



INTEGRATED MANAGEMENT OF CHILDHOOD ILLNESS
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Asthma Bibliography
2002-2005



Pan American Health Organization
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The Asthma Bibliography was made possible through the collaboration of Dr. Alberto Barcelo from the Non communicable diseases Area and Dr. Yehuda Benguigui from Child and Adolescent Health Area with the objective of providing updated references related to prevention, control, diagnosis and treatment of asthma in children.

ASTHMA IN CHILDREN

BIBLIOGRAPHY

CITATIONS FROM MEDLINE, LILACS AND OTHER DATABASES

2000 THROUGH 2005

Table of Contents

SUBJECT SECTION	1
ACARIDS	1
ACUTE ASTHMA	7
AEROBIOLOGY	25
ALLERGENS	25
BETA-ADRENERGIC	46
CLASSIFICATION	46
CLIMATIC FACTORS	53
CLINICAL ASPECTS	55
COMPLICATIONS	57
CORTICOSTEROIDS	81
DIAGNOSIS--reviews	99
DIFFERENTIAL DIAGNOSIS--reviews	111
EDUCATION	117
ENVIRONMENTAL ASPECTS	136
EPIDEMIOLOGY--reviews	149
ETIOLOGY--reviews	155
EXERCISE-INDUCED ASTHMA	168
FOOD	170
GASTROESOPHAGEAL REFLUX	180
GENETICS	182
IMMUNOLOGY--reviews	196
IMMUNOTHERAPY	201
INFLAMMATION	209

INHALATION THERAPY	221
MORTALITY	224
NATURAL HISTORY	230
PHARMACOECONOMICS	232
PHARMACOLOGICAL THERAPY	232
PHYSIOPATHOLOGY--reviews	233
PREVENTION & CONTROL--reviews	238
PROGNOSIS	243
PULMONARY FUNCTION	260
RADIOLOGY	274
RESPIRATORY TRACT DISEASES--reviews	275
RISK FACTORS--reviews	297
VIRUS DISEASE	302
WHEEZING--reviews	309
<i>AUTHOR SECTION</i>	<i>313</i>

SUBJECT SECTION

ACARIDS

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ACUTE ASTHMA

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EXERCISE-INDUCED ASTHMA

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IMMUNOTHERAPY

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AUTHOR SECTION

ANONYMOUS

Action plans in asthma. Drug Ther Bull. 2005; 43(12) : 91-4.p Abstract: Around 5.2 million people in the U.K. have asthma. Symptoms of the disease are often variable, so a fixed treatment regimen is not always appropriate. Personal asthma action plans aim to prompt patients to adjust their medication, or seek medical help, in response to changes in symptoms or peak flow readings. A national clinical guideline in the U.K. recommends that patients with asthma should be offered education in self-management, including a written asthma action plan that focuses on their individual needs. At present, only a minority of people with asthma report receiving such an action plan. Here we discuss the potential content of action plans and review the evidence for their effectiveness.

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Clinical practice guideline: management of sinusitis. Pediatrics. 2001; 108(3) : 798-808.p Abstract : This clinical practice guideline formulates recommendations for health care providers regarding the diagnosis, evaluation, and treatment of children, ages 1 to 21 years, with uncomplicated acute, subacute, and recurrent acute bacterial sinusitis. It was developed through a comprehensive search and analysis of the medical literature. Expert consensus opinion was used to enhance or formulate recommendations where data were insufficient. A subcommittee, composed of pediatricians with expertise in infectious disease, allergy, epidemiology, family practice, and pediatric practice, supplemented with an otolaryngologist and radiologist, were selected to formulate the practice parameter. Several other groups (including members of the American College of Emergency Physicians, American Academy of Otolaryngology-Head and Neck Surgery, American Academy of Asthma, Allergy and Immunology, as well as numerous national committees and sections of the American Academy of Pediatrics) have reviewed and revised the guideline. Three specific issues were considered: 1) evidence for the efficacy of various antibiotics in children; 2) evidence for the efficacy of various ancillary, nonantibiotic regimens; and 3) the diagnostic accuracy and concordance of clinical symptoms, radiography (and other imaging methods), and sinus aspiration. It is recommended that the diagnosis of acute bacterial sinusitis be based on clinical criteria in children <=6 years of age who present with upper respiratory symptoms that are either persistent or severe. Although controversial, imaging

studies may be necessary to confirm a diagnosis of acute bacterial sinusitis in children >6 years of age. Computed tomography scans of the paranasal sinuses should be reserved for children who present with complications of acute bacterial sinusitis or who have very persistent or recurrent infections and are not responsive to medical management. There were only 5 controlled randomized trials and 8 case series on antimicrobial therapy for acute bacterial sinusitis in children. However, these data, plus data derived from the study of adults with acute bacterial sinusitis, support the recommendation that acute bacterial sinusitis be treated with antimicrobial therapy to achieve a more rapid clinical cure. Children with complications or suspected complications of acute bacterial sinusitis should be treated promptly and aggressively with antibiotics and, when appropriate, drainage. Based on controversial and limited data, no recommendations are made about the use of prophylactic antimicrobials, ancillary therapies, or complementary/alternative medicine for prevention and treatment of acute bacterial sinusitis. This clinical practice guideline is not intended as a sole source of guidance in the diagnosis and management of acute bacterial sinusitis in children. It is designed to assist pediatricians by providing an analytic framework for evaluation and treatment. It is not intended to replace clinical judgment or establish a protocol for all patients with this condition.

Cockroach allergen may have greatest impact on childhood asthma. FDA Consum. 2005; 39(3) : 6.p

Combination therapy: addition of other long-term-control medications to inhaled corticosteroids. J Allergy Clin Immunol. 2002; 110(5 Suppl) : S169-80.p

Congress urges "right to carry"--for asthma inhalers. Child Health Alert. 2004; 22 : 3.p

Contraindications to vaccination in children. Mainly immunosuppression and a history of severe reactions. Prescrire Int. 2003; 12(65) : 103-7.p Abstract: (1) A history of severe anaphylactic reaction to a vaccine or one of its components is an absolute contraindication to the use of the same vaccine. (2) Live vaccines (viral or bacterial) are contraindicated in children with impaired immune response; this includes children receiving high-dose steroids. (3) BCG vaccination is contraindicated in HIV-seropositive children regardless of immune status. (4) Vaccination need not be postponed in children with common illnesses such as rhinopharyngitis; in children with a history of asthma or eczema; in children taking antibiotics; or in babies who are breast fed. (5) The contraindications of pertussis vaccination are now well defined (mainly neurological diseases). (6) Very few studies have assessed the adverse effects of vaccination on the outcome of pregnancy or on the unborn child. In practice, vaccination of pregnant women can usually wait until after delivery.

Critical Path Network: education decreases ED visits for young asthma patients. Hosp Case Manag. 2005; 13(1) : 7-8.p

Diagnosis of asthma. CMAJ. 2005; 173(6 Suppl) : S15-9.p

Drugs for asthma. Treat Guidel Med Lett. 2005; 3(33) : 33-8.p Abstract: Patients with mild, infrequent asthma symptoms may require only intermittent, as needed use of an inhaled short-acting beta2-adrenergic agonist. Use of a short-acting beta2-agonist more than twice weekly, other than for exercise-induced bronchospasm, indicates a need for anti-inflammatory treatment. Inhaled corticosteroids are the most effective anti-inflammatory medication;

leukotriene modifiers are less effective alternatives. If regular use of an inhaled corticosteroid in a low dose does not prevent symptoms, a long-acting beta2-agonist should be added; addition of a second drug is more effective than raising the dose of the inhaled steroid. A leukotriene modifier can also be used as the second drug. Omalizumab may be considered as adjunctive therapy for patients more than 12 years old who have allergic asthma not controlled by other drugs. A short course of oral corticosteroids may be useful for acute exacerbations. Treatment of acute severe asthma as a medical emergency is not included here; it has been reviewed elsewhere (ER McFadden Jr, Am J Respir Crit Care Med 2003; 168:740).

Education and follow-up. CMAJ. 2005; 173(6 Suppl) : S51-5.p

Effects of early treatment on the progression of asthma. J Allergy Clin Immunol. 2002; 110(5 Suppl) : S196-219.p

Extract from the Norwegian National Report on Physical Activity and Health. Scand J Med Sci Sports. 2001; 11(4) : 255-7.p Abstract: In 1999 the National Council on Nutrition and Physical Activity in Norway appointed a committee to look into the relationship between health and physical activity, and to provide some guidelines to various populations regarding physical activity. The committee, which consisted of Sigmund B. Stromme, Sigmund A. Anderssen, Ingvar Hjermann, Jorunn Sundgot-Borgen, Sigbjorn Smeland, Sverre Maehlum, and Anita Andaas Aadland, produced a comprehensive 84-page report (rapport nr. 2/2000) on physical activity and health based on the currently available scientific evidence. An extract from the first part of the report, which concentrates on the significance of physical activity for various population groups follows below.

Immunotherapy. CMAJ. 2005; 173(6 Suppl) : S46-50.p

Immunotherapy: new guidelines suggest a 'window' for prevention. Dis Manag Advis. 2003; 9(4) : 59-61, 50.p Abstract: New guidelines suggest that immunotherapy can, in some cases, actually prevent the development of allergic asthma in children with allergic rhinitis. The new recommendations offer advice on when to consider immunotherapy, optimal dosing, and how to handle and store medicines.

Information from your family doctor. Treating my child's asthma. Am Fam Physician. 2005; 71(10) : 1969.p

Inhalation devices. CMAJ. 2005; 173(6 Suppl) : S39-45.p

Interventions show promise in primary prevention of asthma. Dis Manag Advis. 2004; 10(9) : 106-7, 97.p Abstract: It's not clear why some children develop allergies and asthma and some children do not, but scientists know that environmental exposures probably account for the epidemic of the disease that has taken place in the developed world over the last three decades. Consequently, a number of researchers are investigating whether environmental interventions can actually prevent onset of the disease. Taking on such an issue for study is not easy, but early results from one investigation in Canada have thus far yielded promising results.

Leukotriene receptor antagonists--an update. Drug Ther Bull. 2005; 43(11) : 85-8.p Abstract: Montelukast (Singulair-MSD) and zafirlukast (Accolate-AstraZeneca) are oral leukotriene receptor antagonists, licensed for the treatment of patients with asthma. In 1998, soon after their launch, we concluded that there was insufficient evidence to clearly define their place in treatment. Here, we reconsider their role in adults and children with asthma in the light of more recent evidence.

Long-term management of asthma in children: effectiveness of inhaled corticosteroids compared to other medications. J Allergy Clin Immunol. 2002; 110(5 Suppl) : S147-60.p

May--asthma awareness month. School Nurse News. 2002; 19(3) : 8.p

Mometasone (Asmanex Twisthaler) for asthma . Med Lett Drugs Ther. 2005; 47(1223-1224) : 98-9.p

New inner-city asthma interventions put social workers in the driver's seat. Dis Manag Advis. 2003; 9(8) : 111-5.p Abstract: Why? Because research shows that, unlike so many failed strategies, a social worker-based intervention can boost outcomes and cut costs. The critical element seems to be the social worker's ability to remove barriers that commonly sabotage other efforts. See how this alternative approach to asthma DM is being implemented.

Patient education. Asthma first aid for your child. Aust Fam Physician. 2005; 34(7) : 577.p

Pharmacotherapy--add-on therapies. CMAJ. 2005; 173(6 Suppl) : S37-8.p

Pharmacotherapy--first-line maintenance therapy. CMAJ. 2005; 173(6 Suppl) : S28-32.p

Pharmacotherapy--treatment of intermittent asthma with ICSs. CMAJ. 2005; 173(6 Suppl) : S33-6.p

Project cuts admissions for kids with asthma. Hosp Case Manag. 2005; 13(8) : 127-8.p

Resources. "Allergic asthma for dummies"...and a Web-based tool to improve immunizations and health screenings. Child Health Alert. 2005; 23 : 2.p

School transportation modes--Georgia, 2000 . MMWR Morb Mortal Wkly Rep. 2002; 51(32) : 704-5.p Abstract: Moderate physical activity (e.g., walking or bicycling) offers substantial health benefits. Physical activity is especially important for young persons not only because of its immediate benefits but also because participation in healthy behaviors early in life might lead to healthier lifestyles in adulthood. Persons aged > 2 years should engage in > or = 30 minutes of moderately intense physical activity on all or most days of the week. However, sedentary after-school activities (e.g., watching television or using computers), decreased participation in physical education, and fewer students walking or riding their bicycles to school might contribute to the high rate of childhood obesity. Walking to school provides a convenient opportunity for children to be physically active. To examine modes of transportation to school for Georgia children, the Georgia Division of Public Health analyzed data from the Georgia Asthma Survey conducted during May-August 2000. This report summarizes the results of that analysis, which indicate that < 19% of Georgia school-aged children who live < or = 1 mile from school walk to school the majority of days of the week. Statewide surveillance data of school transportation modes should be collected to monitor prevalence of walking to school.

The September epidemic of asthma hospitalizations...and do antibiotics in infancy lead to asthma? Child Health Alert. 2006; 24 : 3.p

Should vitamins be avoided early in life? Child Health Alert. 2005; 23 : 3-4.p

Aalbers R. et al. *Adjustable maintenance dosing with budesonide/formoterol compared with fixed-dose salmeterol/fluticasone in moderate to severe asthma.* *Curr Med Res Opin.* 2004; 20(2) : 225-40.p **Abstract:** **BACKGROUND:** Current asthma guidelines recommend that patients are educated to adjust their medication according to their asthma severity using physician-guided self-management plans. However, many patients take a fixed dose of their controller medication and adjust their reliever medication according to asthma symptoms. **OBJECTIVES:** This study examined whether asthma control improved if patients adjusted the maintenance dose of budesonide/formoterol (Symbicort Turbuhaler* 160/4.5 microg) according to asthma severity compared with traditional fixed dosing (FD) regimens. **METHODS:** Symptomatic patients with asthma (n = 658, mean symptom score 1.5, mean inhaled corticosteroids 735 microg/day, mean forced expiratory volume in 1 second [FEV(1)] 84% predicted) were randomised after 2 weeks' run-in to either: budesonide/formoterol adjustable maintenance dosing (AMD), budesonide/formoterol FD or salmeterol/fluticasone (Seretide Diskus dagger 50/250 microg) FD. In a 4-week double-blind period, both budesonide/formoterol AMD and FD groups received two inhalations twice daily (bid) and salmeterol/fluticasone FD patients received one inhalation bid. In the following 6-month open extension, both FD groups continued with the same treatment. Patients in the AMD group with well-controlled asthma stepped down to one inhalation bid; others continued with two inhalations bid. All AMD patients could increase to four inhalations bid for 7-14 days if symptoms worsened. All patients used terbutaline or salbutamol for symptom relief throughout. The primary variable was the odds of achieving a well-controlled asthma week (WCAW). **RESULTS:** The odds ratio for achieving a WCAW did not differ between the FD regimens; however, during the open period, budesonide/formoterol AMD increased the odds of achieving a WCAW vs. budesonide/formoterol FD (odds ratio 1.335; 95% CI: 1.001, 1.783; p = 0.049) despite a 15% reduction in average study drug use. Budesonide/formoterol AMD patients had a lower exacerbation rate over the study: 40% lower vs. salmeterol/fluticasone FD (p = 0.018); 32% lower vs. budesonide/formoterol FD (NS). During the double-blind period, there were no clinically relevant differences between the budesonide/formoterol FD and salmeterol/fluticasone FD groups. Budesonide/formoterol AMD patients used less reliever medication in the open extension: 0.58 vs. 0.92 occasions/day for budesonide/formoterol FD (p = 0.001) and 0.80 occasions/day for salmeterol/fluticasone FD (p = 0.011). **CONCLUSIONS:** Adjustable maintenance dosing with budesonide/formoterol provides more effective asthma control by reducing exacerbations and reliever medication usage compared with fixed-dose salmeterol/fluticasone.

Aaron S.D. *The use of ipratropium bromide for the management of acute asthma exacerbation in adults and children: a systematic review.* *J Asthma.* 2001; 38(7) : 521-30.p **Abstract:** Ipratropium bromide is a quaternary anticholinergic bronchodilator that is commonly used to treat obstructive lung disease. Although ipratropium is not usually employed as a first-line bronchodilator to treat chronic asthma, it has been used extensively in hospital emergency departments as adjunctive therapy for the emergency treatment of acute asthma exacerbation. This review will summarize the physiological actions of ipratropium and the rationale for its use as an anticholinergic bronchodilator. Evidence available from randomized trials and from two meta-analyses is summarized to determine whether the addition of inhaled ipratropium to inhaled beta2-agonist therapy is effective in the treatment of acute asthma exacerbation in children and adults. Published reports of randomized, controlled trials assessing the use

of ipratropium and concurrent beta2-agonists in adult acute asthma exacerbation were identified by a search of electronic databases, as well as by hand searching. Data from 10 studies of adult asthmatics, reporting on a total of 1377 patients, were pooled in a meta-analysis using a weighted-average method. Use of nebulized ipratropium/beta2-agonist combination therapy was associated with a pooled 7.3% improvement in forced expiratory volume in 1 sec [95% confidence interval (CI), 3.8-10.9%] and a 22.1% improvement in peak expiratory flow (95% CI, 11.0-33.2%) compared with patients who received beta2-agonist without ipratropium. For the three trials in adults reporting hospital admission data (n = 1064), adult patients receiving ipratropium had a relative risk of hospitalization of 0.80 (95% CI, 0.61-1.06). Similarly, randomized controlled studies of pediatric asthma exacerbation and a meta-analysis of pediatric asthma patients suggest that ipratropium added to beta2-agonists improves lung function and also decreases hospitalization rates, especially among children with severe exacerbations of asthma. The adult and pediatric studies did not report any severe adverse effects attributable to ipratropium when it was used in conjunction with beta2-agonists. In conclusion, there is a modest statistical improvement in airflow obstruction when ipratropium is used as an adjunctive to beta2-agonists for the treatment of acute asthma exacerbation. In pediatric asthma exacerbation, use of ipratropium also appears to improve clinical outcomes; however, this has not been definitively established in adults. It would seem reasonable to recommend the use of combination ipratropium/beta2-agonist therapy in acute asthmatic exacerbation, since the addition of ipratropium seems to provide physiological evidence of benefit without risk of adverse effects.

Aboudiab T. et al. *[Does non IgE-dependent sensitization to cow's milk proteins influence chronic cough and asthma in children?].* *Arch Pediatr.* 2003; 10(10) : 911-2.p

Abramson J.M. et al. *Feasibility of school-based spirometry screening for asthma.* *J Sch Health.* 2003; 73(4) : 150-3.p **Abstract:** To determine the feasibility and value of spirometry in school-based asthma screening, spirometry testing was coupled with parent questionnaires in a school-based asthma screening project. Children in grades five to eight of the Catholic school system in Rochester, Minn., performed spirometry with coaching and data acquisition by nurses trained for this activity. Most students completed three tests. For each student, the best test was selected for interpretation. Tests were considered technically unacceptable for screening purposes if the FEV1 was less than 85% and the curve showed evidence of cough, delayed start, poor initial effort, incomplete effort, or non-reproducibility. Students with acceptable tests and FEV1 < 85% as predicted for age, race, and BMI were classified as appropriate for referral for further evaluation of potential asthma. A sensitivity analysis was conducted using different FEV1 thresholds for referral. Children (119, 17.6% of all) with known asthma based on parent-completed questionnaire were not considered for referral. Of the remaining 557 students screened, 535 had technically acceptable tests, and 498 had normal spirometry performance. Using a threshold for referral of FEV1 < 85%, 37 children were candidates for referral for further evaluation of potential asthma. Only four (11%) of these also had questionnaire responses that made them candidates for referral. School-based spirometry screening for asthma is technically feasible but there is little overlap between those who are referral candidates based on spirometry data and those who are referral candidates based on parent-reported symptoms on screening questionnaires. Without further study, spirometry cannot be recommended for school-based asthma screening.

Abu-Hasan M. et al. *Exercise-induced dyspnea in children and adolescents: if not asthma then what?* *Ann Allergy Asthma Immunol.* 2005; 94(3) : 366-71.p **Abstract:** **BACKGROUND:** Exercise-induced dyspnea (EID) in children and adolescents is a common manifestation of asthma and is therefore commonly

attributed to exercise-induced asthma (EIA) when present in otherwise healthy children. **OBJECTIVE:** To report the outcome of evaluations for EID when other symptoms and signs of asthma were absent or if there was no response to previous use of an inhaled beta2-agonist. **METHODS:** We reviewed the results of all exercise tests performed in otherwise healthy patients with EID during 1996 to 2003. Physiologic measures included preexercise and postexercise spirometry with the addition of oxygen uptake, carbon dioxide production, continuous oximetry, and electrocardiogram monitoring during most tests. EIA was diagnosed if symptoms were reproduced in association with a 15% or greater decrease in forced expiratory volume in 1 second from baseline. Endoscopy was performed if stridor and/or decreased maximal inspiratory flow were present. Criteria were established for restrictive abnormalities, physical conditioning, exercise-induced hyperventilation, and normal physiologic limitation. **RESULTS:** A total of 142 patients met our criteria for inclusion. EID had been present in these patients for a mean duration of 30.2 months (range, <1 to 192 months) before evaluation and had been previously attributed to asthma by the referring physician in 98 of them. Symptoms of EID were reproduced during exercise testing in 117 patients. EIA was identified as the cause of EID in only 11 of those 117. Seventy-four demonstrated only normal physiologic exercise limitation; 48 of these 74 had normal to high cardiovascular conditioning, and 26 had poor conditioning. Other diagnoses associated with reproduced EID included restrictive abnormalities in 15, vocal cord dysfunction in 13, laryngomalacia in 2 (1 of whom had unilateral vocal cord paralysis), primary hyperventilation in 1, and supraventricular tachycardia in 1. **CONCLUSION:** The diagnosis of EIA should be questioned as the etiology of EID in children and adolescents who have no other clinical manifestations of asthma and who do not respond to pretreatment with a beta2-agonist. Exercise testing that reproduces symptoms while monitoring cardiac and respiratory physiology is then indicated to identify causes of EID other than EIA.

Ackerman A.D. *Mechanical ventilation of the intubated asthmatic: how much do we really know?* *Pediatr Crit Care Med.* 2004; 5(2) : 191-2.p

Acs N. et al. *Association between bronchial asthma in pregnancy and shorter gestational age in a population-based study.* *J Matern Fetal Neonatal Med.* 2005; 18(2) : 107-12.p **Abstract:** **OBJECTIVE:** To study the association between bronchial asthma during pregnancy and gestational age/birth weight, and also preterm birth and low birth weight. **METHOD:** In the population-based large data set of the Hungarian Case-Control Surveillance System of Congenital Abnormalities, 1980-1996, controls without congenital abnormalities were analysed. **RESULTS:** Of 38,151 newborn infants, 757 (2.0%) had mothers with bronchial asthma during pregnancy, 88% were medically recorded prospectively. Mothers with bronchial asthma in pregnancy had 0.6 week shorter gestational age and a higher proportion of preterm births (14.1% vs. 9.1%). These findings were reflected with a lower mean birth weight (3,102 vs. 3,279 gram) and higher proportion of low birth weight newborns (9.0% vs. 5.6%). **CONCLUSION:** The old fashioned anti-asthmatic drugs were not able to prevent the bronchial asthma-related preterm birth, thus there is an urgent need to use modern inhaled therapies.

Acun C. et al. *Effects of inhaled corticosteroids on growth in asthmatic children: a comparison of fluticasone propionate with budesonide.* *Allergy Asthma Proc.* 2005; 26(3) : 204-6.p **Abstract:** In asthmatic children inhaled corticosteroids are widely used. However, there are some concerns about the systemic adverse effects of these drugs, especially in the growing child. We performed this prospective study in order to compare the effects of 400 microg/day of budesonide (BUD) and 250 microg/day of fluticasone propionate (FP) on growth in prepubertal (aged 4-11.5 years), moderate persisting asthmatic children. One hundred patients (51 boys and 49 girls), who were randomized into two groups, were recruited for the study. The first

group was treated with BUD, 2X 200 microg/day, and the second group was treated with FP, 2X 125 microg/day, by using a medium-size volume-spacer metered-dose inhaler. Growth in children with asthma who were treated by inhaled corticosteroids was calculated by growth velocity over a 12-month period. Comparisons between treatment groups were calculated by t-test and chi-square test. There were no significant differences between BUD and FP groups for sex, age, first height, and growth velocity. Moderate persisting, prepubertal asthmatic children treated with 250 microg/day of FP appeared to have no different linear growth than those children who received 400 microg/day of BUD.

Adams N. et al. *Inhaled beclomethasone versus budesonide for chronic asthma.* *Cochrane Database Syst Rev.* 2002; (1) : CD003530.p **Abstract:** **BACKGROUND:** Beclomethasone dipropionate (BDP) and budesonide (BUD) are used widely in the treatment of chronic asthma. The two drugs have different in vitro pharmacokinetic characteristics. It is unclear whether this translates into clinically significant differences in efficacy or safety when treating children and adults with chronic asthma. **OBJECTIVES:** To assess clinical outcomes in studies which have compared inhaled BDP and BUD in the treatment of chronic asthma. **SEARCH STRATEGY:** We searched the Cochrane Airways Group Trial Register (1999) and reference lists of articles. We contacted trialists and pharmaceutical companies for additional studies and searched abstracts of major respiratory society meetings (1997-1999). **SELECTION CRITERIA:** Prospective, randomised trials comparing BDP to BUD in the treatment of chronic asthma. Two reviewers independently assessed articles for inclusion and methodological quality. **DATA COLLECTION AND ANALYSIS:** One reviewer extracted data; authors were contacted to clarify missing information. Quantitative analyses were undertaken using Review Manager 4.0.3 with Metaview 3.1. **MAIN RESULTS:** 24 studies met the criteria for inclusion (1174 subjects). Methodological quality was variable. A meta-analysis of crossover studies did not demonstrate a significant difference between BDP and BUD for FEV1, morning PEF, evening PEF, asthma symptoms or rescue beta2 agonist use, over a dose range of 400 to 1000 mcg/d. The majority of crossover trials had significant design flaws related to a lack of washout and/or failure to exclude carryover effects so the results must be viewed with caution. A single crossover study with adequate washout showed that BUD 400 mcg/d delivered via Turbohaler dry powder inhaler (DPI) may be more effective than BDP 400 mcg/d delivered via Rotahaler DPI in reducing histamine bronchial hyper-responsiveness: Weighted Mean Difference (WMD) 0.43 log10 PC20 FEV1 (95% Confidence Intervals (CI) 0.05, 0.81 log10 PC20 FEV1). A meta-analysis of two parallel group, dose down-titration studies (231 patients) showed that less BUD delivered via a Turbohaler DPI was required to maintain control in adults asthmatics compared to BDP delivered via metered dose inhaler with or without a spacer: WMD 444 mcg/d (95% CI 332, 556 mcg/d). **REVIEWER'S CONCLUSIONS:** There is limited high quality randomised controlled trial data comparing the relative efficacy of BDP and BUD. Current guidelines (BTS 1997, GINA 1995, NHLBI 1997) assume BDP and BUD to have equal efficacy, such that for each defined level of asthma severity, the recommended doses BDP and BUD are the same. Although there is some data to suggest that BUD via Turbohaler is more effective than BDP via either Rotahaler or MDI (with and without spacer), these comparisons are confounded by use of different delivery devices, and are not sufficient to warrant a change in guideline recommendations.

Adams N.P. et al. *Inhaled fluticasone at different doses for chronic asthma in adults and children.* *Cochrane Database Syst Rev.* 2005; (3) : CD003534.p **Abstract:** **BACKGROUND:** Inhaled fluticasone propionate (FP) is a high-potency inhaled corticosteroid used in the treatment of asthma. **OBJECTIVES:** 1. To assess the efficacy and safety outcomes of inhaled fluticasone at different nominal daily doses in the treatment of chronic asthma. 2. To test for the presence of a dose-response effect. **SEARCH STRATEGY:** We searched the

Cochrane Airways Group Trials Register (January 2005) and reference lists of articles. We contacted trialists and pharmaceutical companies for additional studies and searched abstracts of major respiratory society meetings (1997 to 2004). **SELECTION CRITERIA:** Randomised trials in children and adults comparing fluticasone at different nominal daily doses in the treatment of chronic asthma. Two reviewers independently assessed articles for inclusion and methodological quality. **DATA COLLECTION AND ANALYSIS:** One reviewer extracted data. These were checked and verified by a second reviewer. Quantitative analyses were undertaken using RevMan (Analyses 1.0.2). **MAIN RESULTS:** Forty-three studies (45 data sets with 8913 participants) met the inclusion criteria. Methodological quality was high. In asthmatics with mild to moderate disease who were not on oral steroids a dose-response effect was present with FP for change in morning peak expiratory flow (PEF). For low doses (100 versus 200 microg/day) the weighted mean difference (WMD) was 6.29 litres/min, 95% confidence interval (CI) 2.28 to 10.29. Comparing medium (400 to 500 microg/day) to low dose (200 microg/day) FP the WMD was 6.46 litres/min (95% CI 3.02 to 9.89); this effect was more pronounced in one trial with more severely asthmatic children. For FP 100 versus 400 to 500 microg/day the WMD was 8 litres/min (95% CI 1 to 15) and at high versus low doses (800 to 1000 versus 50 to 100 microg/d) the WMD was 22 litres/min (95% CI 15 to 29). When high and medium doses were compared there was no significant difference in the change in morning PEF: at 400 to 500 versus 800 to 1000 microg/day the WMD was 0.16 litres/min (95% CI 6.95 to 6.63). There was no dose-response effect on symptoms or rescue beta-2 agonist use. The likelihood of hoarseness and oral candidiasis was significantly greater for the higher doses (800 to 1000 microg/day). People with oral steroid-dependent asthma treated with FP (2000 microg/day) were significantly more likely to reduce oral prednisolone than those on 1000 to 1500 microg/day (Peto odds Ratio 2.8, 95% CI 1.3 to 6.3). The highest dose also allowed a significant reduction in daily oral prednisolone dose compared to 1000 to 1500 microg/day (WMD 2.0 mg/day, 95% CI 0.1 to 4.0 mg/day). **AUTHORS' CONCLUSIONS:** Effects of fluticasone are dose dependent but relatively small. At dose ratios of 1:2, there are significant differences in favour of the higher dose in morning peak flow across the low dose range. The clinical impact of these differences is open to interpretation. Patients with moderate disease achieve similar levels of asthma control on medium doses of fluticasone (400 to 500 microg/day) as they do on high doses (800 to 1000 microg/day). More work in severe asthma would help to confirm that doses of FP above 500 microg/day confer greater benefit in this subgroup than doses of around 200 microg/day. In oral corticosteroid-dependent asthmatics, reductions in prednisolone requirement may be gained with FP 2000 microg/day.

Adams N.P. et al. *Inhaled fluticasone versus placebo for chronic asthma in adults and children.* Cochrane Database Syst Rev. 2005; (2) : CD003135.p **Abstract:** **BACKGROUND:** Inhaled fluticasone propionate (FP) is a relatively new inhaled corticosteroid for the treatment of asthma. **OBJECTIVES:** 1. To assess efficacy and safety outcomes in studies that compared FP to placebo for treatment of chronic asthma. 2. To explore the presence of a dose-response effect. **SEARCH STRATEGY:** We searched the Cochrane Airways Group Trial Register (January 2004), reference lists of articles, contacted trialists and searched abstracts of major respiratory society meetings (1997-2004). **SELECTION CRITERIA:** Randomised trials in children and adults comparing FP to placebo in the treatment of chronic asthma. Two reviewers independently assessed articles for inclusion and methodological quality. **DATA COLLECTION AND ANALYSIS:** Two reviewers extracted data. Quantitative analyses were undertaken using RevMan Analyses 4.2.7. **MAIN RESULTS:** Sixty eight studies met the inclusion criteria (11, 104 participants). Methodological quality was high. In non-oral steroid treated asthmatics with mild and moderate disease FP resulted in improvements from baseline compared with placebo across all dose ranges (100 to 1000 mcg/d) in FEV1 (between 0.13 to 0.45 litres);

morning PEF (between 27 and 47 L/min); symptom scores (based on a standardised scale, between 0.5 and 0.85); reduction in rescue beta-2 agonist use (between 1.2 and 2.2 puffs/d). High dose FP reduced the number of patients dependent on prednisolone: FP 1000-1500 mcg/d Peto Odds Ratio 0.07 (95% CI 0.05 to 0.10). FP at all doses led to a greater likelihood of sore throat, hoarseness and oral Candidiasis, but 21 patients would need to be treated for one extra to develop Candidiasis (FP 500 mcg/day), whilst only three or four patients need to be treated to avoid one extra patient being withdrawn due to lack of efficacy at all doses of FP. **AUTHORS' CONCLUSIONS:** Doses of FP in the range 100-1000 mcg/d are effective. In most patients with mild-moderate asthma improvements with low dose FP are only a little less than those associated with high doses when compared with placebo. High dose FP appears to have worthwhile oral-corticosteroid reducing properties. FP use is accompanied by an increased likelihood of oropharyngeal side effects.

Adams N.P. et al. *Fluticasone versus placebo for chronic asthma in adults and children.* Cochrane Database Syst Rev. 2005; (4) : CD003135.p **Abstract:** **BACKGROUND:** Inhaled fluticasone propionate (FP) is a relatively new inhaled corticosteroid for the treatment of asthma. **OBJECTIVES:** 1. To assess efficacy and safety outcomes in studies that compared FP to placebo for treatment of chronic asthma. 2. To explore the presence of a dose-response effect. **SEARCH STRATEGY:** We searched the Cochrane Airways Group Specialised Register (January 2005), reference lists of articles, contacted trialists and searched abstracts of major respiratory society meetings (1997-2004). **SELECTION CRITERIA:** Randomised trials in children and adults comparing FP to placebo in the treatment of chronic asthma. Two reviewers independently assessed articles for inclusion and methodological quality. **DATA COLLECTION AND ANALYSIS:** Two reviewers extracted data. Quantitative analyses were undertaken using RevMan 4.2 **MAIN RESULTS:** Seventy-five studies met the inclusion criteria (14,208 participants). Methodological quality was high. In non-oral steroid treated asthmatics with mild and moderate disease FP resulted in improvements from baseline compared with placebo across all dose ranges (100 to 1000 mcg/d) in FEV1 (between 0.13 to 0.45 litres); morning PEF (between 23 and 47 L/min); symptom scores (based on a standardised scale, between 0.5 and 0.85); reduction in rescue beta-2 agonist use (between 1.2 and 2.2 puffs/day). High dose FP increased the number of patients who could withdraw from prednisolone: FP 1000-1500 mcg/day Peto Odds Ratio 14.07 (95% CI 7.17 to 27.57). FP at all doses led to a greater likelihood of sore throat, hoarseness and oral Candidiasis. Twenty-one patients would need to be treated for one extra to develop Candidiasis (FP 500 mcg/day), whilst only three or four patients need to be treated to avoid one extra patient being withdrawn due to lack of efficacy at all doses of FP. **AUTHORS' CONCLUSIONS:** Doses of FP in the range 100-1000 mcg/day are effective. In most patients with mild-moderate asthma improvements with low dose FP are only a little less than those associated with high doses when compared with placebo. High dose FP appears to have worthwhile oral-corticosteroid reducing properties. FP use is accompanied by an increased likelihood of oropharyngeal side effects.

Adams R.J. et al. *Intranasal steroids and the risk of emergency department visits for asthma.* J Allergy Clin Immunol. 2002; 109(4) : 636-42.p **Abstract:** **BACKGROUND:** In patients with asthma, treatment for associated conditions, such as rhinitis, is recommended. It is unknown whether this treatment can reduce the risk for emergency department (ED) visits for asthma. **OBJECTIVES:** We sought to determine whether treatment with intranasal steroids or prescription antihistamines in persons with asthma is associated with a reduced risk for ED visits caused by asthma. **METHODS:** We performed a retrospective cohort study of members of a managed care organization aged greater than 5 years who were identified during the period of October 1991 to September 1994 as having a

diagnosis of asthma by using a computerized medical record system. The main outcome measure was an ED visit for asthma. RESULTS: Of the 13,844 eligible persons, 1031 (7.4%) had an ED visit for asthma. The overall relative risk (RR) for an ED visit among those who received intranasal corticosteroids, adjusted for age, sex, frequency of orally inhaled corticosteroid and beta-agonist dispensing, amount and type of ambulatory care for asthma, and diagnosis of an upper airways condition (rhinitis, sinusitis, or otitis media), was 0.7 (95% confidence interval [CI], 0.59-0.94). For those receiving prescription antihistamines, the risk was indeterminate (RR, 0.9; 95% CI, 0.78-1.11). When different rates of dispensing for intranasal steroids were examined, a reduced risk was seen in ED visits in those with greater than 0 to 1 (RR, 0.7; 95% CI, 0.57-0.99) and greater than 3 (RR, 0.5; 95% CI, 0.23-1.05) dispensed prescriptions per year. CONCLUSIONS: Treatment of nasal conditions, particularly with intranasal steroids, confers significant protection against exacerbations of asthma leading to ED visits for asthma. These results support the use of intranasal steroids by individuals with asthma and upper airways conditions.

Adams R.J. et al. *How and by whom care is delivered influences anti-inflammatory use in asthma: Results of a national population survey.* J Allergy Clin Immunol. 2003; 112(2) : 445-50.p **Abstract:** BACKGROUND: Studies examining the influence of provider behavior and patterns of care delivery on the use of anti-inflammatory asthma therapy have been limited to selected populations or have been unable to assess the appropriateness of therapy for individuals. We have previously reported the influence of sociodemographic variables and asthma severity on reported use of asthma medications in the United States. OBJECTIVE: We sought to examine the influence of patterns of care delivery and clinician behavioral factors on the use of anti-inflammatory medication by patients with asthma. METHODS: We performed a cross-sectional national random digit dial household telephone survey in 1998 of adult patients and parents of children with current asthma. Respondents were classified as having current asthma if they had a physician's diagnosis of asthma and were either taking medication for asthma or had asthma symptoms during the past year. RESULTS: One or more persons met the study criteria for current asthma in 3273 (7.8%) households in which a screening questionnaire was completed. Of the 2509 persons (721 children <16 years of age) with current asthma interviewed, 507 (20.1%) reported current use of anti-inflammatory medication. In a multiple logistic regression model controlling for asthma symptoms, reported anti-inflammatory use was significantly associated with patients reporting their physician having an excellent ability to explain asthma management (odds ratio [OR], 1.47; 95% CI, 1.09-1.98), scheduling regular visits to a physician for asthma (OR, 1.30; 95% CI, 1.02-1.64), having a written asthma action plan (OR, 1.63; 95% CI, 1.29-2.06), and being of white, non-Hispanic ethnicity (OR, 1.53; 95% CI, 1.19-1.98), along with markers of greater asthma morbidity, missing 6 or more days from work or school in the past year (OR, 1.29; 95% CI, 1.01-1.65), and hospitalization for asthma in the past year (OR, 1.74; 95% CI, 1.19-2.53). Anti-inflammatory use was less likely to be reported with younger age (OR, 0.82; 95% CI, 0.73-0.94), lower long-term asthma symptom burden (OR, 0.82; 95% CI, 0.71-0.94), use of 4 or fewer reliever inhaler canisters in the past year (OR, 0.50; 95% CI, 0.43-0.58), and smoking (OR, 0.50; 95% CI, 0.37-0.68). CONCLUSION: How asthma care is delivered influences the use of anti-inflammatory medication. Strategies to increase regular evaluation by a physician interested in asthma, particularly for minority patients, and to increase a physician's ability to communicate asthma management to patients might improve use of anti-inflammatory therapy among patients with asthma.

Adams W.G. et al. *TLC-Asthma: an integrated information system for patient-centered monitoring, case management, and point-of-care decision support.* AMIA Annu Symp Proc. 2003; 1-5.p **Abstract:** A great deal of successful work has been done in the area of EMR

development, implementation, and evaluation. Less work has been done in the area of automated systems for patients. Efforts to link data at multiple levels - the patient, the case manager, and the clinician have been rudimentary-to-date. In this paper we present a model information system that integrates patient health information across multiple domains to support the monitoring and care of children with persistent asthma. The system has been developed for use in a multi-specialty group practice and includes three primary components: 1) a patient-centered telephone-linked communication system; 2) a web-based alert reporting and nurse case-management system; and 3) EMR-based provider communication to support clinical decision making at the point-of-care. The system offers a model for a new level of connectivity for health information that supports customized monitoring, IT-enabled nurse case-managers, and the delivery of longitudinal data to clinicians to support the care of children with persistent asthma. Systems like the one described are well-suited, perhaps essential, technologies for the care of children and adults with chronic conditions such as asthma.

Addo-Yobo E.O. et al. *Seasonal variability in exercise test responses in Ghana.* Pediatr Allergy Immunol. 2002; 13(4) : 303-6.p **Abstract:** Exercise-induced bronchospasm (EIB) is widely used in epidemiological studies to investigate the prevalence of asthma. We aimed to determine seasonal variations in the prevalence of EIB in Ghanaian school children from urban-rich (UR), urban-poor (UP), and rural (R) schools. We have previously reported the prevalence of EIB in 9-16-year-old children to be 3.1% in the dry season, with UR children having a significantly higher prevalence of both EIB and atopy compared to UP or R children. In the current study, the prevalence of EIB was assessed in the same 1,095 children in the wet season (5 months following the initial study) using the same methodology. Exercise provocation consisted of free running outdoors for 6 min. In the wet season, 17/1,095 children [mean 1.55%, 95% confidence interval (CI): 0.91-2.47] had a positive response to exercise, compared to our previous report of 34 children (mean 3.1%, 95% CI: 2.15-4.32) with EIB in the dry season (dry vs. wet season, difference 1.55, 95% CI: 0.41-2.69). The proportion of children with a positive response to exercise in the UR school fell from 4.2% (25/599) to 1.3% (8/599) (difference 2.9, 95% CI: 1.2-4.5). In the wet season, there was no difference in the prevalence of EIB among the UR, UP, and R children. Only five of 1,095 subjects (mean 0.5%, 95% CI: 0.15-1.07) demonstrated EIB in both seasons. In conclusion, although exercise challenge remains a useful tool for determining asthma prevalence in epidemiological studies, seasonal variations in the pattern of responses may occur and the results should be interpreted with caution.

Adedoyin O.T. et al. *Association of nephrotic syndrome with bronchial asthma: two case reports.* Afr J Med Med Sci. 2003; 32(4) : 419-20.p

Aekplakorn W. et al. *Heterogeneity of daily pulmonary function in response to air pollution among asthmatic children.* Southeast Asian J Trop Med Public Health. 2004; 35(4) : 990-8.p **Abstract:** Several epidemiological studies have demonstrated the association of short-term exposure to air pollution with transient declines in pulmonary function. Although the magnitudes of declines in pulmonary function found in these studies are relatively small, the effects vary among children. This study examined whether the variation is evidence of biological heterogeneity or due to random variation by analyzing data from a panel study of 83 asthmatic school children exposed to SO₂ and PM₁₀ in the Mae Moh district of Thailand. Daily pulmonary function testing was performed on the children for 61 days. General linear mixed models were used to examine and test for the null hypothesis of no variation in the subject-specific slopes of pulmonary functions in response to the air pollutants. The individual daily pulmonary functions measured were FVC, FEV₁, PEF_R, and FEF_(25-75%). These were used as an outcome to compare with air pollutant concentrations as random effects, adjusting for height,

gender, time, and temperature. The results indicate evidence of inter-individual variation for subject-specific changes in FVC, FEV1, and PEFR due to the effects of SO2 and PM10 on children. In conclusion, even at low concentrations of daily SO2 and PM10 in the study area, there is evidence of a heterogeneous response to short-term exposure to SO2 and PM10 in children.

Agertoft L. et al. *Influence of particle size on lung deposition and pharmacokinetics of beclomethasone dipropionate in children.* *Pediatr Pulmonol.* 2003; 35(3) : 192-9.p **Abstract:** We set out to evaluate lung deposition, systemic availability, and basic pharmacokinetic parameters of beclomethasone dipropionate (BDP) in children with chronic asthma. Plasma levels of BDP, 17 and 21 beclomethasone monopropionate (17-BMP and 21-BMP), and beclomethasone were measured after an intravenous infusion of 60 microg BDP and after inhalation of A) 100 microg HFA-BDP, B) 200 microg HFA-BDP, C) 200 microg HFA-BDP after ingestion of charcoal to block gastrointestinal (GI) absorption of drug, and D) 400 microg CFC-BDP. A breath-actuated pMDI (Autohaler) was used for HFA inhalations, and a pMDI with a large volume spacer (Volumatic) for CFC inhalations. Treatments A-D were given in a randomized, cross-over design. Fourteen patients aged 10-14 years completed all 5 study days. The mean systemic bioavailabilities in percent of dose leaving the canister valve (ex-valve) were 70% (100 HFA), 74% (200 HFA), 60% (200 HFA + charcoal), and 27% (400 microg CFC). After HFA treatment, 82% of the systemically available dose was absorbed through the lungs, and 18% from the gastrointestinal tract. The estimated bioavailability of BDP from the GI tract was 68%. BDP was metabolized to 17-BMP within minutes. Mean steady-state volume of distribution of 17-BMP was 84 L, and the mean terminal half-life ($T_{1/2}$) after the four inhalations was 2.7 hr (range, 2.2-3.7 hr). Mean $T_{1/2}$ and clearance after i.v. administration were 1.7 hr and 0.9 L/min, respectively. The HFA Autohaler delivers approximately three times as much BDP to the intrapulmonary airways as a CFC-pMDI with a large volume spacer.

Agertoft L. et al. *Short-term lower-leg growth rate and urine cortisol excretion in children treated with ciclesonide.* *J Allergy Clin Immunol.* 2005; 115(5) : 940-5.p **Abstract:** **BACKGROUND:** Measurement of short-term lower-leg growth rate in children by means of knemometry has become established as an integral part of the available measures of systemic activity of topical steroids in children. **OBJECTIVE:** We sought to determine the effects of clinically effective doses of the novel inhaled corticosteroid ciclesonide on lower-leg growth rate and hypothalamic-pituitary-adrenal axis function in children with asthma. **METHODS:** In a double-blind, placebo-controlled, 4-period crossover study, 24 children aged 6 to 12 years sequentially received ciclesonide (40, 80, and 160 microg) in randomized order once daily in the evening. Each 2-week treatment period was followed by a 2-week washout period. Knemometry was performed at the beginning and end of each treatment period. Cortisol levels in 12-hour overnight urine were measured at the end of each treatment period. **RESULTS:** No statistically significant differences were seen in lower-leg growth rates between any of the ciclesonide treatments and placebo. Lower-leg growth rates were 0.412 mm/wk for placebo, 0.425 mm/wk for 40 microg of ciclesonide, 0.397 mm/wk for 80 microg of ciclesonide, and 0.370 mm/wk for 160 microg of ciclesonide. There was no statistically significant dose-response effect. Likewise, no statistically significant differences or dose-response effects were found for urinary cortisol adjusted for creatinine. **CONCLUSION:** Short-term lower-leg growth rate and hypothalamic-pituitary-adrenal axis function are not affected by treatment with ciclesonide in doses intended for clinical use in children.

Agius A.M. et al. *The role of atopy in Maltese patients with chronic rhinitis.* *Clin Otolaryngol Allied Sci.* 2004; 29(3) : 247-53.p **Abstract:** The global prevalence of allergic rhinitis has been on the

increase and recent clinical experience in Malta has shown a similar trend. The aim of this study was to investigate the role of atopy in 415 patients presenting with rhinitis of at least 3 months duration, and to identify the common allergens responsible. Presenting clinical features, past and family history of seasonal allergic symptoms, exposure to cigarette smoking, pet ownership and occupation were analysed. All patients were skin tested for common allergens. Fifty-five per cent of patients were atopic, the main allergens responsible being house dust mite, cat dander and grass pollen. Rhinorrhoea and sneezing were significantly more common in atopic patients, who were more likely to have a past history and family history of seasonal asthma, eczema or rhinoconjunctivitis. Skin test-negative patients with idiopathic rhinitis were mostly females and tended to present a decade later. Differentiation between atopic and idiopathic chronic rhinitis may be helpful in the clinical setting in order to help predict response to treatment.

Ait-Khaled N. et al. *Implementation of asthma guidelines in health centres of several developing countries.* *Int J Tuberc Lung Dis.* 2006; 10(1) : 104-9.p **Abstract:** **SETTING:** Nine selected out-patient clinics caring for asthma patients in Algeria, Guinea, Ivory Coast, Kenya, Mali, Morocco, Syria, Turkey and Vietnam. **DESIGN:** Prospective enrolment of consecutive patients considered by the practitioner to have asthma with evaluation of adherence of the practitioner with recommended standard case management, including proportion of patients confirmed to have asthma, proportion in whom severity was correctly graded and proportion in whom treatment with inhaled corticosteroids corresponded to severity grade. **RESULTS:** Of 499 consecutive patients, 456 (91%) were enrolled and evaluated. The diagnosis was confirmed in 263 (58%). Agreement between the practitioner and the guidelines in assigning grade of severity was moderate overall ($\kappa = 0.42$). It was higher for assignment of grade using symptoms ($\kappa = 0.51$), but poor for assignment of grade using peak expiratory flow (PEF) rate ($\kappa = 0.29$), with practitioners tending to underestimate the severity. Agreement between the practitioners' assessment of severity and treatment with inhaled corticosteroids was poor ($\kappa = 0.18$), with underutilisation of inhaled corticosteroids. **CONCLUSIONS:** Practitioners caring for asthma patients in this study tended to underutilise the PEF rate in assessing their patients and underutilised treatment of patients with inhaled corticosteroids.

Ajaiyeoba A.I. *Prevalence of atopic diseases in Nigerian children with vernal kerato-conjunctivitis.* *West Afr J Med.* 2003; 22(1) : 15-7.p **Abstract:** A descriptive study of 117 cases of vernal kerato-conjunctivitis (VKC), in children below the age of 18 years, newly presenting to 2 hospitals in Ibadan, Nigeria. All the children had a structured questionnaire administered to them which inquired about demographic and clinical, especially history or presence of other atopic diseases amongst other things. Specifically inquired about were asthma, eczema, allergic rhinitis or hay fever, allergic skin rash e.g. scabies, reaction to drugs and others. The children were also examined to confirm or detect the presence of these atopic diseases. The overall prevalence of atopic conditions was 19.8% amongst cases of VKC. These comprised of 6% asthma, 5% allergic rhinitis and 4.3% eczema. (Total 15.5%). Other forms of atopic conditions like other non-specific allergic skin reactions (0.9%), reaction to certain drugs e.g. chloroquine (0.9%) and other unknown allergic conditions (2.6%). It is suggested that children with VKC should be subjected to detailed enquiry and examination with regards to the presence of other atopic conditions. This will go a long way in understanding the type(s) of allergic response involved and perhaps of management of VKC.

Akahoshi M. et al. *Functional promoter polymorphism in the TBX21 gene associated with aspirin-induced asthma.* *Hum Genet.* 2005; 117(1) : 16-26.p **Abstract:** Asthma is a phenotypically heterogeneous disorder with many etiologic factors and clinical characteristics. T-

bet, a Th1-specific transcription factor of T-box family, has been found to control interferon-gamma (IFN-gamma) expression in T cells. Mice lacking the T-bet gene (tbx21) demonstrate multiple physiological and inflammatory features reminiscent of human asthma. In order to examine whether polymorphisms in the candidate gene, TBX21, located on chromosome 17q21.32, are related to the risk of human asthma phenotypes, we have searched for genetic variations in the human TBX21 gene and identified 24 single nucleotide polymorphisms (SNPs), including five novel SNPs, by direct sequencing in Japanese subjects. Among asthma phenotypes, a promoter -1993T-->C SNP, which is in linkage disequilibrium with a synonymous coding 390A-->G SNP in exon 1, is significantly associated with a risk of aspirin-induced asthma (AIA; $P = 0.004$, $P(c) = 0.016$). This association has also been confirmed in additional independent samples of asthma with nasal polyposis ($P = 0.008$), regardless of aspirin hypersensitivity. Furthermore, our data indicate that the -1993T-->C substitution increases the affinity of a particular nuclear protein to the binding site of TBX21 covering the -1993 position, resulting in increased transcriptional activity of the TBX21 gene. Thus, in addition to the antigen-driven excess Th2 response, increased T-bet (and subsequent IFN-gamma) production in human airways of individuals with the -1993T-->C polymorphism could contribute to the development of certain asthma-related phenotypes, such as AIA.

Akçakaya N. et al. *Psychological problems in Turkish asthmatic children and their families.* Allergol Immunopathol (Madr). 2003; 31(5) : 282-7.p **Abstract:** BACKGROUND: Asthma is a chronic respiratory disorder characterized by recurrent episodes of impaired breathing. The disease causes psychological problems due to hospitalization, long-term medication use, and restricted social life. OBJECTIVE: The aim of this study was to investigate the relationship between the severity and duration of asthma and psychological problems in asthmatic children, as well as the probability of maternal anxiety. METHODS: Thirty-seven children with mild asthma, 55 with moderate asthma and eight with severe asthma were compared with 50 healthy children. The severity of asthma was evaluated using the Pearlman-Bierman classification. Psychological adjustment was measured using the Achenbach child Behavior checklist and Spielberger's scale. RESULTS: Emotional factors and family dynamics were found to be triggering factors for disease attacks in 16% of children with mild asthma, 38% of those with moderate asthma and 63% of those with severe asthma ($p < 0.05$). There was no significant difference in the mean maternal anxiety score between the disease severity groups ($p > 0.05$). The mean depression score was significantly higher in children with moderate and severe asthma than in those with mild asthma ($p < 0.05$). Disease duration showed no effect on depression and anxiety. CONCLUSION: Both asthmatic children and their mothers are negatively affected by the disease.

Akerman M. et al. *Allergen sensitivity and asthma severity at an inner city asthma center.* J Asthma. 2003; 40(1) : 55-62.p **Abstract:** The objective of this study was to examine the relationship of allergen sensitivity to asthma symptoms among inner-city asthmatics seen at our Brooklyn, NY, asthma center. We hypothesized that asthma severity would increase for adults and children with increased cockroach and dust mite allergen sensitivity. Data were gathered from retrospective chart review for all patients who were treated at the center with a diagnosis of asthma and had undergone skin-prick testing (SPT) for allergen sensitivity during 1998 (pediatric, $n = 79$; adult, $n = 29$). Asthma severity (determined by National Heart, Lung and Blood Institute [NHLBI] asthma severity class) was examined in relation to allergen sensitivity. Allergen sensitivity was measured by percent positive to skin-prick testing as well as by relative mean diameter of skin prick test wheals. For adults, mite sensitivity prevalence was 61% and cockroach sensitivity prevalence was 41%. For children, mite sensitivity prevalence was 49%; cockroach sensitivity prevalence was 42%. For adults, asthma severity

correlated significantly with sensitivity to Cladosporium, tree, and grass as measured by percent positive skin tests and by increasing mean diameter of skin test wheals. There was a significant correlation with severity for adult dust mite sensitivity only as measured by increasing mean wheal diameter. Ragweed sensitivity showed a significant correlation with severity only as measured by percent positive skin tests. There was a significant positive association for adults between increasing asthma severity and total number of allergen sensitivities per subject. There was no significant correlation for children between asthma severity and total number of allergen sensitivities per subject. Among children, no specific allergen sensitization showed a significant positive association with asthma severity. By both measures of allergen sensitization, there was a significant negative association for children between Cladosporium and asthma severity. Among our inner-city asthmatic population significant correlation between mite sensitivity and asthma severity was found only in adults. No significant association was seen with cockroach. However, outdoor allergen sensitivity (Cladosporidium, tree, ragweed, and grass) significantly correlated with asthma for adults in this inner city population.

Akil I. et al. *Biochemical markers of bone metabolism and calciuria with inhaled budesonide therapy.* Pediatr Nephrol. 2004; 19(5) : 511-5.p **Abstract:** We investigated the changes in renal excretion of calcium, sodium, and potassium in asthmatic children treated with inhaled budesonide, an inhaled glucocorticoid. Twenty-two asthmatic patients (7 female, 15 male, mean age 10.1+/-4.3 years) treated with 400-600 microg/day inhaled budesonide and 23 healthy children (6 female, 17 male, mean age 10.2+/-2.8 years) were enrolled in the study. The parameters recorded were serum sodium, potassium, calcium, phosphorus, alkaline phosphatase (ALP), type I collagen carboxyterminal telopeptide (ICTP), osteocalcin, intact parathyroid hormone (PTH) levels, first spot morning urine calcium/creatinine ratio, sodium/potassium ratio, and daily renal calcium excretion rate (UCa-ER). These parameters were measured in the control group and pre- and post-budesonide treatment in asthmatic children. Serum electrolytes, ALP, PTH, ICTP, and UCa-ER were in the normal ranges and were not significantly different between controls and asthmatic children. Serum levels of ICTP increased, while levels of osteocalcin decreased after budesonide therapy in the asthmatic group ($P=0.001$, $P=0.005$). UCa-ER was decreased after budesonide therapy in asthmatics ($P=0.000$). In conclusion, moderate doses of inhaled budesonide cause hypocalciuria and decreased bone turnover. These results may be attributed to a mechanism compensating for decreased absorption of calcium in the gut due to the topical effect of swallowed budesonide rather than the systemic effects of the drug. Increased bone metabolism and decreased turnover may have an important role in this compensatory mechanism.

Akinbami L.J. et al. *Racial and income disparities in childhood asthma in the United States.* Ambul Pediatr. 2002; 2(5) : 382-7.p **Abstract:** OBJECTIVE: To examine racial and income disparities in asthma prevalence in US children, and disparities in morbidity and ambulatory health care use among children with asthma. METHODS: Using 1993-1996 National Health Interview Survey data, we measured asthma prevalence and morbidity in children aged 3 to 17 years ($N = 14\ 211$) stratifying by race and poverty status. Measures of morbidity included asthma-related activity limitation and number of bed days. We used the ratio of asthma-related doctor contacts to number of bed days in the past 2 weeks to measure health care use adjusted for severity of illness. RESULTS: An annual average of 7.4% of children aged 3 to 17 years had asthma. There were no significant differences in asthma prevalence between race and poverty groups. In contrast, asthma-related morbidity was higher among black and poor children. Black poor children were most likely to have activity limitations due to asthma: 49% were limited compared with about 20% of black nonpoor, white poor, and white nonpoor children. Among children with activity limitations, black children and white poor children were more likely to have severe

limitations, and white nonpoor children were least likely. Finally, white nonpoor children had the highest level of ambulatory care use for asthma after accounting for disease severity, and black poor children had the lowest level. CONCLUSIONS: We found no significant racial or income disparities in asthma prevalence among children in the United States. However, black children and poor children are at higher risk for activity limitation, more severe activity limitation, and relative underuse of ambulatory health care. Black children living in poverty are at highest risk. Targeted interventions to reduce the burden of asthma morbidity in this population are likely to reduce disparities in asthma morbidity as well as reduce overall childhood asthma morbidity.

- Akinbami L.J. et al.** *Racial and ethnic differences in asthma diagnosis among children who wheeze.* Pediatrics. 2005; 115(5) : 1254-60.p
Abstract: BACKGROUND: Racial and ethnic disparities exist in reported childhood asthma prevalence, but it is unclear if disparities stem from true prevalence differences or a different likelihood of receiving a diagnosis from a health professional. Concern has been raised that asthma may be underdiagnosed, particularly among minority children who have more restricted access to high-quality health care. OBJECTIVE: To examine racial/ethnic differences among currently symptomatic children in acquiring an asthma diagnosis to determine if relative underdiagnosis among minorities exists. Children for whom no symptoms were reported (a group that includes those with well-controlled symptoms) were excluded from the analysis. METHODS: The 1999 National Health Interview Survey includes a nationally representative sample of children with reported wheezing symptoms. We included children 3 to 17 years old in the study and analyzed racial/ethnic differences in asthma diagnosis, controlling for young age, gender, parental education, single-parent household, central-city residence, region of residence, health insurance, having a usual place of care, and parent-reported severity of wheezing symptoms. RESULTS: Among those reported to have wheezed in the past year (n = 946), 83% of Puerto Rican, 71% of non-Hispanic black, and 65% of Mexican children were diagnosed with asthma compared with 57% of non-Hispanic white children. Using non-Hispanic white children as the reference group, the approximate adjusted relative risk for physician diagnosis of asthma given wheezing in the past year was 1.43 (95% confidence interval [CI]: 1.04, 1.63) for Puerto Rican, 1.22 (95% CI: 1.03, 1.37) for non-Hispanic black, and 1.19 (95% CI: 0.94, 1.39) for Mexican children. Minority children were reported to have greater severity of wheezing symptoms. Even after accounting for this increased severity, children in racial and ethnic minority groups were as or more likely to have a reported asthma diagnosis than non-Hispanic white children. CONCLUSIONS: Our findings do not provide evidence for the hypothesis that symptomatic minority children are underdiagnosed with asthma compared with non-Hispanic white children. To the contrary, among currently symptomatic children, minority children were more likely to be diagnosed than non-Hispanic white children even after accounting for the higher wheezing severity among minority children.

- Akinbami L.J. et al.** *Trends in childhood asthma: prevalence, health care utilization, and mortality.* Pediatrics. 2002; 110(2 Pt 1) : 315-22.p
Abstract: OBJECTIVES: Our objective was to use national data to produce a comprehensive description of trends in childhood asthma prevalence, health care utilization, and mortality to assess changes in the disease burden among US children. METHODS: Five data sources from the National Center for Health Statistics were used to describe trends in asthma for children aged 0 to 17 years from 1980 to the most recent year for which data were available. These included the National Health Interview Survey (NHIS), the National Ambulatory Medical Care Survey, the National Hospital Ambulatory Medical Care Survey, the National Hospital Discharge Survey, and the Mortality Component of the National Vital Statistics System. RESULTS: Asthma prevalence increased by an average of 4.3% per year from 1980 to 1996, from 3.6% to 6.2%. The peak prevalence

was 7.5% in 1995. In 1997, asthma attack prevalence was 5.4%, but changes in the NHIS design in 1997 preclude comparison to previous estimates. Asthma attack prevalence remained level from 1997 to 2000. After a decrease between 1980 and 1989, the asthma office visit rate increased by an average of 3.8% per year from 1989 to 1999. The asthma hospitalization rate grew by 1.4% per year from 1980 to 1999. Although childhood asthma deaths are rare, the asthma death rate increased by 3.4% per year from 1980 to 1998. Children aged 0 to 4 years had the largest increase in prevalence and had greater health care use, but adolescents had the highest mortality. The asthma burden was borne disproportionately by black children throughout the period. Racial disparities were largest for asthma hospitalizations and mortality: compared with white children, in 1998-1999, black children were >3 times as likely to be hospitalized and in 1997-1998 >4 times as likely to die from asthma. CONCLUSIONS: Recent data suggest that the burden from childhood asthma may have recently plateaued after several years of increasing, although additional years of data collection are necessary to confirm a change in trend. Racial and ethnic disparities remain large for asthma health care utilization and mortality.

- Akpınarlı A. et al.** *Increased interleukin-4 and decreased interferon gamma production in children with asthma: function of atopy or asthma?* J Asthma. 2002; 39(2) : 159-65.p
Abstract: Both atopy and asthma are claimed to be associated with a Th-2 cytokine pattern. We sought to determine the contribution of atopy and asthma to the observed Th-2/Th-1 imbalance in these conditions. Of 60 children aged 6-16 years that were included in the study, 13 were nonatopic nonasthmatic, 15 atopic nonasthmatic, 14 nonatopic asthmatic, and 18 atopic asthmatic. Atopic children had positive skin prick tests to grass pollens only. All children were studied after an asymptomatic and drug-free period of at least three months. Total IgE was measured in serum. Peripheral blood mononuclear cells were cultured and stimulated in vitro with phytohemagglutinin and interferongamma (IFN-gamma) and interleukin-4 (IL-4) measured in the supernatants. Total IgE was significantly higher in atopic asthmatics compared to nonatopic asthmatics (p = 0.004), and nonatopic nonasthmatics (p = 0.001), but was not different from atopic nonasthmatics (p >0.05). On the other hand, IL-4 was significantly elevated in atopic asthmatics and in nonatopic asthmatics compared to nonatopic nonasthmatics (p = 0.037 and p = 0.009, respectively). Although atopic asthmatics had lower IFN-gamma values than nonatopic asthmatics, the difference did not reach statistical significance. No correlation was detected between any two parameters. Our results suggest that both atopy and asthma contribute to the increased levels of IL-4 and that, whereas nonatopic asthma is associated with increases in both IL-4 and IFN-gamma release by mononuclear cells, only atopic asthma is characterized by a Th-2 type cytokine dominance.

- Al-Abdulhadi S.A. et al.** *Preferential transmission and association of the -403 G --> A promoter RANTES polymorphism with atopic asthma.* Genes Immun. 2005; 6(1) : 24-30.p
Abstract: Asthma is a complex inherited disease. The study was undertaken to identify the association of RANTES promoter polymorphisms with atopy and asthma using family-based association tests (FBATs) and generation-specific case-control analyses. We identified 154 nuclear families (453 individuals) in whom we established RANTES promoter status using the RFLP-PCR method. Of the two known promoter polymorphisms -403G/A and -28C/G, only the former appeared with a clinically relevant frequency. A total of 61 families were eligible for assessment of transmission of the allele with asthma and atopy by the pedigree disequilibrium test (PDT). Overall, allele frequency for -403A was 38.3% and 84 of 89 (94.3%) alleles were transmitted with physician diagnosed asthma (PDA) (P=0.001). All 89 children with atopy received the mutant allele, which was more than expected following Mendelian Laws of transmission (P=0.0001). In 303 unrelated parents, significant associations of the mutant allele were for atopy with or without asthma (P=0.001). In 150 unrelated

children, significant associations were for atopy alone ($P=0.001$) and asthma ($P=0.001$). No associations were found for bronchial hyper-responsiveness (BHR). The $-403\text{ G} \rightarrow \text{A}$ is transmitted with atopy and atopic asthma, although its contribution appears to relate more to atopy than asthma and BHR.

Al-Ayed T.M. et al. *Minimal exhaled nitric oxide production in the lower respiratory tract of healthy children aged 2 to 7 years.* Ann Saudi Med. 2005; 25(2) : 120-3.p **Abstract:** BACKGROUND: Exhaled nitric oxide (eNO) is elevated in inflammatory airway conditions, e.g. asthma. We measured eNO levels in normal preschool children for whom there is little data available and in whom the prevalence of asthma is high. SUBJECTS AND METHODS: Fifty children, 2-7 years old, undergoing elective surgery, excluding airway procedures, were recruited. Children with known respiratory disease or acute viral infections were excluded. Gas for eNO measurement was collected in a non-diffusion bag via 1) the mask after inhalation induction of anesthesia, 2) endotracheal tube (ETT) or laryngeal mask airway (LMA), and 3) during emergence. Measurement was off-line by chemiluminescent analyzer. RESULTS: Mean eNO level by mask was 10.23 ppb (mean value \pm SD of 8.8-11.1 ppb) after induction and 8.35 ppb (mean value \pm SD of 5.9-10.8 ppb) on emergence. Mean eNO for the intubated group ($n=25$) was 0.75 ppb (mean value \pm SD of 0.4-1 ppb) ($P<0.0001$ vs mask); mean eNO for the LMA group ($n=25$) was 2.6 ppb (mean value \pm SD of 2-3.2 ppb), which differed from the mask ($P<0.0001$), and from ETT values ($P<0.0001$). CONCLUSIONS: Most eNO is produced by the upper airway in healthy pre-school children. The lower airway constitutive eNO production is very low. The LMA does not completely isolate the upper airway and current mask collection techniques allow significant contamination of samples by sino-nasal eNO production in young children.

Al-Dawood K.M. *Risk factors associated with hospital emergency visits among asthmatic schoolboys in Saudi Arabia.* East Mediterr Health J. 2002; 8(1) : 31-41.p **Abstract:** This cross-sectional study was carried out to determine the prevalence of a positive history of hospital emergency visits (HHEV) among asthmatic Saudi schoolboys. Data were collected using self-administered questionnaires to parents. The prevalence rate for positive HHEV among questionnaire-diagnosed asthmatic boys (QDAs) was 65.0%. Factors associated with positive HHEV among QDAs were determined. Modifying the preventable factors associated with the total number of hospital emergency room visits is expected to decrease the severity and the disability of this disease.

Al-Dawood K.M. *Schoolboys with bronchial asthma in Al-Khobar City, Saudi Arabia: are they at increased risk of school absenteeism?* J Asthma. 2002; 39(5) : 413-20.p **Abstract:** The objective of this cross-sectional study was to determine the mean period of school absenteeism (MPSA) among asthmatic Saudi schoolboys of Al-Khobar City and to determine the factors associated with the absenteeism. The methodology included the distribution of a self-administered questionnaire, which was completed by the parents of 1482 schoolboys who satisfied the selection criteria of the study. The prevalence rate of questionnaire-diagnosed asthma (QDA) was 9.5% (141/1482). The MPSA among questionnaire-diagnosed asthmatic boys (QDAs) was 13.6 \pm 3.4 days compared to 3.7 \pm 2.2 days among non questionnaire-diagnosed asthmatic boys (non QDAs). Among QDAs, the MPSA was associated significantly and positively with those who were younger, and with decreasing levels of socioeconomic class, histories of pets at home, presence of a currently smoking family member (father or both parents), visit to a hospital emergency room, and admission to hospital. It was significantly and negatively associated with concomitant use of prophylactic medication(s), including those used appropriately. The QDAs from middle and lower socioeconomic classes showed less use of prophylactic medication(s) but more histories of visits to an

emergency room and of admissions to hospital. The multiple linear regression equation for the total period of school absenteeism (TPSA) during the 1995 academic year was generated. Asthmatic school children have a higher MPSA compared to their non asthmatic classmates. The risk of suffering the impacts of this disease is shown to be particularly increased among QDAs belonging to less socioeconomically advantaged families.

Al-Dowaisan A. et al. *Salsola pollen as a predominant cause of respiratory allergies in Kuwait.* Ann Allergy Asthma Immunol. 2004; 92(2) : 262-7.p **Abstract:** BACKGROUND: Respiratory allergies are common in Kuwait, and the role of certain allergens has been previously documented. OBJECTIVE: To evaluate the results of skin prick tests to a range of allergens that were considered relevant to the vegetation surveys and aerobiological studies performed in Kuwait. METHOD: New patients attending our center during August 2002 to February 2003 with asthma or allergic rhinitis underwent skin prick tests to a battery of allergens. RESULTS: A total of 451 patients aged 5 to 60 years (mean age, 29.5 years) were tested. Of these patients, 403 (89.4%) had a positive test result to at least one allergen and were considered allergic. A total of 76.7% of the allergic patients had a positive reaction to Salsola pollen, with a mean wheal diameter of 8.25 mm (median, 8 mm). Chenopodium album was positive in 57.6% and Bermuda grass was positive in 38.2% of the allergic cases. Indoor allergens seemed to play a lesser role than pollens: Dermatophagoides pteronyssinus was positive in only 37.5%, and American and German cockroaches were positive in 33.2% and 22.3%, respectively. All the allergens other than Salsola elicited a mean wheal diameter of less than 6.25 mm (median, $<$ or = 6 mm). CONCLUSIONS: Indoor allergens seem to play a lesser role in respiratory allergies in Kuwait. Most allergic patients become sensitized to pollens; the strongest and most frequent reaction is from Salsola pollen. Salsola imbricata is found growing extensively in most areas of the country, flowering mainly in autumn, when the most common pollen is of the Chenopod-Amaranth type and when most patients with seasonal allergic rhinitis become symptomatic.

Al-Khatib I. et al. *Impact of housing conditions on the health of the people at al-Ama'ri refugee camp in the West Bank of Palestine.* Int J Environ Health Res. 2003; 13(4) : 315-26.p **Abstract:** Al-Ama'ri camp is situated to the south of Ramallah city in the West Bank of Palestine. It is densely populated, with a total population of 4046, divided into 760 households, on a surface area of 93 dunums (93000 m²). In this research, the relationship between the housing conditions at Ama'ri camp and the prevalence and incidence rates of upper respiratory tract diseases has been studied. The diseases and symptoms most encountered in winter, and those include: common cold, cough, pharyngitis, influenza, ear infection, asthma and bronchitis have been studied. It was found that these are diseases directly related to poor housing conditions. Cold housing, presence of dampness and moulds, dust and smoke, burning of biomass fuel, crowding, poor ventilation and inadequate lighting problems are commonly found in the houses of this refugee camp.

Al-Mousawi M.S. et al. *Asthma and sensitization in a community with low indoor allergen levels and low pet-keeping frequency.* J Allergy Clin Immunol. 2004; 114(6) : 1389-94.p **Abstract:** BACKGROUND: Little is known about causes of asthma and sensitization in desert countries. OBJECTIVE: To investigate risk factors associated with asthma and sensitization in Kuwait. METHODS: One hundred sixty children (9-16 years) with physician-diagnosed asthma were recruited and matched (age, sex) with 303 healthy controls. Risk factors were assessed by questionnaires, determination of sensitization status (skin tests and IgE), and home allergen exposure (mite, cat, dog, cockroach; ELISA). RESULTS: Home allergen levels and frequency of pet ownership were very low (cat, 4.1%; dog, 1.5%). The risk of cat sensitization increased significantly among cat owners (odds ratio [OR], 3.53; 95% CI, 1.33-9.41; $P = .01$), and in

children with reported contact with cats during the first year of life (OR, 2.60; 95% CI, 1.17-5.80; P = .019). In the multivariate analysis, maternal atopy (OR, 1.77; 95% CI, 1.13-2.75; P = .01) and cat ownership (OR, 3.32; 95% CI, 1.19-9.25; P = .02) remained significant associates of cat sensitization. Current dog ownership significantly increased the risk of sensitization to dog (OR, 6.05; 95% CI, 1.33-27.54; P = .02). In the multivariate analysis, dog ownership remained the only significant associate of dog sensitization (OR, 6.02; 95% CI, 1.30-27.96; P = .02). Sensitization to *Alternaria* was the strongest independent associate of the asthma group. Family history of asthma, history of whooping cough, current cat ownership, and breast-feeding <2 months were other significant and independent risk factors for asthma. CONCLUSIONS: Pet ownership markedly increased the risk of sensitization to pets. Despite low allergen exposure, the pattern of childhood asthma in Kuwait follows that described in Western communities (strong association with sensitization).

Al-Mutairi S.S. et al. *Utilization of the pulmonary function test laboratory in the evaluation of respiratory disorders in the Al-Amiri Hospital: a secondary medical center.* Med Princ Pract. 2005; 14(3) : 182-8.p **Abstract:** OBJECTIVE: The aim of this study was to describe the current use of pulmonary function tests (PFT) and the degree of matching between the diagnoses at referral and after the test. SUBJECTS AND METHODS: A pre-test questionnaire was administered to 464 (5-88 years) patients referred to the PFT laboratory followed by a complete PFT test. The results of the patients' tests were analyzed in terms of the diagnosis before the test, its relation to symptoms, and the rate of concordance between the diagnoses before and after the test. RESULTS: The most referrals were from the medical Outpatient Department; 61% and the most frequent diagnosis before the test was asthma (31.8%). Of the 464 patients, 34% were currently smoking cigarettes, and the most common symptoms were chronic dyspnea (30.2%) and chronic cough (19.6%). The chronicity of symptoms showed some association with the diagnosis before PFT in the case of chronic obstructive pulmonary disease (COPD) showing the symptom of dyspnea (p = 0.05), and COPD and restrictive lung disease with cough (p < 0.05). The overall rate of concordance in matching diagnoses before and after the test was 60.4% by consultant physicians and 51.9% by non-consultants, with an overall rate of 55% by all physicians. CONCLUSION: Our findings show that there should be better utilization of the PFT laboratory by physicians in all sub-specialities and there is a need to facilitate its use to make a better functional diagnosis.

Al-Riyami B.M. et al. *A relatively high prevalence and severity of asthma, allergic rhinitis and atopic eczema in schoolchildren in the Sultanate of Oman.* Respirology. 2003; 8(1) : 69-76.p **Abstract:** OBJECTIVES: Although asthma, allergic rhinitis and eczema are among the most common chronic diseases in children worldwide, there is very limited information about the burden of these conditions in Oman. The aim of this study was to determine the prevalence and severity of symptoms of asthma, allergic rhinitis and eczema in Omani schoolchildren using the International Study of Asthma and Allergies in Childhood (ISAAC) Phase I questionnaire. METHODS: An Arabic version of the ISAAC Phase I questionnaire was completed by parents of 3893 children aged 6-7 years and self-completed by 3174 children aged 13-14 years, randomly selected from a nationwide sample of public schools. RESULTS: The prevalence rates of reported diagnoses of asthma, allergic rhinitis and eczema were higher in older children (20.7%, 10.5% and 14.4% compared with 10.5%, 7.4% and 7.5%, respectively, in young children). In young children, 277 were current wheezers and of these 40.8% had sleep-disturbing wheeze at least once a week and 45.1% had speech-limiting wheeze during the past year. Similarly, 283 older children were current wheezers, and of these 30.0% had sleep-disturbing wheeze at least once a week and 37.5% had speech-limiting wheeze during the past year. Exercise-induced wheeze was

higher in older children (19.2% vs 6.9%; P < 0.001). Allergic rhinitis and eczema were also associated with significant sleep disturbance and limitation of activity in both age groups. CONCLUSION: Allergic conditions in Omani schoolchildren are common and associated with significant morbidity. Further research is required to identify the local risk factors for allergy to allow better understanding and management of these conditions.

Al-Shawwa B. et al. *Hypercholesterolemia is a potential risk factor for asthma.* J Asthma. 2006; 43(3) : 231-3.p **Abstract:** INTRODUCTION: The effect of hyperlipidemia on asthma has never been addressed. Recent literature implicates a pro-inflammatory role for hypercholesterolemia. This study evaluates the effect of serum cholesterol level on asthma frequency. METHODS: Factors associated with asthma risk were examined in a retrospective study design. Study subjects were between the 4 and 20 years of age who presented to a rural pediatric clinic and whose total serum cholesterol level was obtained. Diagnosis of asthma was determined by the treating physician. Multivariable logistic regression was performed to identify variables that were related to the odds of having asthma. RESULTS: A total of 188 patients were included. Asthma was present in 50 patients. Total serum cholesterol (mean +/- SD) for the asthma group was 176.7 +/- 39.8 compared to 162.9 +/- 12.8 in the non-asthma group (P = 0.028). A total of 21 of the 50 (42%) asthma patients were obese compared to 31 of the 138 (22%) non-asthma patients (p = 0.014). There was no difference between both groups regarding age and gender. Hypercholesterolemia and obesity were identified by logistic regression analysis to increase the probability of asthma independently. CONCLUSION: Hypercholesterolemia is a potential risk factor for asthma independent of obesity.

Albernaz E.P. et al. *[Risk factors associated with hospitalization for bronchiolitis in the post-neonatal period].* Rev Saude Publica. 2003; 37(4) : 485-93.p **Abstract:** OBJECTIVE: To investigate the relationship between socioeconomic factors, maternal characteristics, breastfeeding, and hospitalization for bronchiolitis in the post-neonatal period. METHODS: A nested case-control study with a cohort of 5,304 children born in the city of Pelotas, Brazil, was conducted. The cohort study consisted of four sub-studies with their own methods and logistics. Mothers were interviewed using a standard questionnaire during in-hospital and home visits. Cases were defined as any child aged 28 to 364 days who had been hospitalized for bronchiolitis. RESULTS: Among 5,304 cohort children, 113 (2.1%) were hospitalized for bronchiolitis. The hierarchical multivariate analysis performed using logistic regression showed the following results: family income and gestational age were inversely associated with the risk of hospitalization for bronchiolitis. Breastfeeding showed to have a protective effect; children who were breastfed for less than one month had 7 times less risk for being hospitalized for acute bronchiolitis in the first three months of life. The risk for hospitalization for bronchiolitis is 57% higher in those exposed to maternal smoking than in those non-exposed. CONCLUSIONS: Hospitalization for acute bronchiolitis is inversely associated with family income, gestational age and duration of breastfeeding and positively associated with maternal smoking. There was not an association with either parity or maternal history of asthma.

Alford S.H. et al. *Parental history of atopic disease: disease pattern and risk of pediatric atopy in offspring.* J Allergy Clin Immunol. 2004; 114(5) : 1046-50.p **Abstract:** BACKGROUND: Family history is an important risk factor for atopic disease. However, most studies assess only limited information on family history. Because atopic disease can exhibit transient or persistent patterns, it may be useful to assess information on patterns of disease within families. This approach has been applied in other diseases, such as cancer, to discriminate between predominantly inherited versus

environmentally caused (sporadic) cases. **OBJECTIVE:** In a cohort of children who were followed from birth until age 6 to 7 years, we examined the relationship between parental onset (ie, childhood and adulthood) and duration of atopic disease (ie, persistent disease) and the risk of pediatric atopic disease. Our hypothesis was that different parental disease patterns would be important to pediatric risk of disease. **METHODS:** Data from 476 families in the ongoing Childhood Allergy Study in Detroit, Mich, were analyzed by using logistic regression. We examined the association between parental patterns of disease and disease onset in their children. Results: Father's disease history, particularly asthma history, was more strongly related to pediatric outcomes than mother's history. Asthma status in the fathers, whether it was childhood-only, adulthood-only, or persistent, was associated with current asthma in the children. Childhood-only and persistent asthma in fathers conferred a higher risk of atopy in the study children, whereas adulthood-only disease did not. There was also a significant relationship between persistent allergy in the father and atopy in the study children. **CONCLUSION:** Our data support the hypothesis that there are complex inheritance patterns for allergy and asthma. Therefore, a detailed family history of atopy, including childhood and adulthood experiences, is critical to identifying and classifying risk and disease phenotypes.

Ali M. et al. *NOS1 polymorphism is associated with atopy but not exhaled nitric oxide levels in healthy children.* *Pediatr Allergy Immunol.* 2003; 14(4) : 261-5.p **Abstract:** Exhaled nitric oxide (FENO) is raised in atopy. The mechanism for this is unclear. The aim of this study was to investigate whether the number of AAT repeats in intron 20 of the NOS1 gene, recently associated with variations in FENO in adults with asthma and cystic fibrosis, was associated with the raised FENO in healthy atopic children. Eighty-seven healthy children (44 girls, 42 atopic, age range 6-18 years) underwent measurements of FENO, spirometry, airway responsiveness and skin prick testing. Genotyping was carried out to determine the number of AAT repeats. There was no association between the number of AAT repeats and FENO in either the whole sample of healthy children (n = 87) or in the subsample of healthy atopics (n = 42). However, a greater number of atopic children had two high repeat alleles compared with non-atopic children (33.3% vs. 13.6%, respectively, p = 0.03). This suggests that variations in the NOS1 gene may contribute to atopy without this relationship being reflected by FENO.

Allen D.B. *Effect of inhaled corticosteroids on growth.* *Pediatrics.* 2001; 108(5) : 1234-5.p

Allen-Ramey F.C. et al. *Trends in use of inhaled corticosteroids for asthma management: 1994-1998.* *Ann Epidemiol.* 2004; 14(3) : 161-7.p **Abstract:** **PURPOSE:** To evaluate trends in prescribing of inhaled corticosteroids for asthma between 1994 and 1998 and patterns of prescribing in relation to selected physician characteristics. **METHODS:** Using a HMO database, a physician sample (N = 335) was linked to patient encounter data and pharmacy claims (N = 51,345) for asthma patients ages 5 to 45 years (N = 6,944). Longitudinal and cross-sectional analytic methods were used to examine physician prescribing patterns across the study period. **RESULTS:** The percent of physicians prescribing an inhaled corticosteroid increased over time with consistently greater prescribing among specialists. Annual comparisons by specialty groups revealed that specialists (allergy and pulmonary) prescribed inhaled steroids to a larger proportion of their patients than generalists (family practice, internal medicine, pediatrics, pediatric emergency department); (range: 0.61-0.69 vs. 0.31-0.39, p < .01). The lowest proportions were found among pediatric emergency department physicians (range: 0.00-0.10) and pediatricians (range: 0.17-0.27). **CONCLUSIONS:** Significant linear trends in either physician group were not observed during this 5-year period. Differences across physician groups were evident.

Almqvist C. et al. *Heredity, pet ownership, and confounding control in a population-based birth cohort.* *J Allergy Clin Immunol.* 2003; 111(4) : 800-6.p **Abstract:** **BACKGROUND:** The association between pet ownership in childhood and subsequent allergic disease is controversial. Bias related to selection of pet exposure has been suggested as a reason for contradictory study results. **OBJECTIVE:** The purpose of this investigation was to elucidate how pet exposure depends on family history of allergic disease, smoking, and socioeconomic factors in a prospective birth cohort. **METHODS:** Parents of 4089 two-month-old children answered a questionnaire that included detailed questions about family history of asthma (maternal, paternal, and sibling), rhinoconjunctivitis, atopic eczema/dermatitis syndrome, pollen and pet allergy, smoking habits, parental occupation, and family pet ownership (cat and dog). Dust samples collected from the mothers' beds were analyzed for Fel d 1 and Can f 1 in a subgroup of the cohort. **RESULTS:** Cats were less frequently kept in families with parental asthma, rhinoconjunctivitis, or pet or pollen allergy (3.5% to 5.8%) than in families without parental allergic disease (10.8% to 11.8%). Dogs were less common in families with (3.3%) than in families without (5.9%) parental atopic eczema/dermatitis syndrome. Families with smoking mothers and those with low socioeconomic index kept cats and dogs more frequently. Cat allergen levels were lower in homes with than in homes without maternal pet allergy, and this tended to hold true even for homes without a cat. Cat ownership decreased from birth to 2 years of age, especially in families with parental history of allergic diseases. **CONCLUSION:** There seems to be a selection of pet exposure based on parental history of allergy, maternal smoking, and socioeconomic factors. This has to be taken into consideration in evaluations of risk associations between pet exposure and allergic disease in childhood.

Althman G.A. et al. *Evaluation of bronchial constriction in children with cystic fibrosis after inhaling two different preparations of tobramycin.* *Chest.* 2002; 122(3) : 930-4.p **Abstract:** **OBJECTIVES:** This randomized, double-blind, cross-over study evaluated the risk of bronchoconstriction with two preparations of inhaled tobramycin in children with cystic fibrosis (CF) infected with *Pseudomonas aeruginosa* with and without airway hyperreactivity. **DESIGN:** Of 19 children with CF (age range, 7 to 16 years) with mild-to-moderate pulmonary disease, 10 children were at high risk (HR) for bronchospasm (family history of asthma and previous response to bronchodilators) and 9 children were at low risk (LR) for bronchospasm (no family history of asthma or previous response to bronchodilators). Two solutions of tobramycin were administered: (1) 80 mg in a 2-mL vial diluted with 2 mL of saline solution containing the preservatives phenol and bisulfites (IV preparation); and (2) 300 mg in a preservative-free preparation in a 5-mL solution. Following a bronchodilator-free period of 12 h, the patients inhaled either one or the other preparation in random order on two different occasions, 2 weeks apart. **RESULTS:** Prechallenge and postchallenge results for the LR group showed a percentage of fall in FEV(1) (DeltaFEV(1)) of 12 +/- 9% (mean +/- SD) for the IV preparation, compared to 4 +/- 5% for the preservative-free preparation (p = 0.046). An DeltaFEV(1) of > 10% was seen in six of nine patients for the IV preparation and in one of nine patients for preservative-free preparation. For the HR group, the DeltaFEV(1) was 17 +/- 13% for the IV-preparation group, compared to 16 +/- 12% for the preservative-free group (p = 0.4). In this group, equal numbers of patients (8 of 10 patients) had an DeltaFEV(1) > 10% after inhaling each preparation. The largest DeltaFEV(1) was 44% (HR group with the preservative-free preparation that forced the early termination of inhalation). **CONCLUSIONS:** Both preparations caused significant bronchoconstriction in the HR group, and the preservative-containing IV preparation caused more bronchospasm in LR group than the preservative-free solution. Heightened airway reactivity in children with CF places them at risk of bronchospasm from inhalation therapy.

Altmuller J. et al. *Phenotypic and genetic heterogeneity in a genome-wide linkage study of asthma families.* BMC Pulm Med. 2005; 5 : 1.p
Abstract: BACKGROUND: Asthma is a complex genetic disease with more than 20 genome-wide scans conducted so far. Regions on almost every chromosome have been linked to asthma and several genes have been associated. However, most of these associations are weak and are still awaiting replication. METHODS: In this study, we conducted a second-stage genome-wide scan with 408 microsatellite markers on 201 asthma-affected sib pair families and defined clinical subgroups to identify phenotype-genotype relations. RESULTS: The lowest P value for asthma in the total sample was 0.003 on chromosome 11, while several of the clinical subsets reached lower significance levels than in the overall sample. Suggestive evidence for linkage ($p = 0.0007$) was found for total IgE on chromosomes 1, 7 and again on chromosome 11, as well as for HDM asthma on chromosome 12. Weaker linkage signals could be found on chromosomes 4 and 5 for early onset HDM, and, newly described, on chromosome 2 for severe asthma and on chromosome 9 for hay fever. CONCLUSIONS: This phenotypic dissection underlines the importance of detailed clinical characterisations and the extreme genetic heterogeneity of asthma.

Ameli F. et al. *Nasal endoscopy in asthmatic children: clinical role in the diagnosis of rhinosinusitis.* Rhinology. 2004; 42(1) : 15-8.p
Abstract: The aim of the study was to determine the role of rigid nasal endoscopy in the diagnosis of rhinosinusitis and adenoiditis in asthmatic children. Hundred-forty-five asthmatic children (aged 2-15 years) with recurrent upper respiratory symptoms were evaluated with complete ENT examination and nasal endoscopy by rigid endoscope during local anaesthesia. A step by step endoscopic procedure is described. Endoscopy was successfully performed in 128 patients (88.3%). Purulent rhinosinusitis was diagnosed in 61 subjects (47.6%) and adenoiditis in 45 subjects (35.1%). Rhinosinusitis was associated with adenoiditis in 35 subjects (27.3%), more frequently in younger children (i.e. 2-5 years). Nasal bacteria occurred in 90% of rhinosinusitis patients. Numerous anatomical anomalies were identified. Endoscopy of nasal cavity and rhinopharynx is less traumatic and more readily accepted than other methods. Nasal endoscopy may be proposed as an appropriate routine diagnostic tool in children since it is well tolerated, easily and quickly performed, cost-efficient, and useful in diagnosing rhinosinusitis.

Amin H.S. et al. *Evaluation of near-fatal reactions to allergen immunotherapy injections.* J Allergy Clin Immunol. 2006; 117(1) : 169-75.p
Abstract: BACKGROUND: The overall incidence of near-fatal reactions (NFRs) after immunotherapy injections is unknown. Investigation of NFRs might identify preventive strategies that could avert fatal immunotherapy reactions. OBJECTIVE: We sought to determine the incidence and characteristics of NFRs to allergen immunotherapy. METHODS: In a brief survey of fatal reactions (FRs) and NFRs administered to practicing allergists, 273 of 646 respondents reported NFRs after immunotherapy injections; a NFR was defined as respiratory compromise, hypotension, or both requiring emergency epinephrine. Respondents were mailed a 105-item questionnaire regarding the details of NFRs and circumstances of these events. RESULTS: During the period from 1990 through 2001, the incidence of unconfirmed NFRs was estimated at 23 per year (5.4 events per million injections). There were 68 confirmed NFRs on the basis of responses to the long survey, with a mean case incidence of 4.7 per year or 1 NFR per million injections. Asthma was present in 46% of near-fatal reactors and in 88% of fatal reactors identified in this study. Hypotension was reported in 80% and respiratory failure occurred in 10% of NFRs and exclusively in asthmatic subjects. Epinephrine was delayed or not administered in 6% of NFRs versus 30% of reported FRs (OR, 7.3; 95% CI, 1.4-39.8; $P = .01$). CONCLUSIONS: Confirmed NFRs were 2.5 times more frequent than FRs. Favorable outcomes of NFRs when compared

with FRs could be related to lower asthma prevalence and appropriate management of life-threatening anaphylaxis.

Amirav I. et al. *Safety of inhaled corticosteroids delivered by plastic and metal spacers.* Arch Dis Child. 2003; 88(6) : 527-8.p
Abstract: BACKGROUND: Because of its non-electrostatic properties the metal Nebuchamber (NC) valved holding chamber (VHC) delivers a greater mass of aerosol to the mouth than the polypropylene Aerochamber (AC) VHC. Delivery of more aerosol to the lungs may also increase systemic absorption of inhaled corticosteroids (ICS) and hypothalamo-pituitary-adrenal (HPA) suppression. METHODS: Thirty children (mean 4.3 (SD 0.3) years) received 200 micro g budesonide twice daily by NC or AC, both with the mask provided, in a randomised, two month crossover trial. Twenty four hour urinary free cortisol (UFC) was determined as a measure of HPA suppression. RESULTS: UFC decreased from 42.3 (7.8) nmol UFC/nmol creatinine control to 26.2 (2.4) ($p = 0.06$ v control) after AC, and to 24.5 (2.5) ($p = 0.04$ v control) after NC ($p = 0.4$ AC v NC). CONCLUSIONS: Despite a greater total dose delivered to the mouth, NC is not associated with greater HPA suppression when using 400 micro g/day budesonide under real life conditions in young children.

Amirav I. et al. *Measurement of peak inspiratory flow with in-check dial device to simulate low-resistance (Diskus) and high-resistance (Turbohaler) dry powder inhalers in children with asthma.* Pediatr Pulmonol. 2005; 39(5) : 447-51.p
Abstract: Drug delivery and lung deposition from a dry powder inhaler (DPI) are dependent on the peak inspiratory flow (PIF) through the DPI. Therefore, when prescribing a DPI, it is important to know whether a child is able to generate sufficient PIF through a particular device. Using a PIF meter (In-Check Dial) that mimics the internal resistance of DPIs, two commonly used devices (high-resistance Turbohaler (TH) and low-resistance Diskus (DK)) determined the PIF generated by asthmatic children through each of them. Two hundred and twenty-three children were studied, of whom 100 (mean age, 9.1 +/- 3.0 years; range, 3-15 years) were experienced with the use of a DPI (>1 month of regular DPI use), and 123 (mean, 5.5 +/- 1.9 years; range, 3-9 years) were inexperienced (no previous DPI use). All of the experienced patients generated more than 30 l/min through both devices, but a PIF of 60 l/min through the TH was obtained by only 68 (68%) of them. The age above which a minimal PIF of 30 l/min (for DK) or 60 l/min (for TH) could be achieved in new DPI users (inexperienced) was 4 years and 9 years, respectively. Even among experienced patients, many young children may not generate optimal PIFs through high-resistance DPIs. When DPI treatment is considered for young children, some devices may be successfully introduced at a younger age. It may thus be important to measure PIF in children who use a DPI or in whom DPI use is contemplated. This evaluation can be easily undertaken in the clinic with the In-Check Dial device.

Amirav I. et al. *Comparison of efficiency and preference of metal and plastic spacers in preschool children.* Ann Allergy Asthma Immunol. 2004; 93(3) : 249-52.p
Abstract: BACKGROUND: The metal NebuChamber valved holding chamber (VHC) has gained wide acceptance among children with asthma. Due to its nonelectrostatic properties and larger volume, the 250-mL, metal NebuChamber delivers a greater mass of aerosol to a filter at the mouth compared with the commonly used 150-mL polypropylene AeroChamber VHC. Such in vitro results have been used to suggest that this may provide increased efficacy with the NebuChamber. No comparative efficacy data exist for preschool children with asthma. OBJECTIVE: To compare efficiency and preference of metal and plastic spacers in preschool children. METHODS: Children with mild-to-moderate persistent asthma received 200 microg of budesonide twice daily by NebuChamber or AeroChamber, both with the mask provided in a randomized, 2-month, crossover trial. Symptom diary cards, beta-

agonist use, and preference by children and parents were compared. RESULTS: Thirty children (mean +/- SD age, 4.3 +/- 0.3 years) completed the study. There was no difference between the AeroChamber and NebuChamber in clinical efficacy outcomes. There was no difference between the AeroChamber and NebuChamber in parents' view of ease of use, design, acceptability by the children, and overall satisfaction. CONCLUSIONS: Despite a greater total dose delivered to the mouth, the NebuChamber appears no more effective than the AeroChamber and it is not preferred by patients or parents. More parents chose to continue to use the NebuChamber after the study.

Anak S. et al. *Possible curative effect of intensive chemotherapy on asthma in children.* *Pediatr Hematol Oncol.* 2001; 18(6): 421-2.p

Anarella J. et al. *A survey of Medicaid recipients with asthma: perceptions of self-management, access, and care.* *Chest.* 2004; 125(4) : 1359-67.p Abstract: STUDY OBJECTIVES: To understand how Medicaid recipients with asthma view their experience with care. DESIGN: Survey sent to Medicaid managed care enrollees. SETTING: A survey designed to assess general health status, access to care, medication-taking behaviors, and overall satisfaction was sent to 25,171 patients with moderate-to-severe asthma. RESULTS: A total of 92% of patients rated their asthma care as good or excellent, 64% of adults reported their health as fair or poor, while only 27% of children reported their health as being fair or poor. Respondents were well-educated regarding their asthma, with 87% reporting knowing what to do for severe asthma attacks, 78% knowing the early warning signs of an asthma attack, and 77% recognizing aggravating factors. Eighty-nine percent of respondents rated the quality of the information given to them by their provider as very good or good. While 75% of patients reported using inhaled steroids, only 38% of those reported using them on a daily basis. Forty percent of patients reported using inhaled steroids only when they have symptoms. Forty-six percent of adults either smoke cigarettes or are exposed to smoking in the home, while 35% of children are exposed to smoke in the home. CONCLUSION: Asthmatic patients rated the quality of the information that their physicians provide very highly and reported that they understand how to treat exacerbations. However, they do not take prescribed inhaled steroids on a daily basis. In addition, many asthmatic patients reside in homes where cigarette smoking is present.

Anbar R.D. *Self-hypnosis for anxiety associated with severe asthma: a case report.* *BMC Pediatr.* 2003; 3 : 7.p Abstract: BACKGROUND: Management of asthma can be complicated by both medical and psychiatric conditions, such as gastroesophageal reflux, chronic sinusitis, and anxiety. When symptoms of asthma are interpreted without regard to such conditions treatment may yield a suboptimal outcome. For example, anxiety-associated dyspnea, tachypnea, and chest tightness can be mistakenly interpreted as resulting from an exacerbation of asthma. Medical treatment directed only for asthma may thus lead to overuse of asthma medications and increased hospitalizations. CASE PRESENTATION: The described case illustrates how a systemic steroid-dependent patient with asthma benefited from receiving care from a pediatric pulmonologist who also was well versed in the diagnosis and treatment of anxiety. By using self-hypnosis, the patient was able to reduce her dependence on bronchodilators. Following modification of her medical therapy under supervision of the pulmonologist, and regular use of hypnosis, the patient ultimately was weaned off her systemic steroid therapy. CONCLUSIONS: This report emphasizes that anxiety must be considered as a comorbid condition in the treatment of asthma. Self-hypnosis can be a useful skill in the treatment of a patient with anxiety and asthma.

Andersen G. *Biomonitoring.* *NCSL Legisbrief.* 2004; 12(44) : 1-2.p

Anderson E.W. et al. *Schools' capacity to help low-income, minority children to manage asthma.* *J Sch Nurs.* 2005; 21(4) : 236-42.p Abstract: This article describes the challenges and strengths of asthma management in 14 low-income, predominantly African American urban elementary schools serving more than 5,000 students. Asthma prevalence was 24.5%. Teachers, school principals, parents, and children described how asthma was managed at school. Data from classmates of students with asthma showed that they had moderate to high levels of information about the disease. Data from teachers indicated the great need for practical instruction on how they might effectively support a child with asthma in the classroom and on the playground. Principals raised concerns about expectations for the functioning of school staff and implementation of school policies especially related to asthma emergencies. Parents reported a range of problems their children face at school. Data from children with asthma showed that 75% believed asthma affected their school work. Findings from this study should be useful to school personnel, health providers, and others who assist children and their families to manage asthma at school. Data suggest that making school nursing services available is warranted, given the impact of asthma on the school community.

Anderson G.P. *The immunobiology of early asthma.* *Med J Aust.* 2002; 177 Suppl : S47-9.p Abstract: What do we know? CD4+ T cells are strongly implicated in asthma pathogenesis. The "T(H)2 hypothesis" postulates two patterns of cytokine secretion by stimulated CD4+ T cells: a "T(H)1" response and a "T(H)2" response. T(H)2-type cytokines (interleukins IL-4, IL-5, IL-9, IL-13) regulate eosinophilia, mast cell growth, IgE and mucus production and have been proposed as key regulatory factors in asthma. T(H)1-type cytokines include interferon-gamma, IL-2, IL-12, IL-18, and tumour necrosis factor beta. T(H)2 responses are reciprocally inhibited by T(H)1 responses in animal models, but this may not be so in asthma in humans. In humans, T(H)1- and T(H)2-type cytokines are often coexpressed in early asthma. What do we need to know? Is cross-regulation between T(H)1 and T(H)2 immune biases truly lost in early asthma? Can induction of T(H)1-type responses actually protect against asthma, as predicted by the "hygiene hypothesis"? If so, how might this induction be achieved safely in infants? Can the in-utero environment be subtly manipulated to minimise asthma risk? Does early childhood treatment with current anti-asthma drugs lead to long-term immune changes?

Anderson H.R. et al. *Bronchodilator treatment and deaths from asthma: case-control study.* *BMJ.* 2005; 330(7483) : 117.p Abstract: OBJECTIVE: To investigate the association between bronchodilator treatment and death from asthma. DESIGN: Case-control study. SETTING: 33 health authorities or health boards in Great Britain. PARTICIPANTS: 532 patients under age 65 who died from asthma and 532 controls with a hospital admission for asthma matched for period, age, and area. MAIN OUTCOME MEASURES: Odds ratios for deaths from asthma associated with prescription of bronchodilators and other treatment, with sensitivity analyses adjusting for age at onset, previous hospital admissions, associated chronic obstructive lung disease, and number of other drug categories. RESULTS: After full adjustment, there were no significant associations with drugs prescribed in the 4-12 months before the index date. For prescriptions in the 1-5 years before, mortality was positively associated with inhaled short acting beta2 agonists (odds ratio 2.05, 95% confidence interval 1.26 to 3.33) and inversely associated with antibiotics (0.59, 0.39 to 0.89). The former association seemed to be confined to those aged 45-64, and the association with antibiotics was more pronounced in those under 45. Significant age interactions across all periods suggested inverse associations with oral steroids confined to the under 45 age group. An inverse association with long acting beta2 agonists and a positive association with methylxanthines in the 1-5 year period were non-significant. CONCLUSION: There was no evidence of adverse effects on mortality with medium to long term use of inhaled long

acting beta2 agonist drugs. The association with short acting beta(2) agonists has several explanations, only one of which may be a direct adverse effect.

Anderson K. et al. *Breath sounds, asthma, and the mobile phone.* Lancet. 2001; 358(9290) : 1343-4.p **Abstract:** The sounds generated by breathing in asthma are widely accepted as an indicator of disease activity. We have investigated the use of a mobile phone and electronic signal transfer by e-mail and voice mail to study tracheal breath sounds in individuals with normal lung function and patients with chronic or exercise-induced asthma. Spectrograms from patients with active asthma and impaired lung function were significantly different from people without asthma ($p < 0.0001$). Our results suggest that mobile phone recordings clearly discriminate tracheal breath sounds in asthma and could be a non-invasive method of monitoring airway diseases.

Anderson M.E. et al. *Successful school-based intervention for inner-city children with persistent asthma.* J Asthma. 2004; 41(4) : 445-53.p **Abstract:** OBJECTIVE: Because children attend school daily, school-based interventions for children with persistent asthma could provide effective disease management for inner-city asthmatic children. The Kunsberg School in Denver, Colorado, enrolls children with chronic diseases, including asthma, into a daily program of school-based disease management. This study sought to determine the impact of the Kunsberg program on asthma utilization. METHODS: Children attending Kunsberg ($n=18$) who received primary care at Denver Health were compared with a group of matched control children who also received primary care at Denver Health, but did not attend Kunsberg ($n=36$). Asthma-related utilization for an average of 2.9 years before and after Kunsberg enrollment was assessed. RESULTS: The 18 Kunsberg and 36 control subjects were mostly minority children in low-income families, without significant demographic differences between groups. Compared with controls, the Kunsberg cohort experienced fewer hospitalizations (0.5 vs. 0.9 hospitalizations/subject/ year, $p=0.05$), fewer emergency department (ED) visits (1.4 vs. 2.8 ED visits/ subject/year, $p=0.04$), and fewer follow-up visits for asthma (3.7 vs. 5.0 visits/subject/ year, $p=0.01$) in the time period (mean 2.9 years; range 1-6 years) following the intervention. Hospital- and clinic-based asthma utilization costs decreased 80% following enrollment in the school (8122 dollars/year to 1588 dollars/year per child), compared to a 19% decrease in the control group. Among the Kunsberg children with hospitalizations prior to school enrollment ($n=8$), hospital days decreased from 3.5 days to 0.1 days annually ($p < 0.01$), ED visits decreased from 2.1 to 0.6 visits annually ($p=0.02$), and follow-up visits decreased from 6.8 to 2.1 visits annually ($p=0.02$). As part of their school program, 89% of Kunsberg enrollees received inhaled corticosteroids daily on a monitored basis while at school. Conclusions: The Kunsberg school program improved asthma control and reduced disease severity for at-risk inner-city asthmatic children, leading to cost reduction for asthma management. Directly observed controller therapy at school can be an important component of a school-based program for children with chronic conditions.

Andrew W. *Bronchial Boogie.* Community Pract. 2006; 79(3) : 78-9.p

Aneeshkumar M.K. et al. *Complete tracheal rings: lower airway symptoms can delay diagnosis.* Eur Arch Otorhinolaryngol. 2005; 262(2) : 161-2.p **Abstract:** Bronchial asthma is a very common condition seen in children diagnosed by clinical examination. While treating these children, all the other possible causes of breathlessness including complete tracheal rings should be considered. Further investigations in the form of endoscopy may need to be carried out in doubtful cases.

Annesi-Maesano I. *[Asthma epidemiology].* Rev Prat. 2005; 55(12) : 1295-8.p **Abstract:** Asthma is excessively common among the individuals (up to 10% in adults and 35% in children). Asthma is differently distributed in the world. Asthma incidence is 1%/y in average. Children are at greater risk of asthma than adults, which could be due to a cohort effect. Severe asthma is reported by 1-3% of the general population (children and adults respectively). Recent population-based data show that the asthma prevalence increase observed worldwide in the past 30 years has now stopped in industrialised countries. Such phenomenon has been paralleled by an increase in the use of asthma medications. The development and phenotypic expression of asthma depends on a complex interaction between genetic and environmental factors. Gene-environment interactions already in early life should be explored to understand asthma epidemiological evolution.

Annett R.D. et al. *Predicting children's quality of life in an asthma clinical trial: what do children's reports tell us?* J Pediatr. 2001; 139(6) : 854-61.p **Abstract:** OBJECTIVE: To define predictors of disease-specific quality of life (QOL) and the relationship between asthma symptoms and disease-specific QOL. STUDY DESIGN: Three hundred thirty-nine children participated at 4 of 8 Childhood Asthma Management Program clinical centers. Included in the analyses were 2 weeks of asthma symptom data, child-reported health status, and QOL scores from the Pediatric Asthma Quality of Life Questionnaire. Data were obtained 12 months after randomization into the Childhood Asthma Management Program. RESULTS: Children were rated at baseline as having "moderate" asthma (63%) and "mild" asthma (37%). QOL scores were correlated with the child-reported anxiety measures. Factor analysis of the QOL measure resulted in 2 factors. Stepwise multiple regression indicated that the strongest independent predictors of QOL were the child's anxiety level, age, sex, and a measure of the child's tendency to minimize or exaggerate symptoms. CONCLUSIONS: Children had few asthma symptoms in the 2 weeks before their 12-month follow-up clinic visit and a generally positive QOL, suggesting that mild-to-moderate asthma does not significantly impair QOL. A child's QOL was predicted primarily by their level of anxiety.

Annett R.D. et al. *Association of hypothalamic-pituitary-adrenal axis function with neuropsychological performance in children with mild/moderate asthma.* Child Neuropsychol. 2005; 11(4) : 333-48.p **Abstract:** The present study examines the relationship between hypothalamic-pituitary-adrenal (HPA) axis function and child psychological/neuropsychological function in a group of children with mild to moderate asthma. The goal of the study was to determine whether child neuropsychological functioning and psychological functioning were associated with cortisol production in response to adrenocorticotropic hormone (ACTH) stimulation when assessed as area under the curve. Data for this study were gathered from 63 children who participated in an ancillary study within the Childhood Asthma Management Program (CAMP) during the pre-randomization phase of the CAMP trial. At 2 of the 8 CAMP clinical centers participants completed an ACTH stimulation test after an overnight stay in the General Clinical Research Center. Gender differences on baseline cortisol and change in cortisol 30 minutes after infusion of ACTH were present. Results further indicated significant associations between cortisol production and measures of child neuropsychological function. Stepwise multiple regression analysis revealed that cortisol change could be predicted by measures of gender, working memory, and arousal maintenance, providing support for the hypothesis that cortisol plays a modest role in the neuropsychological function of children with mild and moderate asthma. In contrast, cortisol production was not associated with child reports of psychological functioning. Limitations to the methods employed in this study are discussed.

Annus T. et al. *Wheezing in relation to atopy and environmental factors in Estonian and Swedish schoolchildren.* Clin Exp Allergy. 2001; 31(12) : 1846-53.p **Abstract:** **BACKGROUND:** The prevalence of asthma and allergic diseases is significantly lower in post socialist Eastern Europe than in Western industrialized countries. The reason for this difference is largely unknown. Different types of childhood wheezing could be related to different risk factors. **OBJECTIVE:** To compare the prevalence of respiratory symptoms, asthma and atopic diseases among Estonian and Swedish schoolchildren and to evaluate characteristics for wheezing in the two countries. **METHODS:** In a prevalence study, population-based random samples of 10-11-year-old schoolchildren in Tallinn (n = 979), Estonia and in Linköping (n = 911) and Östersund (n = 1197), Sweden were studied by a parental questionnaire and skin prick tests (SPT). All 275 children with wheeze in the past 12 months and 710 randomly selected controls within the original cohorts were invited to a case-control study involving a parental questionnaire, examination for flexural dermatitis and bronchial challenge with hypertonic saline. The study adhered to the International Study of Asthma and Allergies in Childhood (ISAAC) Phase II protocol. **RESULTS:** The prevalence of current wheezing was similar (8-10%) in the three centres, while diagnosed asthma and atopic symptoms were more common in Sweden and cold-related respiratory symptoms were more prevalent in Estonia. Frequent wheezing was more common in Sweden than in Estonia (but significantly so only in Östersund). Wheezing children in Sweden had a high rate of positive SPT (49% in Linköping and 58% in Östersund) bronchial hyper-responsiveness (BHR) (48% in Linköping and Östersund) and anti-asthmatic treatment (63% in Linköping and 81% in Östersund). In Estonia, the proportion of wheezing children with positive SPT, BHR and anti-asthmatic treatment was only 26%, 13% and 17%, respectively. Domestic crowding was inversely related to wheezing in one of the study areas (Östersund). The mean baseline forced expiratory volume in one second (FEV1) was higher in Estonia than in Sweden, both in wheezing and non-wheezing children. **CONCLUSIONS:** Our study suggested that although wheezing symptoms were equally common in Estonia and Sweden, they were less severe in Estonia. More frequent symptoms and a high rate of atopy, BHR and anti-asthmatic medication characterized wheezing children in Sweden. In contrast, BHR, atopy and medication were uncommon among wheezing children in Estonia.

Antonio M.A. et al. [Evaluation of the nutritional status of children and adolescents with asthma]. Rev Assoc Med Bras. 2003; 49(4) : 367-71.p **Abstract:** **OBJECTIVE:** The aim of this study was to analyze the nutritional state of children and adolescents with asthma, and to relate this to patient age at the onset of disease, severity of the disease, family per capita income, and the level of maternal schooling. **METHODS:** A cross sectional study involved 66 patients from the Immunology, Allergy and Pulmonology outpatient clinic of the Hospital das Clinicas of the State University of Campinas (HC/UNICAMP). All of the patients suffered from atopic asthma and ranged in age from 4 to 14 years old. The patients were compared to 124 controls. **RESULTS:** There were no differences among male patients and the controls in the distribution of the z-scores for weight/age (p=0.24), height/age (p=0.61), body mass index (p=0.21), upper arm circumference (p=0.94) and triceps skinfold (p=0.49) in relation to disease severity, age at the first occurrence of disease, family per capita income, and the level of maternal schooling. Similarly, there were no significant differences in the z-scores for weight/age (p=0.13), height/age (p=0.46), body mass index (p=0.13), upper arm circumference (p=0.06) among female patients and their controls. However, there was a difference (p=0.002) between the triceps skinfold of female patients (-0.74 +/- 0.84) and the controls (0.17 +/- 1.21). No child with asthma was obese (z-scores for body mass index > or =2). There were no significant differences in of the anthropometrical measurements among patients in relation to family per capita income, the level of maternal schooling, severity of the disease, and age at first occurrence the disease, but the mean weight of boys suffering from moderate asthma was lower than that of the

other patients (p=0.02). **CONCLUSIONS:** The nutritional status of the patients studied was satisfactory so that their body composition was unaffected by the disease, on environment, or by any interaction between these two factors. Our results reinforce the view that an anthropometrical evaluation should be done periodically to assess the consequences of the disease and the impact of any interventions and therapeutic measures used. This will provide a better evaluation of the patient's overall health.

Antonucci R. et al. *Intrauterine smoke exposure: a new risk factor for bronchopulmonary dysplasia?* J Perinat Med. 2004; 32(3) : 272-7.p **Abstract:** **OBJECTIVE:** To evaluate the role of intrauterine smoke exposure and other variables on the development of bronchopulmonary dysplasia (BPD) in infants with birth weight < 1500 g (VLBW). **METHODS:** This case-control study investigated 277 VLBW infants (141 cases, 136 controls) admitted at birth to neonatal intensive care unit and survived to discharge. A retrospective telephone interview provided detailed parental information supplementing clinical data. Logistic regression assessed the effects of birth weight < 1000 g, gestational age < 30 weeks (GA<30), respiratory distress syndrome (RDS), neonatal mechanical ventilation > 7 days (MV>7), patent ductus arteriosus (PDA), intrauterine smoke exposure > or = 3 months (ISE), and of parental history of asthma on BPD (oxygen dependency at 28 days with characteristic radiographic abnormalities) occurrence. **RESULTS:** Including all variables, only GA<30, RDS and MV>7 were significantly associated with BPD. ISE did not contribute significantly to this model (odds ratio [OR] 1.94; 95% confidence interval 0.88-4.26). Excluding iatrogenic variable MV>7, GA<30, RDS, PDA and ISE (OR 2.21; 95% confidence interval 1.03-4.76) were significantly associated with BPD. Analyzing GA as a continuous variable, the OR was 0.63 for each additional week. **CONCLUSIONS:** Prolonged mechanical ventilation, RDS and low gestational age were the major BPD determinants. Intrauterine smoke exposure seems to influence independently BPD development.

Aoki M. et al. *A novel single-nucleotide substitution, Leu 467 Pro, in the interferon-gamma receptor 1 gene associated with allergic diseases.* Int J Mol Med. 2003; 12(2) : 185-91.p **Abstract:** We identified a novel heterozygous single-nucleotide substitution 1400 T right curved arrow C (Leu 467 Pro) in the seventh exon of the interferon-gamma receptor 1 (IFNGR1) gene. This substitution was detected in 6 of the 89 allergic patients but not in the 72 non-allergic subjects. There was a difference in the L467P frequency between the allergic patients and the non-allergic subjects (Fisher's exact test: p=0.033). The 6 patients with L467P have allergic diseases such as bronchial asthma and/or allergic rhinitis. Furthermore, a familial analysis for L467P revealed a linkage between allergic diseases and L467P. Serum IgE levels of the patients with L467P were higher than those of the non-allergic subjects (p=0.001). Our previous studies have been shown that interferon-gamma (IFN-gamma) production by PBMCs in the allergic patients was lower than that in the non-allergic subjects. In this study, although IFN-gamma production in the allergic patients with L467P was equivalent to that in the non-allergic subjects, their serum IgE levels were high and they had allergic diseases. Our results suggest that some allergic patients have IFNGR dysfunction, and that L467P in the IFNGR1 gene is one of candidate susceptibility genes for allergic diseases.

Arbes S.J. Jr et al. *House dust mite allergen in US beds: results from the First National Survey of Lead and Allergens in Housing.* J Allergy Clin Immunol. 2003; 111(2) : 408-14.p **Abstract:** **BACKGROUND:** Although exposure to house dust mite allergen is a major risk factor for allergic sensitization and asthma, nationwide estimates of dust mite allergen levels in US homes have not been reported. **OBJECTIVE:** The purpose of this study was to estimate the prevalence of dust mite allergen in beds of US homes and to identify predictors of dust mite allergen concentration. **METHODS:** Data

were obtained from the first National Survey of Lead and Allergens in Housing, a cross-sectional survey of 831 permanently occupied noninstitutional housing units that permitted resident children. Dust mite allergen concentration (Der f 1 plus Der p 1) was determined from a dust sample collected from a bed. The percentages of homes with concentrations at or greater than detection, 2.0 microg/g bed dust, and 10.0 microg/g bed dust were estimated. Independent predictors of allergen concentration were assessed with multivariable linear regression. RESULTS: The percentages of US homes with dust mite allergen concentrations at or greater than detection, 2.0 microg/g, and 10.0 microg/g were 84.2% (SE, 1.73), 46.2% (SE, 2.0), and 24.2% (SE, 2.1), respectively. Independent predictors of higher levels were older homes, non-West census regions, single-family homes, no resident children, lower household income, heating sources other than forced air, musty or mildew odor, and higher bedroom humidity. CONCLUSION: Most US homes have detectable levels of dust mite allergen in a bed. Levels previously associated with allergic sensitization and asthma are common in US bedrooms. Predictors can be used to identify conditions under which homes are more likely to have increased dust mite allergen levels.

Arias J. et al. [*Exposition and sensitization to Tyrophagus putrescentiae in a allergic population to Dermatophagoides pteronyssinus in Huelva, Spain*]. Allergol Immunopathol (Madr). 2005; 33(4) : 214-20.p **Abstract:** BACKGROUND: In this work we analyzed the allergological importance of Tyrophagus putrescentiae (Tp) in Huelva (SE Spain). We studied the level of exposition and the grade of sensitization to Tp in a group of patients sensitized to Dermatophagoides pteronyssinus (Dpt). The allergenic cross-reactivity between Dpt and Tp was determined by RAST inhibition. METHODS AND RESULTS: We analyzed house dust samples from the dwellings of allergic patients with documented Dpt sensitization. Skin test (ST), conjunctival provocation (CP) and/or specific IgE (RAST) to Tp were performed when Tp was identified in the house dust sample of the patient. Among the 136 dust samples studied, Dpt was the most frequently identified mite species (94.8%) and Tp was found in third position (41.1%) after Glycyphagus domesticus (54.4%). Among the 45 patients studied, 23 (51.1%) presented, at least, two positive tests, 18 (40%) were not sensitized to Tp and 4 (8.8%) showed contradictory results. 26 patients (57.7%) inhabited in urban areas and 19 (42.2%) in rural regions. We determined specific IgE (RAST) to Tp in 25 patients, and the results were positive in 12, with only 7 with values greater than 2 kU/L. No significant correlation were found between IgE-antibody levels to Dpt and Tp. The RAST inhibition studies confirmed the low cross-reactivity between these mites and only in one patient Dpt partially inhibited the IgE-binding to Dpt extract. CONCLUSIONS: Tp was the second more frequent storage mite in the house dust samples from patients allergic to Dpt in Huelva. However, only half of the exposed patients were sensitized to Tp and the majority inhabited in urban areas. No significant correlation were found between IgE-antibody levels to Dpt and Tp. The RAST inhibition studies confirmed the low cross-reactivity between these mites.

Arikan C. et al. *Allergic disease after pediatric liver transplantation with systemic tacrolimus and cyclosporine a therapy*. Transplant Proc. 2003; 35(8) : 3039-41.p **Abstract:** Cyclosporine A (CsA) and tacrolimus (Tac), both calcineurin inhibitors, have been used extensively for immunosuppressive therapy in pediatric liver transplant recipients. They share a similar mechanism of action, the inhibition of cytokine gene transcription primarily interleukin-2 (IL-2) in T lymphocytes. Despite the strong immunosuppressive property, there are several reports of food allergy in pediatric transplant recipients under Tac immunosuppression, but not CsA. In this paper we report on 3 of 50 pediatric liver transplant recipients diagnosed with food allergy and asthma while receiving systemic Tac/CsA immunosuppression and the discuss the role of calcineurin inhibitors in this situation.

Arocha-Sandoval F. et al. [*Oropharyngeal bacteria in asthmatic patients in the city of Maracaibo, Venezuela*]. Invest Clin. 2002; 43(3) : 145-55.p **Abstract:** Bronchial asthma is an intercurrent disease that affects a major portion of the population. Neither its etiopathogenesis nor its complications have been fully established. The purpose of this study was to determine the composition of oropharyngeal bacterial flora in asthmatic patients and compare it with oropharyngeal bacterial flora in a group of healthy patients in order to establish its relationship with the pathogenesis of asthma and its complications. A sample consisting of 116 pharyngeal swabs was analysed from march 1995 to december 1996. 58 of the total amount of pharyngeal swabs corresponded to asthmatic patients (during asthmatic crisis), while the other 58 corresponded to healthy subjects. Common bacteriological culture techniques were carried out in order to obtain the bacteriological diagnosis. The results showed that isolation of transitory flora bacteria in asthmatic patients was 75.8%, which was significantly higher ($p < 0.05$) than in the control group (27.5%). Streptococcus pyogenes was the most frequent isolated bacteria in the group of asthmatic patients (17.2%), while Escherichia coli was the most frequent bacteria in the control group. No significant difference was found regarding sex and the presence of transitory flora bacteria. It was also found that enterobacteria and non fermenting negative gram bacillus increased with age in both groups; a higher incidence was observed in the group of 40-year-old subjects. These finding confirm the existence of a relationship between the asthmatic condition and the percentage of transitory bacterial flora carriers. The explanation to this phenomenon might be the frequent use of antibiotics and the possible contamination of the micro-nebulization equipment used for the treating the asthma crisis. This data must be considered when applying empiric therapy in asthmatic patients complicated with pneumonia. The possibility that certain infectious agents, including bacteria, could play a role in asthma pathogenesis is one of the questions that should be answered in future studies on this topic.

Aronson N. et al. *Management of chronic asthma*. Evid Rep Technol Assess (Summ). 2001; (44) : 1-10.p

Arora P. et al. *Vitamin A status in children with asthma*. Pediatr Allergy Immunol. 2002; 13(3) : 223-6.p **Abstract:** Low vitamin A levels have been found in a number of diseases in children. The aim of this study was to examine the vitamin A status in children with asthma and to correlate the changes with severity of disease. Serum levels of vitamin A, retinol-binding protein (RBP), and albumin were estimated in 35 asthmatic children (24 males) in the age group of 2-12 years (mean 5.89 years) and 29 controls (19 males). Both study and control groups were similar with respect to age, sex, and overall nutritional status. Twenty-four children in the study group (68.6%) had moderate to severe persistent asthma and eight children had mild persistent asthma. Only three patients suffered from mild intermittent asthma. Vitamin A levels in children with asthma (mean +/- SD 22.14 +/- 5.38 microg/dl) were found to be significantly lower than their controls (mean +/- SD 27.54 +/- 4.83 microg/dl) ($p = 0.0001$). Age, age of onset of asthma, and gender had no correlation with serum vitamin A levels. Low serum vitamin A levels (< 20 microg/dl) were observed four times more commonly in the study group (28.6%) than controls (6.9%). Severity of asthma had a negative correlation with serum vitamin A levels ($r = -0.61$, $p = 0.0001$). Children with severe persistent asthma had markedly low serum vitamin A levels (mean +/- SD 13.42 +/- 5.19 microg/dl) as compared with mild intermittent asthma (mean +/- SD 24.61 +/- 2.32 microg/dl). Therapeutic trials are needed to prove whether low vitamin A levels contribute to asthma severity and the clinical utility of vitamin A supplementation in asthmatic children.

Arshad S.H. et al. *Primary prevention of asthma and atopy during childhood by allergen avoidance in infancy: a randomised controlled study*. Thorax. 2003; 58(6) : 489-93.p **Abstract:** BACKGROUND: Recent increases in the prevalence of asthma and atopy emphasise

the need for devising effective methods for primary prevention in children at high risk of atopy. **METHOD:** A birth cohort of genetically at risk infants was recruited in 1990 to a randomised controlled study. Allergen avoidance measures were instituted from birth in the prophylactic group (n=58). Infants were either breast fed with mother on a low allergen diet or given an extensively hydrolysed formula. Exposure to house dust mite was reduced by the use of an acaricide and mattress covers. The control group (n=62) followed standard advice as normally given by the health visitors. At age 8, all 120 children completed a questionnaire and 110 (92%) had all assessments (skin prick test, spirometry, and bronchial challenges). **RESULTS:** In the prophylactic group eight children (13.8%) had current wheeze compared with 17 (27.4%) in the control group (p=0.08). Respective figures were eight (13.8%) and 20 (32.3%) for nocturnal cough (p=0.02) and 11 of 55 (20.0%) and 29 of 62 (46.8%) for atopy (p=0.003). After adjusting for confounding variables, the prophylactic group was found to be at a significantly reduced risk for current wheeze (odds ratio (OR) 0.26 (95% confidence interval (CI) 0.07 to 0.96)), nocturnal cough (OR 0.22 (95% CI 0.06 to 0.83)), asthma as defined by wheeze and bronchial hyperresponsiveness (OR 0.11 (95% CI 0.01 to 1.02)), and atopy (OR 0.21 (95% CI 0.07 to 0.62)). **CONCLUSION:** Strict allergen avoidance in infancy in high risk children reduces the development of allergic sensitisation to house dust mite. Our results suggest that this may prevent some cases of childhood asthma.

Arshad S.H. et al. *Rhinitis in 10-year-old children and early life risk factors for its development.* Acta Paediatr. 2002; 91(12) : 1334-8.p **Abstract:** **AIM:** To study the prevalence, characteristics of and risk factors for childhood rhinitis. **METHODS:** In a whole population birth cohort study (n = 1,456) the prevalence and characteristics of rhinitis among 10-y-old children were examined. At this age 1373 children (94%) completed standardized questionnaires, 1,043 (72%) skin-prick testing, 953 (65%) serum inhalant immunoglobulin E antibody screening and 784 (54%) methacholine bronchial challenges. **RESULTS:** At the age of 10 y the prevalence of hayfever ever was 18.6% and current nasal symptoms (rhinitis) 22.6%. Rhinitis at 10 y was largely seasonal and associated with low morbidity, although 62.7% of cases required pharmacological treatment. Atopy (positive skin test) and other allergic states were associated with rhinitis (p < 0.001). Wheeze or diagnosed asthma was higher with coexistent rhinitis. Among wheezing children physician-diagnosed asthma (p < 0.024) and inhaled corticosteroid use (p < 0.001) were greater with the presence of rhinitis. Significant bronchial hyperresponsiveness (methacholine concentration giving a 20% fall in forced expiratory volume in 1 s <4.0 mg ml(-1)) was greater if rhinitis was present even when the child did not wheeze (p < 0.001). Risk factor analysis for rhinitis identified the independent significance for atopy (p < 0.001) and eczema (p = 0.009) at the age of 4 y plus paternal rhinitis (p < 0.001), maternal rhinitis (p = 0.033) and maternal food allergy (p = 0.016). **CONCLUSION:** Rhinitis is common at the age of 10 y, with strong associations with atopy, wheezing, asthma and bronchial hyperresponsiveness. An inherited predisposition towards atopy appears to predominate over environment in the aetiology of this state.

Asero R. et al. *Clinical features of patients showing Candida hypersensitivity: an observational study.* J Investig Allergol Clin Immunol. 2004; 14(4) : 309-11.p **Abstract:** **BACKGROUND:** The significance of *Candida albicans* as an allergen is still unclear. This study aimed at investigating the clinical features of patients monosensitized to *Candida*. **METHODS:** Thirty-four adult patients monosensitized to the yeast *Candida albicans* selected from a population of >7000 subjects and referred for suspect respiratory allergy were studied. Ninety subjects monosensitized to different airborne allergens served as controls. Both patients and controls underwent a clinical examination at the ENT department to detect possible nasal polyps. **RESULTS:** Male and female patients were equally distributed (17/17). The mean age of the patients was 58.4

years (range 23-75 years; median 59 years) vs 29.9 years (range 9-62 years) in controls (p < 0.001). At baseline examination, 15 (44%) patients vs 5/90 (6%) controls were diagnosed as having nasal polyposis (p < 0.001). Polyposis was bilateral in 13/15 (87%) patients; 3 had "massive" polyps, and 4 had a clinical history of prior surgical intervention to remove nasal polyps. Eight patients (24%) had asthma, previously diagnosed as intrinsic in six cases. No patient had a history of aspirin-induced asthma (i.e. ASA triad). After one year 1/11 (9%) patients without polyps at the baseline examination had developed bilateral nasal polyposis. **CONCLUSION:** *Candida*-hypersensitivity is uncommon, occurs in older ages, and is strongly associated with nasal polyposis.

Assefa D. et al. *Effect of deep inspiration on airway caliber in children with asthma.* Pediatr Pulmonol. 2004; 38(5) : 406-12.p **Abstract:** The objective of this study was to assess the effect of deep inspiration (DI) on airway caliber in school-age children with asthma. Thirty children with asthma (10 from each group of mild, moderate, and severe persistent asthma as defined by the National Asthma Education and Prevention Program guidelines of the National Heart, Lung, and Blood Institute) were enrolled, and their results were compared to those obtained in 7 healthy children. Subjects performed a partial expiratory flow volume curve (P) initiated from approximately 70% of vital capacity (VC) followed by a maximal expiratory flow volume (M) maneuver begun from total lung capacity (TLC). The M/P ratio at 30% of the VC (M/P30) was calculated. Specific airway conductance (sGaw) was measured before and immediately after DI, using standard techniques. Differences in M/P30 and sGaw ratios between asthma and control groups were compared with Student's unpaired t-tests. One-way ANOVA was used to compare the effect of DI on M/P30 and sGaw ratios among the various asthma severity groups. The M/P30 ratio (mean +/- 1 SD) was significantly lower in children with moderate and severe persistent asthma (0.73 +/- 0.21 and 0.72 +/- 0.1, respectively) than in healthy controls (1.69 +/- 0.62) (P < 0.05). In mild persistent asthmatics, there was limited bronchodilation (M/P30 = 1.1 +/- 0.35, P = 0.052). There was a significant inverse correlation between M/P30 ratio and severity of asthma (r = -0.684, P < 0.01). The mean sGaw ratio was decreased in asthmatic subjects compared to healthy controls (0.98 +/- 0.17 vs. 1.13 +/- 0.16, P = 0.062). In conclusion, in school-age children, the effects of DI on airway caliber are similar in direction to those observed in adults, i.e., bronchodilation in healthy and mild asthmatics, and bronchoconstriction (BC) in moderate to severe asthmatics. This finding suggests that forces that determine airway caliber in school-age children are similar to those forces in adults.

Auinger P. et al. *Trends in otitis media among children in the United States.* Pediatrics. 2003; 112(3 Pt 1) : 514-20.p **Abstract:** **BACKGROUND:** The prevalence of repeated otitis media (OM) increased during the 1980s, but it is unknown if the increase has continued. **OBJECTIVES:** To determine trends in the prevalence of OM, early-onset OM, and repeated OM among US children from 1988 to 1994 and to identify factors that may explain any observed changes. **METHODS:** The Third National Health and Nutrition Examination Survey was administered in 2 phases: phase I (1988-1991) and phase II (1991-1994), each comprising a national probability sample. OM (ever having had OM), early-onset OM (first episode at <12 months of age), and repeated OM (>or=3 episodes) were assessed for 8261 children <6 years of age. **RESULTS:** After controlling for risk factors for OM, the prevalence of OM from phase I to phase II increased from 66.7% to 69.7% (odds ratio [OR] = 1.1; 95% confidence interval [CI] = .99, 1.1), early-onset OM increased from 41.1% to 45.8% (OR = 1.1; 95% CI = 1.03, 1.2), and repeated OM increased from 34.8% to 41.1% (OR = 1.2; 95% CI = 1.1, 1.4). This observed increase corresponds to 561,000 and 720,000 more children having early-onset OM and repeated OM, respectively. Child care use, early breastfeeding termination, asthma, and access to health care did not significantly increase from phase I to phase II.

The prevalence of early-onset OM and repeated OM was higher for affluent children, but the greatest increase in prevalence was among impoverished children. There was an increase in allergic conditions from phase I to phase II for poor children (22.6% to 30.2%). CONCLUSIONS: The prevalence of early-onset OM and repeated OM continued to increase among preschool children in the United States. Further research to investigate this increasing prevalence should explore changes in management practice and an increase in prevalence of allergic conditions among poor children.

Ault A. *Report blames global warming for rising asthma.* Lancet. 2004; 363(9420): 1532.p

Austin J.B. et al. *Childhood asthma in the Highlands of Scotland-morbidity and school absence.* Scott Med J. 2004; 49(1): 18-21.p
Abstract: BACKGROUND: The prevalence of childhood asthma in Scotland is one of the highest in the world. The morbidity secondary to allergic diseases is significant in terms of costs to the nation and effects on the family including the child. AIMS: The aims of this study were to describe the prevalence of asthma, eczema and hay fever in the Highlands of Scotland and in the Shetland Isles and to examine factors in relation to quality of life and social deprivation. METHOD: A total population survey of 12 year old children using a parent completed questionnaire. RESULTS: 86.3% (2658/3080) returned questionnaires. Of the 2549 questionnaires analysed, 476 (18.7%) reported asthma ever, 362 (14.2%) wheeze in last 12 months, 508 (19.9%) reported hay fever ever and 555 (21.8%) reported eczema ever. Of the children reporting asthma or wheeze, 35.4% (229/647) had missed school because of asthma or wheeze, 38.0% (246/647) had missed physical education. 62.5% (354/566) of subjects with wheeze ever reported sleep disturbance. Deprivation measured by DEPCAT scores was associated with maternal smoking and bronchitis in the child but not with allergic diseases. CONCLUSION: Compared with previous studies, the prevalence of asthma was unchanged but eczema has increased in Highland adolescents. Allergic disease has a significant impact on school attendance and physical activity. Deprivation was associated with maternal smoking and bronchitis in the child but not with allergic diseases. The impact of allergic diseases in rural areas may be different from urban areas.

Avila-Castanon L. et al. *Formoterol vs. albuterol administered via Turbuhaler system in the emergency treatment of acute asthma in children.* Allergol Immunopathol (Madr). 2004; 32(1): 18-20.p
Abstract: BACKGROUND: Formoterol is a new beta 2 agonist with a duration of 8-12 hours. Albuterol is a beta 2-agonist with rapid onset of action and a duration of approximately 6 hours. OBJECTIVE: The aim of the present study was to compare the onset of action between formoterol and albuterol, both administered through a Turbuhaler. MATERIAL AND METHOD: In a double-blind, parallel-group study design 36 patients were randomly allocated to receive either formoterol 12 microg or salbutamol 200 microg. The two drugs were administered through a Turbuhaler system. Response (% forced expiratory volume in one second [FEV1]) was evaluated 3, 30 and 60 minutes after drug administration. RESULTS: The %FEV1 values at 3, 30 and 60 minutes were similar in both groups: 82.15.0 for formoterol and 82.14.4 for albuterol at 60 minutes ($p > 0.05$). CONCLUSIONS: Formoterol 12 microg has a similar onset of action and potency to albuterol 200 microg when administered via a Turbuhaler in children with a mild acute asthma crisis.

Avila Castanon L. et al. *[The response to PPD and its relation to allergic diseases in children vaccinated at birth with BCG].* Rev Alerg Mex. 2003; 50(2): 48-53.p
Abstract: BACKGROUND: The increase of the atopic disorders can be partially explained by two factors, the infectious disease in developed and developing countries, and the

changes in immunization programs, infections such as measles, whooping cough or tuberculosis can modify the immune response. Recent studies have demonstrated that an inverse relation could exist between the response to late cutaneous hypersensitivity to Mycobacterium tuberculosis and atopic condition. Also, a strong positive response has been associated with low levels of IgE and Th1 cytokines. However some authors have not found positivity between low prevalence in allergic diseases and PPD. OBJECTIVE: To determine the reaction to PPD in children vaccinated with BCG at birth and its disorders. MATERIAL AND METHOD: The study sample included male and female children from 2 to 7 years old, vaccinated with BCG at birth, this fact was corroborated with the post vaccination scar. They had all been diagnosed with allergic disease with clinical compatible data, positive Prick test, elevated serum IgE, and absence of any associated immune deficiency. RESULTS: A total of 50 patients, with a mean age of 4.7 years (2.0 to 7.7 years) were studied. 72% (36) were males and 28% (14) females. Twenty-two percent had diagnosis of asthma, 8% allergic rhinitis, and 62% both diagnosis. The average diameter of tuberculin induration was of 5 mm; 5 patients (10%) had positive reaction ($+10$ mm); 23 patients (46%) were between 5-9 mm; 8 patients (16%) between 1-4 mm, and 14 of the patients (28%) without reactivity. CONCLUSION: We demonstrated that the vaccination with BCG do not protect against the development of allergy, and the negative tuberculin response may mean a reduced cell response. So, it is necessary to assess the cell immunity and revaccination with BCG, with determination of immunological markers, before and after, such as IL 4, IL 2, INF and allergy symptoms.

Avital A. et al. *Exhaled nitric oxide and asthma in young children.* Pediatr Pulmonol. 2001; 32(4): 308-13.p
Abstract: Exhaled nitric oxide (eNO) has been used to diagnose asthma in adults and children using either the slow vital capacity method (SVCm) or, in younger children, the tidal breathing method (TBm). Adenosine 5'-monophosphate (AMP) challenge also has been found to be a sensitive and specific test for the diagnosis of asthma. In the present study, we used the AMP provocation concentration that caused wheezing (PCW) to confirm the diagnosis of asthma ($PCW < \text{or} = 200$ mg/mL). We studied 36 children (2-7 years) with mild intermittent asthma, 13 children (3-7 years) with moderate persistent asthma treated with inhaled steroids, 20 nonasthmatic children (2-7 years) with chronic cough and recurrent pneumonia, and 15 healthy children (4-6 years). Expired gas was collected in collection bags by the TBm, and eNO was measured. We evaluated the efficacy of eNO values in diagnosing asthma. The mean eNO level of the mild intermittent asthmatic children (5.6 ± 0.4 ppb) not receiving inhaled corticosteroids was significantly higher ($ANOVA P < 0.0001$) than that of the moderate persistent asthmatics who were treated with inhaled steroids, the nonasthmatic children with chronic cough, and the group of healthy children (3.7 ± 0.6 ppb, $P < 0.05$; 3.2 ± 0.3 ppb, $P < 0.001$; 2.2 ± 0.2 ppb, $P < 0.001$, respectively). The points of intersection for sensitivity and specificity curves of eNO to differentiate mild intermittent asthmatics from nonasthmatic children with chronic cough and from healthy children were 77% and 88% for eNO values of 3.8 ppb and 2.9 ppb, respectively. We conclude that eNO collected by the TBm can differentiate steroid-naive young children with intermittent asthma from healthy children, from nonasthmatic children with chronic cough, and from asthmatic children treated with inhaled steroids.

Azofra J. et al. *Limpet anaphylaxis: cross-reactivity between limpet and house-dust mite Dermatophagoides pteronyssinus.* Allergy. 2003; 58(2): 146-9.p
Abstract: BACKGROUND: Limpet is a mollusc that is frequently found along the shores of warm seas. Few allergic reactions to limpet have been described, and cross-reactivity with house-dust mites has not been established. METHODS: We report five patients with anaphylactic reactions due to limpet ingestion. A limpet extract was prepared and skin prick tests (SPT), radioallergosorbent assays (RAST), sodium dodecylsulfate

polyacrylamide gel electrophoresis (SDS-PAGE), and IgE-immunoblotting were performed. In order to evaluate cross-reactivity, an immunoblotting inhibition assay with *Dermatophagoides pteronyssinus* was also done. RESULTS: All patients were asthmatics sensitized to house-dust mites. In each case, severe bronchospasm was evidenced, and three required mechanical ventilation. Positive SPT with limpet extract was found in the four patients tested. RAST showed specific IgE on each patient's sera. Immunoblotting showed several allergenic fractions with a wide molecular weight range (15-250 kDa). *D. pteronyssinus* inhibited IgE-binding molecules above 50 kDa in the limpet extract, particularly one molecule of 75 kDa. CONCLUSIONS: We describe five patients with IgE-mediated limpet allergy. Severe bronchospasm was the most important symptom. Cross-reactivity with *D. pteronyssinus* was demonstrated.

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Ba M. et al. [Child asthma in Senegal: epidemiological and clinical features in hospitals]. *Dakar Med.* 2002; 47(2) : 128-33.p

Abstract: This report is a retrospective study carried out from records of diseased of asthma, followed up in a paediatric national center of reference during the period from 1st of November 1987 to 31 st of august 1993. The goal was to describe the epidemiological and clinical factors linked to that affection in order to better contribute to improve its management. For all the diseaseds of this report we notice and analysed the socio economical data, the promoting factors the occurring mode of the disease, the main clinical manifestations of the affection and their consequences. The morbid association and the data of the paraclinical exploration particularly the functional breathing exploration. Thus we noticed that the consultation in a specialized center occurs relatively late because of bad orientation of the diseaseds. In effect the mean age of diseaseds at the first consultation is 7.5 years while the disease begins in average at 3.5 years. By elsewhere we notice that 15% of these diseaseds live in an aggressive mesologic medium. With an atopy in 78.4% of the cases, loaded personal case history in 96.6% of the cases and that the releasing factors are not known for most of them (81.9%). Asthma in our diseaseds is not very frequent (77%) in general with a moderate intensity of crises (69%). However disturbances of physical activity are noted among 23% of the sample which corresponds nearly to the number of subjects with severe respiratory obstruction (25%). We quoted that there is a relation ship between the frequency of the cases the intensity of the crisis and the disturbances of physical activities of the diseaseds ($x^2:25.9$, $df = 2$, $p= 0,000002$). Tacking count of all these factors may serve to set up a asthma prevention and treatment project in Senegal based on populations education and care providers training.

Baars R.M. et al. *The European DISABKIDS project: development of seven condition-specific modules to measure health related quality of life in children and adolescents.* *Health Qual Life Outcomes.* 2005; 3 : 70.p **Abstract:** BACKGROUND: The European DISABKIDS project aims to enhance the Health Related Quality of Life (HRQoL) of children and adolescents with chronic medical conditions and their families. We describe the development of the seven cross-nationally tested condition-specific modules of the European DISABKIDS HRQoL instrument in a population of children and adolescents. The condition-specific modules are intended for use in conjunction with the DISABKIDS chronic generic module. METHODS: Focus groups were used to construct the pilot version of the DISABKIDS condition-specific HRQoL modules for asthma, juvenile idiopathic arthritis, atopic dermatitis, cerebral palsy, cystic fibrosis, diabetes and epilepsy. Analyses were conducted on pilot test data in order to construct field test versions of the modules. A series of factor analyses were run, first, to determine potential structures for each

condition-specific module, and, secondly, to select a reduced number of items from the pilot test to be included in the field test. Post-field test analyses were conducted to retest the domain structure for the final DISABKIDS condition-specific modules. RESULTS: The DISABKIDS condition-specific modules were tested in a pilot study of 360 respondents, and subsequently in a field test of 1152 respondents in 7 European countries. The final condition-specific modules consist of an 'Impact' domain and an additional domain (e.g. worry, stigma, treatment) with between 10 to 12 items in total. The Cronbach's alpha of the final domains was found to vary from 0.71 to 0.90. CONCLUSION: The condition-specific modules of the DISABKIDS instrument were developed through a step-by-step process including cognitive interview, clinical expertise, factor analysis, correlations and internal consistency. A cross-national pilot and field test were necessary to collect these data. In general, the internal consistency of the domains was satisfactory to high. In future, the DISABKIDS instrument may serve as a useful tool with which to assess HRQoL in children and adolescents with a chronic condition. The condition-specific modules can be used in conjunction with the DISABKIDS chronic generic module.

Bacharier L.B. et al. *Long-term effect of budesonide on hypothalamic-pituitary-adrenal axis function in children with mild to moderate asthma.* *Pediatrics.* 2004; 113(6) : 1693-9.p **Abstract:**

OBJECTIVE: To determine the safety of long-term (36 months) administration of an inhaled corticosteroid (budesonide) on hypothalamic-pituitary-adrenal (HPA) axis function in children with mild to moderate asthma. **METHODS:** This was an ancillary study of the Childhood Asthma Management Program (CAMP). Sixty-three children who had mild to moderate asthma and were enrolled in CAMP underwent evaluation of HPA axis function before and 12 and 36 months after receiving continuous therapy with either an inhaled anti-inflammatory agent (budesonide 400 microg/day or nedocromil 16 mg/day) or placebo. HPA axis function was assessed by serum cortisol levels 30 and 60 minutes after 0.25 mg of adrenocorticotrophic hormone (ACTH) and 24-hour urinary free cortisol excretion. **RESULTS:** There were no differences in serum cortisol levels after ACTH stimulation between treatment groups, regardless of time after ACTH administration or months of follow-up. Urinary cortisol excretion per body surface area was similar in both treatment groups at 36 months, after adjusting for age at randomization, race, gender, and clinic. Cumulative inhaled corticosteroid exposure did not influence serum cortisol response to ACTH or urinary free cortisol excretion at 36 months. **CONCLUSIONS:** We found no effects of chronic budesonide treatment at a dose of 400 micro g/day on HPA axis function in children with mild to moderate asthma and demonstrated the absence of a cumulative effect on HPA axis function over a 3-year period.

Bager P. et al. *Smallpox vaccination and risk of allergy and asthma.* *J Allergy Clin Immunol.* 2003; 111(6) : 1227-31.p **Abstract:**

BACKGROUND: It has been proposed that childhood vaccinations may influence the development of allergy. Atopy and allergic diseases have increased after routine smallpox vaccination was stopped in the 1970s. **OBJECTIVE:** We examined whether administration of smallpox vaccination during childhood was associated with a decreased risk of atopy, allergic rhinitis, and asthma. **METHODS:** The occurrence of atopy, allergic rhinitis, and asthma was studied in nearly 2000 women participating in a national birth cohort study. Detailed information on smallpox vaccination was available from school health records. Atopic status was assessed serologically by a specific response to 11 common inhalant allergens by using serum samples obtained from the women during the period 1997 to 2001. Information on allergic rhinitis and asthma was available from telephone interviews. **RESULTS:** We found no association between having been vaccinated against smallpox in childhood and risk of atopy or allergic rhinitis. Smallpox vaccination was associated with a slightly decreased risk of asthma. There was no association between age at smallpox vaccination and risk of atopy,

allergic rhinitis, or asthma. Adjusting for birth cohort, sibship size, age of the woman's mother at birth, and social class in childhood did not change these results. **CONCLUSION:** Our findings do not suggest that childhood vaccination against smallpox, even if given early in life, influences the development of atopy or allergic rhinitis. The association with asthma should be interpreted with caution and needs further study.

Bahceciler N.N. et al. *Inhaled corticosteroids and bone density of children with asthma.* J Asthma. 2002; 39(2) : 151-7.p **Abstract:** In this cross-sectional study, we aimed to compare anteroposterior (AP) spine and total body bone mineral density (BMD) measurements of children with asthma treated with long-term inhaled budesonide (n = 52, mean age 6.4+/-2.2yr, M/F = 22/30) (Group I) with those of asthmatic children who had never received treatment with inhaled corticosteroids (Group II) (n = 22, mean age 6.8+/-2.2, M/F = 10/12). Boys and girls were comparable for age, weight, height, cumulative corticosteroid (CS) dosage, duration of disease and inhaled corticosteroid (ICS) treatment within each group. The mean total accumulated dosage of budesonide for children in Group I was 154.0+/-135.3mg (mean daily dosage = 419+/-154 microg) and the mean treatment duration was 13.0+/-9.8 months. The two groups were comparable with respect to age, gender, weight, height, Tanner's stage and duration of disease. There was no significant difference between subjects in the two groups for total (p = 0.214) and (AP) spine BMD results (p = 0.661), respectively. Our results provide additional support for the safety of ICS therapy on bone density of asthmatic children.

Bahna S.L. *Is it time to reduce our phobia of inhaled corticosteroids?* Pediatrics. 2004; 113(6) : 1813-4.p

Bakhireva L.N. et al. *Asthma medication use in pregnancy and fetal growth.* J Allergy Clin Immunol. 2005; 116(3) : 503-9.p **Abstract:** **BACKGROUND:** Given the high prevalence of asthma in pregnancy, it is important to understand the relationship between asthma medications and fetal growth in the context of appropriate treatment. **OBJECTIVE:** This study examines the effect of inhaled corticosteroids, systemic corticosteroids, and beta(2)-agonists on fetal growth in 654 infants born to women with asthma compared with 303 infants born to controls without asthma. **METHODS:** Subjects for this prospective study were enrolled throughout North America between 1998 and 2003 and followed up by the Organization of Teratology Information Services. Incidence of small for gestational age (SGA) infants and mean birth size measures were compared among groups. **RESULTS:** Mean birth weight of full-term infants born to mothers who used systemic corticosteroids (3373 g) was lower than in the beta(2)-agonist group (3552 g) and controls without asthma (3540 g; P < .05) after adjustment for other risk factors. However, no differences in the incidence of SGA for weight were observed among groups. Adjusted mean birth length was slightly shorter in the systemic steroid group compared with controls (P=.02). Incidence of SGA for length and head circumference and mean head circumference did not vary among groups (P>.05). **CONCLUSION:** The treatment of asthma with systemic corticosteroids resulted in a deficit of about 200 g in birth weight compared with controls and exclusive beta(2)-agonist users and no increased incidence of SGA. These results suggest that asthma management with beta(2)-agonists and/or inhaled corticosteroids during pregnancy does not impair fetal growth, whereas systemic corticosteroids have a minimal effect which should be weighed against the necessity to control severe asthma.

Balatsinou L. et al. *Asthma worsened by benzoate contained in some antiasthmatic drugs.* Int J Immunopathol Pharmacol. 2004; 17(2) : 225-6.p **Abstract:** Here, we report our experience on benzoate hypersensitivity. Drug and food additives are known to induce

pseudo-allergic reactions such as urticaria, eczema, asthma and rhinitis. These reactions are often under-diagnosed, above all in allergic patients treated with additive containing drugs. On the contrary, attention to the additives present in some drug formulations and foods may often permit more correct diagnosis.

Balatsouras D.G. et al. *Improvement of otitis media with effusion after treatment of asthma with leukotriene antagonists in children with co-existing disease.* Drugs Exp Clin Res. 2005; 31 Suppl : 7-10.p **Abstract:** Otitis media with effusion (OME) is a common pediatric disease and there is great controversy concerning its management. Mechanical, medical and surgical treatments have not proven adequate in resolving the disease and serve mainly to manage complications. Leukotriene inhibitors are new drugs that have been approved recently for the treatment of asthma in children. The aim of this study was to evaluate the impact of leukotriene inhibitor therapy for asthma on the clinical course of OME in children with co-existing disease. Fifty children with bilateral OME and asthma, divided equally into two groups, were studied. The children in the first group were treated with budesonide and terbutaline inhalers together with the leukotriene inhibitor montelukast, whereas the children in the second group were treated with the inhalers alone. Duration of treatment was 30 days. Pneumatic otoscopy, tympanometry and pure-tone audiometry were performed at the beginning and at the end of treatment. Fifteen (60%) of the children receiving inhalers and montelukast and nine (36%) of those receiving only inhalers were found free of OME after 30 days of therapy. Thus, it may be concluded that a statistically significant beneficial effect on the clinical course of OME resulted from the addition of montelukast to the treatment of children with co-existing asthma and OME. Given that no medication has been shown to be effective in OME therapy, further investigation of the possible effects of leukotriene inhibitors is warranted.

Bambule G. *[Endoscopic surgery of chronic sinusitis].* Rev Med Suisse Romande. 2001; 121(10) : 735-41.p **Abstract:** Between 1984 and 2000 the author has performed endoscopic sinus surgery (ESS) in 1072 patients with chronic sinusitis resistant to medical therapy. In 201 patient (19%) the operation was limited to the maxillary sinus and in 871 patients (81%) multiple cavities were involved. Ethmoidectomy was performed for 749 patients (70%) of which polyposis was found in 315 (29%), bilateral in (87%). History of previous sinus surgery was found in 399 patients (37%). This retrospective study with a long-term follow-up (average 8.6 years) analyzes the objective and subjective result in 212 patients after ESS for pansinus polyposis. Subjective success rates were noted in 92% of patients after 1 year; in 78% after 5 years and in 82% 8.6 years after ESS. The best results were obtained in nasal breathing which was significantly improved in 91% of patients, the poorest results were noted in olfaction which was improved in 60% of cases. Objectively, the endoscopic findings were normal in 86% of cases after 1 year; in 81.6% after 5 years and in 79.2% 8.6 years after ESS. 26 patients (12.2%) underwent revision surgery. In 100 patients (47%) the polyposis was massive, associated with allergy in 82 cases (39%), asthma in 67 patients (31%), Aspirin sensitivity in 24 patients (11.1%) and Samter's syndrome in 19 patients (9%). In 1072 patients major complications occurred in 4 cases (0.4%). On case of delayed hemorrhage required cautery of the sphenopalatine artery and transfusions. Three other cases of CSF leak were repaired during ESS without sequel.

Banasiak N.C. et al. *Leukotrienes: their role in the treatment of asthma and seasonal allergic rhinitis.* Pediatr Nurs. 2005; 31(1) : 35-8.p

Bandi V. et al. *Deposition pattern of heliox-driven bronchodilator aerosol in the airways of stable asthmatics.* J Asthma. 2005; 42(7) : 583-6.p **Abstract:** To compare the deposition patterns of heliox-driven

and air-driven radiolabeled bronchodilator aerosol, a prospective randomized study was undertaken at the Ben Taub Hospital in Houston, Texas. The working hypothesis was that nebulization with heliox would improve the peripheral deposition of a bronchodilator aerosol. Twelve mild-moderate known asthmatics were recruited for the study. They were asked to withhold medications for 8-24 hours prior to reporting for the study. Each subject was randomized to receive either heliox or oxygen for delivery of albuterol labeled with Tc-99m DTPA. Prior to the nebulization, baseline spirometry was performed. Following nebulization, the subjects were scanned for 1,000,000 counts on the ADAC Genesis Scanner. A postbronchodilator spirometry was then performed. Subjects returned about a week later, this time to have the same process repeated with the other gas. The normalized pixel counts were obtained, and the frequency distribution histograms were constructed for each of the deposition images. Skew and kurtosis were calculated. A lower skew and kurtosis value suggests a more peripheral distribution of the bronchodilator, whereas a higher pixel count corresponds with an increased area and uniformity of deposition. There were no statistically significant differences in baseline PFTs on the 2 days of the study. The pixel count was statistically higher after the heliox-driven nebulization than the air-driven nebulization. The skew and kurtosis values were lower after the heliox-driven nebulization than after the air-driven nebulization of radiolabeled aerosol. All patients had a good bronchodilator response with either driving gas. However, the degree of improvement was more with heliox-driven nebulization than with air-driven nebulization. We conclude that aerosol delivery with heliox results in more uniform and peripheral deposition. Thus, this mode of delivery can be used when uniform, peripheral deposition is desired as with drug delivery during an exacerbation or with aerosolized gene therapy.

Banuelos Arias Adel C. et al. [Skin tests, serum specific IgE and total IgE in the diagnosis of patients with perennial allergic rhinitis]. *Rev Alerg Mex.* 2003; 50(4) : 147-53.p Abstract: BACKGROUND: Skin tests are the most used diagnostic method of allergic rhinitis, which, in addition to identify specific allergen, can determine the relative sensitivity of one patient to the allergen. OBJECTIVE: To assess the association between skin test reactivity and total and specific serum IgE levels on the diagnosis of patients with perennial allergic rhinitis. MATERIAL AND METHODS: We measured the response to skin test reactivity and total and specific serum IgE levels in 69 patients with perennial allergic rhinitis. RESULTS: The skin test reactivity showed responses to: Dermatophagoides pt in 62 patients (90%), house dust in 57 (83%), cat in 41 (59%), dog in 23 (33%), and Lolium p in 16 (23%). The mean level of total IgE was of 378 UI (19 to 4,036) and that of specific IgE was of 39.2 UI (0.2 to 98.6). Total IgE > 200 UI was observed in fifty two patients (75%), which was significantly lesser than the frequency of specific IgE > 0.35 UI (at least for an allergen), which was 94% ($p < 0.05$, Z). At least two tests of skin reactivity were positive for 90% of the patients. This frequency was similar to the 95% for the specific IgE but different to the 75% for the total IgE ($p < 0.05$, X2). The correlation between the results of the skin test reactivity and the specific seric IgE showed Spearman r from 0.23 to 0.35 ($p < 0.05$). The correlation between the total IgE and the specific IgE showed a Spearman r of 0.08 ($p < 0.05$) and between the total IgE and the skin test reactivity an r of 0.15 ($p < 0.05$). CONCLUSION: In the diagnosis of perennial allergic rhinitis, the results of the skin test reactivity and the specific serum IgE are correlated but these two results are non consistent with the results of the total serum IgE.

Baraldi E. et al. Low exhaled nitric oxide in school-age children with bronchopulmonary dysplasia and airflow limitation. *Am J Respir Crit Care Med.* 2005; 171(1) : 68-72.p Abstract: Bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, may be associated with long-term airflow limitation. Survivors of BPD may develop asthma-like symptoms in childhood, with a variable response to beta(2)-agonists. However, the pathologic

pathways underlying these respiratory manifestations are still unknown. The aim of this study was to measure exhaled nitric oxide (FE(NO)) and lung function in a group of 31 school-age survivors of BPD. They showed variable degrees of airflow obstruction (mean FEV(1) 77.8 +/- 2.3% predicted) unresponsive to beta(2)-agonists in 72% of the subjects. Their FE(NO) values (geometric mean [95% confidence interval]: 7.7 [+/- 1.1] ppb) were significantly lower than in a group of healthy matched control subjects born at term (10.7 [+/- 1.1] ppb, $p < 0.05$) and a group of preterm children without BPD (9.9 [+/- 1.1] ppb, $p < 0.05$). The children with BPD were also compared with a group of 31 patients with asthma with a comparable airflow limitation (FEV(1) 80.2 +/- 2.1% predicted) and showed FE(NO) values four times lower than in those with asthma (24.9 [+/- 1.2] ppb, $p < 0.001$). In conclusion, unlike children with asthma, school-age survivors of BPD have airflow limitation associated with low FE(NO) values and lack of reversibility to beta(2)-agonists, probably as a result of mechanisms related to early life structural changes in the airways.

Baraldi E. et al. Cysteinyl leukotrienes and 8-isoprostane in exhaled breath condensate of children with asthma exacerbations. *Thorax.* 2003; 58(6) : 505-9.p Abstract: BACKGROUND: Cysteinyl leukotrienes (Cys-LTs) and isoprostanes are inflammatory metabolites derived from arachidonic acid whose levels are increased in the airways of asthmatic patients. Isoprostanes are relatively stable and specific for lipid peroxidation, which makes them potentially reliable biomarkers for oxidative stress. A study was undertaken to evaluate the effect of a course of oral steroids on Cys-LT and 8-isoprostane levels in exhaled breath condensate of children with an asthma exacerbation. METHODS: Exhaled breath condensate was collected and fractional exhaled nitric oxide (FE(NO)) and spirometric parameters were measured before and after a 5 day course of oral prednisone (1 mg/kg/day) in 15 asthmatic children with an asthma exacerbation. Cys-LT and 8-isoprostane concentrations were measured using an enzyme immunoassay. FE(NO) was measured using a chemiluminescence analyser. Exhaled breath condensate was also collected from 10 healthy children. RESULTS: Before prednisone treatment both Cys-LT and 8-isoprostane concentrations were higher in asthmatic subjects (Cys-LTs, 12.7 pg/ml (IQR 5.4-15.6); 8-isoprostane, 12.0 pg/ml (9.4-29.5)) than in healthy children (Cys-LTs, 4.3 pg/ml (2.0-5.7), $p=0.002$; 8-isoprostane, 2.6 pg/ml (2.1-3.0), $p<0.001$). After prednisone treatment there was a significant decrease in both Cys-LT (5.2 pg/ml (3.9-8.8), $p=0.005$) and 8-isoprostane (8.4 pg/ml (5.4-11.6), $p=0.04$) concentrations, but 8-isoprostane levels remained higher than in controls ($p<0.001$). FE(NO) levels, which fell significantly after prednisone treatment ($p<0.001$), did not correlate significantly with either Cys-LT or 8-isoprostane concentrations. CONCLUSION: After a 5 day course of oral prednisone there is a reduction in Cys-LT and 8-isoprostane levels in EBC of children with an asthma exacerbation, although 8-isoprostane levels remain higher than in controls. This finding suggests that corticosteroids may not be fully effective in reducing oxidative stress in children with an exacerbation of asthma.

Baraldi E. et al. Safety and success of exhaled breath condensate collection in asthma. *Arch Dis Child.* 2003; 88(4) : 358-60.p Abstract: BACKGROUND: Exhaled breath condensate (EBC) is a rapidly expanding area of research to study airway inflammation through the detection of volatile and non-volatile substances in the airways. AIMS: To determine the safety and feasibility of EBC procedure in a group of children with asthma of varying severity. METHODS: In a cross sectional study of children aged 4-17 years, 18 healthy and 91 asthmatic children (69 in stable condition and 22 with asthma exacerbation) underwent the EBC procedure. Outcomes assessed included completion of the procedure, decrease in FEV1, change in fractional exhaled nitric oxide (FE(NO)), and adverse effects. No pretreatment with beta2 agonists was given. All children were able to successfully complete the EBC procedure. RESULTS:

Median fall in FEV1 after the procedure was -1% (IQR -3.5, 1.8) in asthmatics and was comparable to that observed in healthy children. In only one asthmatic child did the drop in FEV1 exceed 12%. No significant changes in FE(NO) were observed after EBC. CONCLUSION: This study suggests that EBC is a simple and well tolerated method for evaluating biological samples from the lower airway. The procedure was safe in children with asthma exacerbation, and the success rate was 100% in children aged 4 years and above.

Barbato A. et al. *Asthma prevalence and drug prescription in asthmatic children.* Allerg Immunol (Paris). 2003; 35(2) : 47-51.p **Abstract:** A cross-sectional study was conducted on among 28,856 children aged from birth to 14 years to determine the prevalence of asthma and assess its treatment in a sample of asthmatic children. Children diagnosed with asthma were identified by a sensitive algorithm applied to the information stored in the computerized medical records between 1997 and 1998. Pediatricians then reviewed and validated the diagnosis. Specific information was obtained, after age stratification under 5 yrs and over 6 yrs, from the medical records and by interview regarding their personal details and treatment of asthmatic patients. In all, 1,263 cases of asthma were identified (64% males) with a prevalence of 6.3% among males and 4% among females in under 5 year-olds, and 3.9% for males and 2.1% for females in over 6 year-olds. The prevalence of asthma diagnosed directly by the pediatrician was consequently higher among under 5 year-olds, in both genders, than among the older children. Contrary to the international guidelines, pediatricians prescribed more oral corticosteroids and nebulized short-acting beta-2 agonists for children under 5 yrs olds than for over 6 year-olds (13.3% Vs 4.8% and 25% Vs 10.9%, respectively, $p < 0.001$). For the $> = 6$ year-olds, the most commonly prescribed treatments were oral antihistamines (13.9% Vs 12.6%), inhaled corticosteroids via metered-dose inhaler (30.8% Vs 28.7%) and sodium cromoglycate (12.1% Vs 4.8%, $p < 0.001$).

Barben J. et al. *Repeatability of bronchial responsiveness to mannitol dry powder in children with asthma.* Pediatr Pulmonol. 2003; 36(6) : 490-4.p **Abstract:** Our objective was to determine the repeatability of bronchial responsiveness to mannitol dry powder (MDP) as an objective marker of asthma in children. MDP challenge was performed in children with stable asthma at the same time of the day on two separate occasions within a week. The test was terminated after a 15% fall of forced expiratory volume in 1 sec (FEV1) and the provocative dose to produce a 15% fall in FEV1 (PD15) were calculated. Seventeen children (aged 9-16 years) on inhaled corticosteroids (200-1,500 mcg) were studied. Mean baseline FEV1 before the challenges were 95% (81-119) and 96% (74-121), respectively, with a standard deviation of differences of 5.2%. PD(15) values ranged from 7-387 mg, with a geometric mean of 38 mg for the first and 49 mg for the second test. Of the 17, all but two pairs of tests achieved a PD15 within one dose of capsules. Four children had a negative challenge on two occasions. A high relative reliability was reflected by a concordance coefficient of 0.86. In conclusion, MDP is a convenient challenge which is easy to administer and is well-tolerated by children. It is a highly reproducible test of airway responsiveness in children with moderate to severe persistent asthma on inhaled corticosteroids within 7 days under laboratory conditions.

Barben J.U. et al. *Effect of detergent-coated versus non-coated spacers on bronchodilator response in children with asthma.* J Paediatr Child Health. 2003; 39(4) : 270-3.p **Abstract:** OBJECTIVE: Previous studies have demonstrated that coating spacers with ionic detergents minimizes the static charge and thereby improves in vivo drug deposition. The present study aims to examine the effect of coated spacers versus non-coated spacers in the clinical situation. METHODS: A randomized, double-blind study in children with

asthma and a ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC) of $<$ or $=72\%$ predicted was carried out. Spirometry was performed at baseline and at 10 min and 20 min after inhalation of two puffs of salbutamol (100 microg/puff) through either a detergent-coated or a non-coated spacer. RESULTS: Fifty children were studied (mean age 11.6 years, range 7-18 years): 26 in the group using coated spacers (CG); and 24 in the group using non-coated spacers (NCG). The mean percentage change in FEV1 from baseline 10 min after inhalation was 18.8% (range 5-50%) in the CG versus 18.5% (range 3-35%) in the NCG. At 20 min after inhalation, the per cent increase in FEV1 was 19.8% (range 0-50%) in the CG versus 19.5% (range 9-35%) in the NCG. There was no significant difference between groups in the percentage change in FEV1 after 10 min ($P = 0.91$), or after 20 min ($P = 0.93$). CONCLUSIONS: There was no improvement in bronchodilatation from detergent-coated spacers in the present study, possibly because a maximal bronchodilator response was achieved with the lower output.

Barbieri E.A. et al. *A syndrome of hypoplastic sinuses, hydrocephalus, bronchiectasis, and hypogammaglobulinemia with functional antibody deficiency in twin girls.* Ann Allergy Asthma Immunol. 2005; 94(6) : 693-9.p **Abstract:** BACKGROUND: A variety of syndromes are known to be associated with immune deficiency, some as a major part of the syndrome and some as an occasional finding. OBJECTIVES: To report a newly defined syndrome of hydrocephalus, hypoplastic sinuses, cartilaginous webbing of the bronchi, bronchiectasis, and hypogammaglobulinemia with functional antibody deficiency in identical twin girls. METHODS: Spirometry, radiography, computed tomography (CT), bronchoscopy, and laboratory tests were performed for diagnosis. RESULTS: A girl (twin A) was evaluated at the age of 7 years for chronic cough and wheeze that worsened with exercise. Hydrocephalus had been diagnosed a year before evaluation. She was treated for cough variant asthma and was lost to follow-up until the age of 10 years. The cough had worsened progressively, and dyspnea was now apparent. Spirometry was consistent with reversible airway obstruction. A chest radiograph was suggestive of bronchiectasis. A chest CT scan showed bilateral upper lobe bronchiectasis. Hypogammaglobulinemia and functional antibody deficiency were noted. A CT scan of the sinuses revealed aplasia or severe hypoplasia of all the paranasal sinuses. Bronchoscopy revealed a grossly abnormal bronchial structure and atrophic-appearing bronchial mucosa. Twin B also had a history of hydrocephalus. Although she had no respiratory symptoms, chest CT revealed bronchiectasis, and she had obstruction on spirometry. Laboratory analysis revealed hypogammaglobulinemia and functional antibody deficiency. She became symptomatic 2 years after twin A. CONCLUSIONS: This is a newly reported syndrome of hydrocephalus, absent sinuses, abnormalities of the bronchi, and functional antibody deficiency, which initially presented as cough and wheeze.

Barlow J. et al. *Increasing touch between parents and children with disabilities: preliminary results from a new programme.* J Fam Health Care . 2002; 12(1) : 7-9.p **Abstract:** Initial findings are presented from a specially devised touch therapy programme for parents of children with disabilities. A total of 42 parent children have completed the programme. Therapists teach parents simple massage techniques during one-hour sessions held once a week for eight weeks. The children had a range of disabilities including cerebral palsy, asthma, sensory impairments and Down's syndrome. Parents reported improvements in children's muscle tone, joint mobility, sleep patterns, bowel movements and response to other forms of therapy, e.g. physiotherapy. Parents also reported that they themselves had benefited, e.g. by feeling "closer" to their child and less stressed.

Barlow J.H. et al. *Psycho-educational interventions for children with chronic disease, parents and siblings: an overview of the research*

evidence base. *Child Care Health Dev.* 2004; 30(6) : 637-45.p
Abstract: **BACKGROUND:** The role of psycho-educational interventions in facilitating adaptation to chronic disease has received growing recognition and is in keeping with policy developments advocating greater involvement of patients in their own care. The purpose of this paper is to provide an overview of the current literature regarding the effectiveness of psycho-educational interventions for children and adolescents with chronic disease, their parents and siblings. **METHODS:** Electronic searches were conducted using AMED, CINAHL, Cochrane Database, DARE, HTA, MEDLINE, NHS EED, PsycLIT, PsycINFO, and PubMed. Inclusion criteria were systematic reviews, meta-analyses and overviews based on traditional reviews of published literature. The titles of papers were reviewed, abstracts were obtained and reviewed, and full copies of selected papers were obtained. **RESULTS:** No reviews of psycho-educational interventions were found for either parents or siblings. Twelve reviews of interventions for children and adolescents were identified: chronic disease in general (three); chronic pain (one); asthma (three); chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) (one); diabetes (two); juvenile idiopathic arthritis (JIA) (one) and one informational intervention for paediatric cancer patients. The main focus was on disease management (particularly in asthma and diabetes) with less attention being paid to psychosocial aspects of life with a chronic condition. Overall, there is evidence of effectiveness for interventions incorporating cognitive-behavioural techniques on variables such as self-efficacy, self-management of disease, family functioning, psychosocial well-being, reduced isolation, social competence, knowledge, hope, pain (for chronic headache), lung function (asthma), days absent from school (asthma), visits to A & E (asthma), fatigue (CFS), and metabolic control (diabetes). A number of gaps and limitations were identified across all disease categories, such as inadequate description of interventions, small sample sizes, and lack of evidence regarding cost-effectiveness. **CONCLUSION:** This overview has highlighted the need to extend the evidence base for psycho-educational interventions, particularly in a UK context. It is essential that effective interventions are implemented and embedded in service provision in order to maximize empowerment through self-care for children, adolescents and their parents.

Barnes K.C. et al. *A novel promoter polymorphism in the gene encoding complement component 5 receptor 1 on chromosome 19q13.3 is not associated with asthma and atopy in three independent populations.* *Clin Exp Allergy.* 2004; 34(5) : 736-44.p **Abstract:** **BACKGROUND:** The inflammatory functions of complement component 5 (C5) are mediated by its receptor, C5R1, which is expressed on bronchial, epithelial, vascular endothelial and smooth muscle cells. A susceptibility locus for murine allergen-induced airway hyper-responsiveness was identified in a region syntenic to human chromosome 19q13, where linkage to asthma has been demonstrated and where the gene encoding C5R1 is localized. **OBJECTIVE:** The aim of this study was to screen for novel polymorphisms in the C5R1 gene and to determine whether any identified polymorphisms are associated with asthma and/or atopy and whether they are functional. **METHODS:** Single-nucleotide polymorphism (SNP) detection in the gene encoding C5R1 was performed by direct sequencing. Genotyping was performed in three populations characterized for asthma and/or atopy: (1) 823 German children from The Multicenter Allergy Study; (2) 146 individuals from Tangier Island, Virginia, a Caucasian isolate; and (3) asthma case-parent trios selected from 134 families (N=783) in Barbados. Functional studies were performed to evaluate differences between the wild-type and the variant alleles. **RESULTS:** We identified a novel SNP in the promoter region of C5R1 at position -245 (T/C). Frequency of the -245C allele was similar in the German (31.5%) and Tangier Island (36.3%) populations, but higher in the Afro-Caribbean population (53.0%; $P=0.0039$ to <0.0001). We observed no significant associations between the -245 polymorphism and asthma or atopy phenotypes. Upon examination of the functional consequences of the -245T/C polymorphism, we did not observe any

change in promoter activity. **CONCLUSION:** This new marker may provide a valuable tool to assess the risk for C5a-associated disorders, but it does not appear to be associated with asthma and/or atopy.

Barnes N. et al. *The national montelukast survey.* *J Allergy Clin Immunol.* 2005; 115(1) : 47-54.p **Abstract:** **BACKGROUND:** Randomized controlled trials have demonstrated the efficacy of montelukast for treating asthma; whether this can be extrapolated to clinical effectiveness in routine practice has yet to be established. **OBJECTIVE:** To examine the use, effectiveness, and tolerability of montelukast in clinical practice for treating asthma and to explore prognostic factors that could predict a favorable response to the drug. **METHODS:** This was a retrospective, cross-sectional, observational study of clinical outcomes seen in patients prescribed montelukast for asthma that used routinely collected clinical information. Data were collected on all consenting patients who had been prescribed montelukast for asthma irrespective of the continuation or duration of treatment. Independent observers, treating physicians, and patients assessed certain outcomes after the initiation of montelukast, including the general asthma response and changes in activity-related symptoms. **RESULTS:** Fifty-six centers in the United Kingdom (20 primary care and 36 secondary care) participated. The analysis was based on 1351 eligible patients for whom essential data were available. Eight hundred thirty patients (66.4%; 95% CI, 63.8% to 69.0%) were recorded as having shown an improvement in their asthma control, and 103 (8.2%; 95% CI, 6.8% to 9.9%) experienced a dramatic improvement. The greatest proportion of patients responding was seen in those with mild to moderate asthma. Montelukast was well tolerated; no new adverse events were recorded. **CONCLUSIONS:** Montelukast is an effective, well-tolerated treatment for asthma in routine practice. The overall response rate and tolerability seen in this survey are similar to those reported in randomized clinical trials.

Barr J. et al. *The relation between adrenal function and the severity of bronchial hyperresponsiveness in children as measured by the methacholine provocation test.* *J Pediatr Endocrinol Metab.* 2002; 15(3) : 307-12.p **Abstract:** **BACKGROUND:** There is no satisfactory explanation why some individuals experience severe attacks of asthma, yet others, exposed to similar stimuli, have a milder form of the disease. **OBJECTIVE:** We tested the hypothesis that children with more severe disease may have relative adrenal insufficiency compared to the children with milder disease. **PATIENTS AND METHODS:** Sixteen children with chronic asthma aged 8-16 years old were studied. Adrenal function was evaluated by the 24-h excretion of urinary free cortisol (UFC) before and after ACTH stimulation, and by plasma cortisol levels before and 60 min after ACTH administration. The severity of bronchial hyperresponsiveness was evaluated by the methacholine provocation test. **RESULTS:** Nine children had 20% fall in forced expiratory volume in 1 sec (FEV1) after a provocative concentration (PC20FEV1) of methacholine ≥ 2.5 mg/ml and were considered as having mild-moderate bronchial hyperresponsiveness (Group A). Seven children had a PC20FEV1 of < 2.5 mg/ml and were considered as having severe bronchial hyperresponsiveness (Group B). No significant difference was found between the peak plasma cortisol response to ACTH between the two groups (634 \pm 182 and 586 \pm 137 nmol/l, respectively). However, there was a significant statistical difference ($p < 0.01$) in the 24-h UFC response to ACTH between the children from Group A (345 \pm 107 nmol/m²) and the children from Group B (161 \pm 125 nmol/m²). **CONCLUSIONS:** Based on the low levels of 24-h UFC secretion in severely asthmatic children in our study, we propose the encouragement of provision of a short course of inhaled steroids to be kept at home for the emergency therapy of those children identified as having high-risk asthma.

Barracough R. et al. *Apparent but not real increase in asthma prevalence during the 1990s.* Eur Respir J. 2002; 20(4) : 826-33.p **Abstract:** The authors investigated changes in asthma prevalence and perception of bronchoconstriction over 6 yrs in adults of Newcastle-upon-Tyne. Postal questionnaires were sent to 6,000 subjects aged 20-44 yrs in 1992-1993 and 1998-1999. Random samples of 600 responders had assessments of atopy, airway responsiveness, and their ability to perceive methacholine-induced bronchoconstriction. The prevalences of asthmatic symptoms, physician-diagnosis, and medication use increased by an average of 4.4%, particularly in subjects aged <30 yrs (8.7 versus 2.7). Atopy prevalence increased from 25% to 31% but atopics and nonatopics had similar mean changes in questionnaire data (5.2 versus 3.4). The probability of a positive methacholine test decreased as did the mean methacholine dose/response slope (0.00527 to 0.00379), indicating lower levels of airway responsiveness. This can be largely explained by an increase in use of inhaled corticosteroids (5.0-9.3%). The proportion of subjects perceiving bronchoconstriction during methacholine tests increased from 63 to 77%. The authors conclude that current changes in asthma epidemiology in adults may result from increased awareness of symptoms (and/or an increased willingness to report them), and from an increased willingness of physicians to make the diagnosis and prescribe treatment, not from increased disease prevalence.

Barreto M. et al. *Additive effect of eosinophilia and atopy on exhaled nitric oxide levels in children with or without a history of respiratory symptoms.* Pediatr Allergy Immunol. 2005; 16(1) : 52-8.p **Abstract:** Although atopy and blood eosinophilia both influence exhaled nitric oxide (eNO) measurements, no study has quantified their single or combined effect. We assessed the combined effect of atopy and blood eosinophilia on eNO in unselected schoolchildren. In 356 schoolchildren (boys/girls: 168/188) aged 9.0-11.5 yr, we determined eNO, total serum IgE, blood eosinophil counts and did skin prick tests (SPT) and spirometry. Parents completed a questionnaire on their children's current or past respiratory symptoms. Atopy was defined by a SPT >3 mm and eosinophilia by a blood cell count above the 80th percentile (>310 cells/ml). eNO levels were about twofold higher in atopic-eosinophilic subjects than in atopic subjects with low blood eosinophils [24.3 p.p.b. (parts per billion) vs. 14.1 p.p.b.] and than non-atopic subjects with high or low blood eosinophils (24.3 p.p.b. vs. 12.2 p.p.b. and 10.9 p.p.b.) (p <0.001 for both comparisons). The additive effect of atopy and high eosinophil count on eNO levels remained unchanged when subjects were analyzed separately by sex or by a positive history of wheeze (n=60), respiratory symptoms other than wheeze (n=107) or without respiratory symptoms (n=189). The frequency of sensitization to Dermatophagoides (Dpt or Dpf) was similar in atopic children with and without eosinophilia (66.2% and 67.4%, respectively); eosinophilia significantly increased eNO levels in Dp-sensitized children as well in children sensitized to other allergens. In a multiple linear regression analysis, eNO levels were mainly explained by the sum of positive SPT wheals and a high blood eosinophil count (t=4.8 and 4.3, p=0.000), but also by the presence of respiratory symptoms (especially wheeze) and male sex (t=2.6 and 2.0, p=0.009 and 0.045, respectively). Measuring eNO could be a simple, non-invasive method for identifying subjects at risk of asthma in unselected school populations.

Barrett J.C. et al. *Managing asthma within the context of the rural family.* Public Health Nurs. 2001; 18(6) : 385-91.p **Abstract:** The purpose of this qualitative study was to describe the experiences of rural families caring for children with asthma. The chief caregivers from six rural families were interviewed about the family's daily experiences in living with asthma, their knowledge of asthma triggers, and strategies for managing asthma. Parental knowledge about asthma and asthma management strategies was quite good. The cost of asthma regimens and school policies about medications were

major barriers to better control. Other management strategies were directed at maintaining normality of family life.

Barton C.A. et al. *Interactions between psychosocial problems and management of asthma: who is at risk of dying?* J Asthma. 2005; 42(4) : 249-56.p **Abstract:** Adjustment for psychosocial and family problems is common in epidemiological research. Recursive partitioning algorithms, such as CHi Square Automatic Interaction Detection (CHAID), can be used to explore complex interactions between these factors and predictor and outcome variables. We investigated the nature of interactions between asthma management variables and psychosocial problems and how these interactions changed the risk of asthma mortality; 50 cases of asthma death and 201 emergency department controls were recruited. A validated questionnaire was used to collect data. An extended version of CHAID was used to identify statistically significant (p < or = 0.05) interactions controlling for asthma severity. Family problems were associated with increased risk of mortality for patients aged > 31 years (OR = 6.5; 95% CI 2.6-16.1) but not for younger patients. Males were at increased risk overall, but females with family problems (OR = 4.3; 95% CI 1.7-10.7) were at greater risk than males (OR = 3.1; 95% CI 1.2-7.9) with family problems. Alcohol use increased risk of mortality for individuals with verbal instructions (OR = 5.4; 95% CI 1.5-19.5) or without a written action plan (OR = 4.4; 95% CI 1.0-19.4). Individuals with severe asthma and who reported having lung function tests were at increased risk for mortality if family (OR = 8.2; 95% CI 1.6-41.6) or financial problems (OR = 11.5; 95% CI 2.0-65.9) were present. This analysis highlights some important interactions and the magnitude of additional risk for mortality associated with psychosocial or family problems. Psychosocial problems need to be identified and addressed as part of asthma management, because even with best practice, these problems place patients at an increased risk of dying.

Basaran S. et al. *Effects of physical exercise on quality of life, exercise capacity and pulmonary function in children with asthma.* J Rehabil Med. 2006; 38(2) : 130-5.p **Abstract:** OBJECTIVE: To investigate the effects of regular submaximal exercise on quality of life, exercise capacity and pulmonary function in asthmatic children. PATIENTS AND METHODS: Sixty-two children with mild-moderate asthma (mean age 10.4 (SD 2.1) years) were randomly allocated into exercise and control groups. The exercise group underwent a moderately intensive basketball training program for 8 weeks. A home respiratory exercise program was advised to both groups. Pediatric Asthma Quality of Life Questionnaire (PAQLQ) was used for the evaluation of activity limitation, symptoms and emotional functions. Exercise capacity was evaluated through the physical work capacity (PWC 170 test) on a cycle ergometer and 6-minute walk test. Spirometric tests were also performed and medication and symptom scores were recorded. RESULTS: Although PAQLQ scores improved in both groups, the improvement in the exercise group was significantly higher. The exercise group performed better in the PWC 170 and 6-minute walk tests, whereas no improvement was detected in the control group at the end of the trial. Medication scores improved in both groups, but symptom scores improved only in the exercise group. No significant changes were detected in pulmonary function in either group, except for peak expiratory flow values in the exercise group. CONCLUSION: Eight weeks of regular submaximal exercise has beneficial effects on quality of life and exercise capacity in children with asthma. Submaximal basketball training is an effective alternative exercise program for asthmatic children.

Basheti I.A. et al. *Counseling about turbuhaler technique: needs assessment and effective strategies for community pharmacists.* Respir Care. 2005; 50(5) : 617-23.p **Abstract:** Optimal effects of asthma medications are dependent on correct inhaler technique. In a telephone survey, 77/87 patients reported that their Turbuhaler technique had not been checked by a health care professional. In a

subsequent pilot study, 26 patients were randomized to receive one of 3 Turbuhaler counseling techniques, administered in the community pharmacy. Turbuhaler technique was scored before and 2 weeks after counseling (optimal technique = score 9/9). At baseline, 0/26 patients had optimal technique. After 2 weeks, optimal technique was achieved by 0/7 patients receiving standard verbal counseling (A), 2/8 receiving verbal counseling augmented with emphasis on Turbuhaler position during priming (B), and 7/9 receiving augmented verbal counseling plus physical demonstration (C) (Fisher's exact test for A vs C, $p = 0.006$). Satisfactory technique (4 essential steps correct) also improved (A: 3/8 to 4/7; B: 2/9 to 5/8; and C: 1/9 to 9/9 patients) (A vs C, $p = 0.1$). Counseling in Turbuhaler use represents an important opportunity for community pharmacists to improve asthma management, but physical demonstration appears to be an important component to effective Turbuhaler training for educating patients toward optimal Turbuhaler technique.

Bashir S.A. *Home is where the harm is: inadequate housing as a public health crisis.* Am J Public Health. 2002; 92(5) : 733-8.p Abstract: Overcrowding and poor-quality housing have a direct relationship to poor mental health, developmental delay, heart disease, and even short stature.

Bassuny W.M. et al. *Association study between interleukin-12 receptor beta1/beta2 genes and type 1 diabetes or asthma in the Japanese population.* Immunogenetics. 2003; 55(3) : 189-92.p Abstract: Interleukin-12 (IL-12) secreted from macrophages or dendritic cells plays an important role in the protection against intracellular pathogens as well as the developmental commitment of T helper 1 cells. IL-12 exerts its biological effects through binding to specific IL-12 receptors (IL-12Rs) termed IL-12Rbeta1 and IL 12Rbeta2. In this paper, we performed association studies between the three reported polymorphisms (Q214R, M365T and G378R) of the IL-12Rbeta1 gene or the newly identified polymorphisms (P238L, IVS9 -7G>A, IVS13 -121G>A, A643T, P779P and c.3283T>G) of the IL-12Rbeta2 gene, and the development of type 1 diabetes or atopic asthma as representative Th1- and Th2- dominant diseases, respectively. The association study of each polymorphism of the IL-12Rbeta1 or IL-12Rbeta2 gene and type 1 diabetes or asthma showed that these IL-12R genes did not contribute to the development of type 1 diabetes or asthma in the Japanese population. Further analysis in individuals with susceptibility to intracellular pathogens may elucidate the importance of the IL-12R genes.

Bastida Segura D.L. et al. *[Allergic asthma and interleukins 2, 4, 5, 6 and 12 and gamma interferon levels].* Rev Alerg Mex. 2004; 51(3) : 107-15.p Abstract: BACKGROUND: Asthma is an inflammatory chronic illness, in which mastocyt cells, basophils, T lymphocytes, eosinophils and cytokines play a role. Its association with the production of TH2 cytokines is not well known, but it is considered an aberrant immune response, yielding the activation and recruitment of a number of effector cells (mastocyt/eosinophils) and the appearance of clinical symptoms. OBJECTIVE: To determine the serum values of the interleukins 2, 4, 5, 6 and 12 and gamma interferon in relation to the severity degree of asthma and the time of immunotherapy in patients with stable chronic allergic bronchial asthma. MATERIAL AND METHODS: Clinical records of allergic asthmatic patients from the external consultation at Servicio de Alergia e Immunologia Clinica were reviewed in a period of 12 months (1st January 2002 to 1st January 2003) and those of healthy volunteers, forming three groups: Group 1, allergic asthmatics with immunotherapy less than 24 months; Group 2, allergic asthmatics with more than 24 months of immunotherapy, and Group 3, healthy volunteers (control group). Previous informed consent, a serum sample was taken of all subjects. RESULTS: Ninety-two subjects were included: 41 (45%) allergic asthmatics and 51 (55%) healthy volunteers. Significant differences were found in interleukins 2, 4, 5,

6 and 12 levels between healthy volunteers and asthmatics without relating the immunotherapy time. In the total group gamma interferon levels were not found. A relation of interleukins Th2 levels with the severity degree of asthma was not found. Differences of serum interleukins Th1 and Th2 in allergic patients related to immunotherapy time were not significant; even though, irrespective of immunotherapy time, IgG levels were always high. CONCLUSIONS: Patients with allergic asthma have a predominance of serum interleukins Th2 and, despite of the immunotherapy, in the maintaining phase, these continue high, which may be due to an immune system dysregulation maybe including other factors. Immunotherapy continues being one of the most useful specific treatments in allergic diseases, demonstrated by its satisfactory clinical response, reduced drugs' use and modification in severity and evolution of the disease.

Batista B.H. et al. *[Progressive bulbar palsy (Fazio-Londe disease): case report].* Arq Neuropsiquiatr. 2002; 60(3-B) : 830-4.p Abstract: Progressive bulbar palsy, also called Fazio -Londe disease, is characterized by progressive impairment of cranial nerves in children. It was first reported by Fazio in 1892 and until now only 30 cases have been published in the literature. Both sexes can be affected and clinical course can be divided on early (< 6 years age, predominance of respiratory symptoms) and late course (6-20 years of age, predominance of motor symptoms on superior limbs). We report a 4 years old boy that started with intense stridor and respiratory distress, initially being diagnosed as an acute asthma attack. Clinical signs worsened and 12 months latter he already had impairment of cranial nerves V, VII, VIII, IX and X confirmed by clinical examination and neurophysiological evaluation.

Batista R. et al. *Lack of detectable allergenicity of transgenic maize and soya samples.* J Allergy Clin Immunol. 2005; 116(2) : 403-10.p Abstract: BACKGROUND: The safety issues regarding foods derived from genetically modified (GM) plants are central to their acceptance into the food supply. The potential allergenicity of proteins newly introduced in GM foods is a major safety concern. OBJECTIVE: We sought to monitor, in potentially sensitive human populations, the allergenicity effects of 5 GM materials obtained from sources with no allergenic potential and already under commercialization in the European Union. METHODS: We have performed skin prick tests with protein extracts prepared from transgenic maize (MON810, Bt11, T25, Bt176) and soya (Roundup Ready) samples and from nontransgenic control samples in 2 sensitive groups: children with food and inhalant allergy and individuals with asthma-rhinitis. We have also tested IgE immunoblot reactivity of sera from patients with food allergy to soya (Roundup Ready) and maize (MON810, Bt11, Bt176) samples, as well as to the pure transgenic proteins (CryIA[b] and CP4 5-enolpyruvylshikimate-3-phosphate synthase). RESULTS: None of the individuals undergoing tests reacted differentially to the transgenic and nontransgenic samples under study. None of the volunteers tested presented detectable IgE antibodies against pure transgenic proteins. CONCLUSION: The transgenic products under testing seem to be safe in terms of allergenic potential. We propose postmarket testing as an important screening strategy for putative allergic sensitization to proteins introduced in transgenic plants.

Baxt W.G. *Prospective application of an asthma severity rule.* Acad Emerg Med. 2002; 9(8) : 868-9.p

Bearison D.J. et al. *Medical management of asthma and folk medicine in a Hispanic community.* J Pediatr Psychol. 2002; 27(4) : 385-92.p Abstract: OBJECTIVE: To describe beliefs about asthma and asthma treatment in a Hispanic (Dominican-American) community to determine how alternative belief systems affect compliance with medical regimens. METHOD: Twenty-five mothers of children with

asthma were interviewed in their homes, in their primary language, Spanish. Mothers were questioned about their beliefs regarding asthma etiology, treatment, prevention of acute episodes, and use of prescribed medications. **RESULTS:** Most mothers (72%) said that they did not use prescribed medicines for the prevention of asthma; instead, they substituted folk remedies called "zumos." The home remedies were derived from their folk beliefs about health and illness. Most mothers (60%) thought that their child did not have asthma in the absence of an acute episode. Eighty-eight percent said that medications are overused in this country and that physicians hide therapeutic information from them. **CONCLUSIONS:** Mothers' reliance on home remedies for asthma prevention leads to a high rate of noncompliance with prescribed regimens. Yet they perceive themselves as compliant with an effective regimen that differs from standard medical practice. Further studies should explore ways of promoting physician/patient communication in order to find ways of coordinating medical and folk beliefs to enhance compliance with medically prescribed regimens.

Beasley R. *A historical perspective of the New Zealand asthma mortality epidemics.* *J Allergy Clin Immunol.* 2006; 117(1) : 225-8.p

Bechger T.M. et al. *A limited dependent variable model for heritability estimation with non-random ascertained samples.* *Behav Genet.* 2002; 32(2) : 145-51.p **Abstract:** In a questionnaire study, a random sample of Dutch families was asked whether they suffered from asthma and related symptoms. From these families, a selected sample was invited to come to the hospital for further phenotyping. Families were selected if at least one family member reported a history of asthma and the twins were 18 years of age or older. Not all families that were thus selected volunteered, leaving us with a fraction of the original sample. The aim of this paper is to describe a limited dependent variable model that can be used in such situations in order to obtain estimates that are representative of the population from which the sample was originally drawn. The model is a linear (DeFries-Fulker) regression model corrected for sample selection. This correction is possible when (some of) the characteristics that determine whether subjects volunteer (or not) are known for all subjects, including those that did not volunteer. The questionnaire study is of interest by itself but serves mainly to provide a concrete illustration of our method. The present model is used to analyze the data and the results are compared to those obtained with other methods: raw (or direct) likelihood estimation, multiple imputation, and sample weighting. Throughout, Rubin's general theory of inference with missing data serves as an integrating framework.

Beckett W.S. *The air pollution detectives.* *Am J Respir Crit Care Med.* 2001; 164(4) : 515-6.p

Beckham S. et al. *A community-based asthma management program: effects on resource utilization and quality of life.* *Hawaii Med J.* 2004; 63(4) : 121-6.p **Abstract:** **OBJECTIVE:** The Waianae Coast Comprehensive Health Center (WCCHC) developed an integrated community-based asthma management program in an effort to reduce inappropriate medical utilization and improve quality of life in their pediatric asthma population. **METHODS:** Over a period of three years, eighty-eight children with asthma participated in the community-based asthma management program. During this time, an automated asthma tracking system was developed, the WCCHC established a standard system of care based on the National Asthma Education and Prevention Program Expert Panel Report Guidelines for the Diagnosis and Management of Asthma (NAEPP Asthma Guidelines) adapted for cultural sensitivity, and a coordinated team care approach was implemented in the asthma management program. **RESULTS:** During the pilot study, forty children participated in the program. Among these forty individuals, there was a significant decrease in both per capita expenditures and asthma related visits after community health worker (CHW) intervention. Average per

capita charges decreased from dollar 735 to dollar 181, Emergency Department (ED) visits decreased from 60 to 10, and the overall asthma related visits decreased from 1.5 to 0.25 per person after the initial CHW encounter. These results were replicated during the 2000-2001 intervention period where average per capita charges decreased from dollar 310 to dollar 129 and ED encounters dropped from 32 to 10 after the first CHW encounter. In addition, the number of high utilizers-defined as those presenting to the ED two or more times for asthma-related diagnoses- sharply decreased from 176 in 1998 to only 16 in 2001. Quality of life improved, with 72% fewer nighttime and 96% fewer daytime symptoms reported after CHW intervention during the pilot study. During the year 2000, symptoms during exercise and asthma related doctor visits decreased 59% and 67% respectively after CHW intervention. **CONCLUSION:** The community-based asthma management program demonstrated success in improving utilization patterns and reducing asthma-related expense among program participants. Improvement was also noted in quality of life as expressed through frequency and time of asthma symptoms. Other health care institutions may also be positively impacted by developing multidisciplinary team implemented, culturally-adapted, and scientifically-based disease management programs.

Bede O. et al. *Urinary magnesium excretion in asthmatic children receiving magnesium supplementation: a randomized, placebo-controlled, double-blind study.* *Magnes Res.* 2003; 16(4) : 262-70.p **Abstract:** The aims of this study were to establish whether a magnesium (Mg) deficit indicated by a decreased urinary excretion exists and to determine whether 12-week oral Mg supplementation affects the Mg status and bronchodilator use in children with stable bronchial asthma. The effects of long-lasting Mg supplementation were investigated in 89 children 4 to 16 years of age with mild or moderate persistent bronchial asthma in a randomized, double-blind, placebo-controlled, prospective study. Each subject received one capsule of Mg citrate per day (= 7 years: 200 mg, > 7 years: 290 mg) or one capsule of placebo containing 260 mg glucose during 12 weeks. Evaluation was performed at 4-week intervals. Venous blood serum total and free Mg and urine Mg levels were determined at the beginning and end of the 12-week period. Parents recorded the number of bronchodilator doses twice daily. A urinary Mg loss (6.81 +/- 3.9 versus 2.79 +/- 1.39 mmol/day, p = 0.01) was observed in the placebo-treated persistent moderate asthmatics. Bronchodilator use was significantly higher after 8 and 12 weeks in the placebo-treated than in the Mg-treated patients with moderate asthma (31.1 +/- 1.8 versus 29.5 +/- 1.2 puffs per patient/4 weeks, p < 0.05, and 31.0 +/- 2.3 versus 29.3 +/- 0.9 puffs per patient/4 weeks, p < 0.05, respectively). Long-lasting Mg supplementation is clearly of benefit in mildly to moderately asthmatic children and is recommended as a concomitant drug in stable asthma.

Behrens T. et al. *The use of synthetic bedding in children. Do strategies of change influence associations with asthma?* *J Asthma.* 2005; 42(3) : 203-6.p **Abstract:** **BACKGROUND:** Epidemiological data suggest in contrast to clinical recommendations a negative effect of synthetic bedding on asthma and respiratory symptoms. **OBJECTIVE:** To assess the effects of bedding filled with synthetic material on the risk of asthma and respiratory symptoms in 6- to 7-year-old children, taking into account allergy-related change of bedding material. **METHODS:** We analyzed data from the ISAAC Phase III cross-sectional survey (1999/2000) in Munster, Germany. Data were collected by parental report from representative school-based samples of 6- to 7-year old children (n = 3,529). We calculated prevalence ratios with 95% confidence intervals for the association between respiratory symptoms suggestive of asthma and synthetic pillows and blankets and adjusting for potential confounders. **RESULTS:** In the preliminary analyses, synthetic pillows and synthetic blankets were positively associated with the studied respiratory outcomes. For example, a high number of wheezing attacks was positively associated with synthetic pillows (PR = 4.44;

95% CI 2.84-6.94) and synthetic blankets (PR = 3.80; 95% CI 2.48-5.82). However, in the restricted analysis, excluding participants reporting allergy-related change of bedding (pillows n = 440; blankets n = 437), the positive associations disappeared for all studied outcomes. CONCLUSIONS: Our findings suggest that allergy-related choice of bedding is an important factor in the assessment of the relation between synthetic bedding and asthma symptoms. Ignoring those changes can lead to false-positive risk estimates. Prospective studies that allow to disentangle the temporal sequence of disease, exposure, and change of bedding should help to further clarify this issue.

Behrens T. et al. *Self-reported traffic density and atopic disease in children. Results of the ISAAC Phase III survey in Muenster, Germany.* *Pediatr Allergy Immunol.* 2004; 15(4) : 331-9.p **Abstract:** Positive associations between traffic exposure and atopic respiratory disorders in children have been described in several studies. We analyzed data related to self-reported truck traffic density and several symptoms and diagnoses of asthma and hay fever (12-month wheezing and rhinitis symptoms, diagnoses of asthma and hay fever) from the ISAAC Phase III survey in Muenster, Germany, using core written and video questionnaires. Data were collected from representative school-based samples (n = 7345) of 6-7- and 13-14-yr-olds. In 13-14-yr-olds, according to exposure levels categorized into rare, frequent, and constant, with the 'never'-category used as reference, the sex-adjusted prevalence ratios were 1.29 (95% CI = 1.08-1.53), 1.58 (1.29-1.94), and 1.57 (1.18-2.10) for wheeze in the past 12 months, and 1.20 (1.06-1.34), 1.35 (1.17-1.55), and 1.69 (1.42-2.0) for rhinitis symptoms in the past 12 months. Prevalence ratios in 6-7-yr-olds and results for a diagnosis of asthma were less consistent while no positive association was detected between hay fever and truck traffic in both age groups. When analyses were based on a more general traffic indicator (self-reported traffic noise), no consistent associations were observed. Our data provide support for the hypothesis that residential exposure to truck traffic may adversely affect the health of children.

Bell M.L. et al. *The avoidable health effects of air pollution in three Latin American cities: Santiago, Sao Paulo, and Mexico City.* *Environ Res.* 2006; 100(3) : 431-40.p **Abstract:** Urban centers in Latin America often face high levels of air pollution as a result of economic and industrial growth. Decisions with regard to industry, transportation, and development will affect air pollution and health both in the short term and in the far future through climate change. We investigated the pollution health consequences of modest changes in fossil fuel use for three case study cities in Latin America: Mexico City, Mexico; Santiago, Chile; and Sao Paulo, Brazil. Annual levels of ozone and particulate matter were estimated from 2000 to 2020 for two emissions scenarios: (1) business-as-usual based on current emissions patterns and regulatory trends and (2) a control policy aimed at lowering air pollution emissions. The resulting air pollution levels were linked to health endpoints through concentration-response functions derived from epidemiological studies, using local studies where available. Results indicate that the air pollution control policy would have vast health benefits for each of the three cities, averting numerous adverse health outcomes including over 156,000 deaths, 4 million asthma attacks, 300,000 children's medical visits, and almost 48,000 cases of chronic bronchitis in the three cities over the 20-year period. The economic value of the avoided health impacts is roughly 21 to 165 billion Dollars (US). Sensitivity analysis shows that the control policy yields significant health and economic benefits even with relaxed assumptions with regard to population growth, pollutant concentrations for the control policy, concentration-response functions, and economic value of health outcomes. This research demonstrates the health and economic burden from air pollution in Latin American urban centers and the magnitude of health benefits from control policies.

Bellamy S.L. et al. *Analysis of clustered and interval censored data from a community-based study in asthma.* *Stat Med.* 2004; 23(23) : 3607-21.p **Abstract:** Many authors in recent years have proposed extensions of familiar survival analysis methodologies to apply in dependent data settings, for example, when data are clustered or subject to repeated measures. However, these extensions have been considered largely in the context of right censored data. In this paper, we discuss a parametric frailty model for the analysis of clustered and interval censored failure time data. Details are presented for the specific case where the underlying time to event data follow a Weibull distribution. Maximum likelihood estimates will be obtained using commercially available software and the empirical efficiency of these estimators will be explored via a simulation study. We also discuss a score test to make inferences about the magnitude and significance of over-dispersion in clustered data settings. These methods will be illustrated using data from the East Boston Asthma Study.

Ben-Gashir M.A. et al. *Predictors of atopic dermatitis severity over time.* *J Am Acad Dermatol.* 2004; 50(3) : 349-56.p **Abstract:** BACKGROUND: Atopic dermatitis (AD) is a chronic relapsing disease that has increased in prevalence during the last 4 decades. However, little is known about factors that affect disease severity. METHODS: We carried out a longitudinal observational study that included children aged 5 to 10 years recruited from general practices in the United Kingdom. General practitioners identified potential patients and the United Kingdom diagnostic criteria for AD were used to verify the diagnosis in children. The scoring AD index was used to assess disease severity. In addition, information was obtained from parents at the first interview as to age of onset, social class, ethnic group, child's atopy, family history of atopy, and other potential risk factors using a 5-page piloted questionnaire. The aim was to document risk factors for AD severity over time by sequential repeated interview and clinical examination during a 2-year period. The scoring AD index was skewed to the right so nonparametric tests were used for statistical significance. RESULTS: In all, 137 children (65 boys [47%] and 72 girls) with AD were recruited and seen up to 4 times; 40 in March 1998, 104 in October 1998, 116 in March 1999, and 120 at the final visit in October 1999, giving our study an 88% follow-up rate. The severity scores were ranked into 3 categories (80% mild, 18% moderate, and 2% severe) according to suggested guidelines. From this population we were able to show that those with eczema that commenced during the first year of life, which was accompanied by asthma, hay fever, or both, and associated with living in an urban area, had more severe disease independent of other potential risk factors. CONCLUSION: This study has systematically studied AD severity in a community-based design. Researchers and clinicians should be aware of those factors reported in our study as patients exposed to these factors may have a different disease outcome. Further studies on disease severity are needed.

Ben Mustapha M.A. et al. *[Pressurized metered dose inhalers for the Tunisian asthmatic].* *Tunis Med.* 2003; 81(6) : 407-14.p **Abstract:** For an experience done on one hundred (100) asthmatics twenty seven (27) year old, getting the "presurize doser aerosol, we fix to show how many the user of this treatment accept it as a the main goal, the inhale technique and its clinic affect. The first prescription, thirty four percent (34%) of asthma seack are afraid and judge that their disease is dangerous and not treated. The prealable learning of using technic had been realised just for seventy percent (70%) of asthmatic seattle to control the inhale technic show that only fifteen percent (15%) inhale correctly and seventy percent (70%) are not consent of the necessity of the write coordination. To conclude, we are conducted to show and insist on the prealable learning, maintaining and finally the "auto-inhale" system which permit to contourn the problem hand-breathes (lung) cordination.

- Bencivenga M. et al.** *Contribution of air-proof doors and windows to asthma in Campania Plain (Italy).* Int J Environ Health Res. 2004; 14(3) : 231-5.p **Abstract:** The relation between the prevalence of doctor-diagnosed asthma in children and the presence of air-proof doors and windows (doors and windows with rubber gaskets) in their homes was investigated by a cross-sectional survey in the area of Campania Plain, South Italy. Information on the occurrence of asthma and home/family characteristics, including parental smoking habit and level of education, was obtained by a questionnaire given to school children, aged 8-14 years, and their parents. After possible confounders were controlled, the risk of developing asthma was found to be significantly higher in children living in houses equipped with air-proof doors and windows (Odds ratio = 1.30, 95% Confidence interval = 1.1-1.5). By reducing the air exchange, these fixtures are likely to produce increased levels of indoor pollutants. No interaction was found between the two variables 'air-proof doors and windows' and 'parental smoking habit'.
- Bender B.G. et al.** *Retrospective and prospective parental reports of sleep in children with asthma.* J Allergy Clin Immunol. 2004; 114(4) : 985-8.p
- Bender B.G. et al.** *Patient-identified barriers to asthma treatment adherence: responses to interviews, focus groups, and questionnaires.* Immunol Allergy Clin North Am. 2005; 25(1) : 107-30.p **Abstract:** This article reviews 32 patient-interview studies that revealed that the most common barriers to adherence revealed by patients included concerns about drug safety and cost and a belief that the patient's asthma was not severe enough to require daily treatment. Important but less commonly cited concerns included worry about dependence or diminished effectiveness with long-term use of the medication. Children and their parents expressed concerns about safety, dependence, peer stigmatization, and parent-child conflict over taking medication. Low-income and minority patients cited similar concerns and barriers that included cost, difficulty of obtaining medication, daily life hassles, and a general distrust of the medical establishment. The information obtained from patients' perspectives indicates the need to reappraise current strategies for the management of asthma, including a more flexible approach to the use of expert guidelines for the treatment of asthma.
- Bender B.G. et al.** *Minimizing attrition in a long-term clinical trial of pediatric asthma.* Ann Allergy Asthma Immunol. 2003; 91(2) : 168-76.p **Abstract:** **BACKGROUND:** Despite increased attention focused on the need to prevent patient attrition in long-term clinical trials, high dropout rates have threatened the success of numerous studies. **OBJECTIVE:** To evaluate the disease, demographic, and psychological factors associated with missed visits and study dropout to help improve patient management in long-term clinical trials. **METHODS:** Predictors of attrition were examined within the Childhood Asthma Management Program (CAMP), a large, multicenter clinical trial that followed up 1,041 children with asthma for 4 to 6 years. **RESULTS:** Eighty-two percent of patients attended all study visits. The tendency to miss visits was increased among older children with milder asthma, lower intellectual and social competence, and more symptoms of behavioral problems and emotional distress. Forty-two patients who missed 3 or more visits in a row and did not attend the final visit were considered study dropouts; these patients at baseline had milder asthma; lower cognitive, academic, and social competence skills; and more family conflict and distress than found among participants who remained in the study. The 49 children who had erratic attendance but did not drop out also had lower intellectual and academic skills and less family social support. **CONCLUSIONS:** The 4% dropout rate in CAMP was lower than reported in any previous long-term asthma trial. The findings of milder disease, decreased psychological resources, and increased distress in problem-attendance patients can assist in identifying patients who are at risk for missed visits or dropout during the trial either to block their entry into the trial or to focus efforts at maintaining their attendance once enrolled in the trial.
- Bener A. et al.** *Association between childhood atopic disease and parental atopic disease in a population with high consanguinity.* Coll Antropol. 2005; 29(2) : 677-82.p **Abstract:** The aim of the study was to investigate the association between asthma, allergic rhinitis, and eczema in Qatari schoolchildren with allergic conditions in their parents. A cross-sectional study was conducted among 3500 Qatari schoolchildren aged 6-14 years in period: February, 2003-February, 2004. A questionnaire was used to collect the clinical history of asthma and allergic rhinitis in their parents and siblings. It was found that 21.6% of asthmatic children had mothers with asthma and 18.2% fathers with asthma. This contrasted with 6.8% of non-asthmatic children who had fathers with asthma and 9.4% mothers with asthma. As for allergic rhinitis, 26.5% of asthmatic children had mothers with allergic rhinitis and 25.3% fathers with allergic rhinitis. The frequency of either parent of the asthmatic children having allergic rhinitis was 41.8% and for both parents was 10.0%. The frequency of siblings having asthma was 36.6%, allergic rhinitis 16.4%, and eczema 29.1%. The present study revealed a strong association between respiratory allergies and eczema in parents, and their asthmatic children.
- Bener A. et al.** *Pet ownership: its effect on allergy and respiratory symptoms.* Allerg Immunol (Paris). 2004; 36(8) : 306-10.p **Abstract:** **BACKGROUND:** Studies have shown that pets are very important sensitizing agents in patients with asthma. Respiratory disorders such as asthma and allergic rhinitis are common in the State of Qatar. **OBJECTIVE:** The aim of the present study was to determine whether exposure to pets and domestic animals plays a significant role in the development of asthma and allergic rhinitis among Qatari population. **DESIGN:** A hospital-based prospective descriptive study conducted. **SETTING:** Allergy Laboratory at the Hamad General Hospital and Hamad Medical Corporation, State of Qatar. **PATIENTS:** Adult patients over 12 years of age diagnosed with bronchial asthma and/or allergic rhinitis who were referred for allergy skin prick test. 1106 adult patients recruited with respiratory diseases of suspected allergic origin who attended Allergy Clinic at the Hamad General Hospital, during three years from January 2001 to April 2003. Total of 1106 whom 607 were females (54.9 %) and 499 were males (45.1%) and their mean was age 30 years (12-48). **METHODS:** Skin Prick Test (SPT) was performed on 1106 patients for common allergens whom the blood sample was taken for measuring total IgE concentration. **RESULTS:** There were 1106 patients studied and 496 patients (44.9%) had positive and 610 (55.1%) had negative skin prick tests. Out of 1106 patients, 311 patients (28.1%) had asthma; 503 patients had allergic rhinitis (45.5%) and 87 patients (7.8%) had skin allerg. Three hundred and forty (340/1106=30.7%) of the 1006 subjects studied had at least one animal at home, and the remaining 69.3% had never had pets in the home. A further 12% reported having had pets in the past, but not anymore. Cats (26.7%), goats (15%) and birds (14.7%), animals were the most common present within the house and was the most frequently seen pet types when compared to other pet types. The risk of having asthma (RR: 1.29; 95% CI: 1.07-1.55; p=0.008), allergic rhinitis (RR: 1.48; 95% CI: 1.24-1.77; p<0.0001) and eczema (RR: 3.56; 95% CI:1.24-1.77; p<0.0001) was significantly higher in subjects with animals than in patients without. **CONCLUSION:** In the present study, the prevalence of asthma, rhinitis, and skin allergy was significantly more common in families with animals than in those without.
- Benicio M.H. et al.** *Wheezing conditions in early childhood: prevalence and risk factors in the city of Sao Paulo, Brazil.* Bull World Health Organ. 2004; 82(7) : 516-22.p **Abstract:** **OBJECTIVE:** To investigate the prevalence and risk factors for wheezing disorders in early childhood in Sao Paulo, Brazil, the largest metropolitan area of

South America. **METHODS:** A population-based cross-sectional survey of 1132 children aged 6-59 months was carried out between 1995 and 1996 to obtain information on recent wheezing and on independent variables such as demographic, socioeconomic, environmental, maternal and nutritional variables and immunization status. Intestinal parasitic infections were diagnosed using standard techniques. Multiple unconditional logistic regression was used to describe associations between outcome and independent variables. **FINDINGS:** The prevalence of recent wheezing (one or more reported episodes in the past 12 months) was 12.5%; 93% of children with wheezing were also reported to have a medical diagnosis of asthma. Recent wheezing was associated with low per capita income, poor quality of housing, day-care attendance, low birth weight and infection with intestinal helminths. **CONCLUSION:** Wheezing in early childhood in Sao Paulo, although more common than in most developing countries, remains less prevalent than in urban areas of industrialized countries. Low income and conditions associated with poverty (poor housing, low birth weight and parasitic infections) are some of the main risk factors for wheezing disorders among young children in this city.

Benito-Fernandez J. et al. *Salbutamol via metered-dose inhaler with spacer versus nebulization for acute treatment of pediatric asthma in the emergency department.* *Pediatr Emerg Care.* 2004; 20(10) : 656-9.p **Abstract:** **OBJECTIVES:** To assess the effectiveness of salbutamol delivered via a metered-dose inhaler with spacer versus a nebulizer for acute asthma treatment in the pediatric emergency department. **METHODS:** All consecutive children younger than 14 years old who required treatment of acute asthma exacerbation in the emergency department during May 2002 (prospective cohort, n = 321) and May 2001 (retrospective cohort, n = 259) were included. Inhaled salbutamol was administered by metered-dose inhaler with a spacer (and a face mask in children younger than 2 years old) in the prospective cohort and by nebulizer in the retrospective cohort. **RESULTS:** There were no significant differences between the two cohorts in the mean (+/-SD) age (44.50 +/- 38.64 vs. 48.37 +/- 43.55 months) and asthma treatment, arterial oxygen saturation (96.34 +/- 2.12% vs. 96.19 +/- 6.32%), and heart rate (123.71 +/- 23.63 vs. 129.41 +/- 34.55 beats/min) before emergency department consultation. The number of doses of inhaled bronchodilators was also similar (1.42 +/- 1.01 vs. 1.45 +/- 0.98) as well as the number of children that required a stay in the observation unit, admission to the hospital, or returned for medical care. The overall mean length of stay in the emergency department was slightly shorter in the prospective cohort (82 +/- 48 vs. 89 +/- 52 minutes). **CONCLUSIONS:** The administration of bronchodilators using a metered-dose inhaler with spacer is an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the emergency department.

Benito Fernandez J. et al. *[Bronchodilators via metered-dose inhaler with spacer in the pediatric emergency department: what is the dosage?].* *An Pediatr (Barc).* 2006; 64(1) : 46-51.p **Abstract:** **INTRODUCTION:** Bronchodilators administered through a metered-dose inhaler (MDI) with spacer are as effective as nebulizers in the treatment of acute asthma exacerbations in childhood. However, consensus is lacking on the most suitable dosage. **OBJECTIVE:** To assess the effectiveness of distinct salbutamol and terbutaline doses delivered via an MDI with spacer for the treatment of acute asthma in the pediatric emergency department. **METHODS:** This was a prospective, double-blind randomized study. All consecutive children (n = 324) between 2 and 14 years of age with acute asthma exacerbations treated in the pediatric emergency department between October 1 and November 30, 2004, were included. Two treatment groups were established: one group received a number of puffs equivalent to half the child's weight (1 puff of salbutamol = 100 microg and 1 puff of terbutaline = 250 microg) and the other group received a number of puffs equivalent to one-third of the child's weight. **RESULTS:** Three hundred twenty-four episodes

were studied; there were 164 children in the first group and 160 in the second. There were no significant differences between the two groups in the mean (6 SD) age (58.34 +/- 34.72 vs 66.04 +/- 36.45 months), arterial oxygen saturation (95.49 +/- 1.93 vs 95.56 +/- 1.97) or pulmonary score (4.04 +/- 1.55 vs 3.97 +/- 1.51) at recruitment and after treatment in the emergency department (arterial oxygen saturation [96.34 +/- 1.60 vs 96.18 +/- 1.77], pulmonary score [1.87 +/- 1.33 vs 1.64 +/- 1.31]). The number of doses administered (2.17 +/- 0.91 vs 2.24 +/- 1.00) and the hospitalization rate (8.56 % vs 6.87 %) were also similar in both groups. **CONCLUSIONS:** The distinct bronchodilator doses administered via an MDI with spacer showed similar effectiveness. These findings should contribute to a reevaluation of the use of high doses of bronchodilators, at least in most acute asthma exacerbations in children.

Bensch G. et al. *One-year efficacy and safety of inhaled formoterol dry powder in children with persistent asthma.* *Ann Allergy Asthma Immunol.* 2002; 89(2) : 180-90.p **Abstract:** **BACKGROUND:** The long-term efficacy and safety of formoterol dry powder capsules for inhalation in pediatric asthma have not previously been evaluated. **OBJECTIVE:** We examined the effectiveness of inhaled formoterol over a period of 12 months in asthmatic children who were still symptomatic despite anti-inflammatory treatment. **METHODS:** After a run-in period, 518 patients (5 to 12 years old) were randomized in a double-blind manner to receive 12 or 24 microg formoterol dry powder (Foradil, Novartis Pharma AG, Basel, Switzerland) or placebo twice daily for 12 months. The drug was administered by inhaler (Aerolizer, Novartis Pharma AG) and was given in addition to their anti-inflammatory treatment. The primary variable was the area under the curve for forced expiratory volume in 1 second measured over 12 hours after the morning dose of study medication. **RESULTS:** The area under the curve for forced expiratory volume in 1 second after the first dose of treatment and after 3 and 12 months of treatment was significantly greater for patients receiving formoterol 12 microg and 24 microg than for patients receiving placebo (all P < or = 0.0062). Compared with placebo, both doses of formoterol significantly improved morning and evening premedication peak expiratory flow rate (all P < 0.001). In the group treated with formoterol 24 microg, median symptom score and median dose of rescue medication at night were lower than during the run-in period, whereas the opposite occurred in the placebo group. The incidence of hospitalizations for asthma was higher in the formoterol groups than in the placebo group. **CONCLUSION:** Our results indicate that, in asthmatic children who are still symptomatic despite anti-inflammatory therapy, the addition of formoterol consistently improves airflow obstruction and nocturnal symptoms and reduces the use of rescue medication. However, this treatment requires close disease monitoring to detect early signs of acute exacerbation.

Bentur L. et al. *Measurement of inspiratory flow in children with acute asthma.* *Pediatr Pulmonol.* 2004; 38(4) : 304-7.p **Abstract:** Dry-powder inhalers (DPIs) have been proposed for treatment of acute asthma. Different DPIs vary in their inspiratory resistance and have different recommended optimal peak inspiratory flows (PIFs). Reduced PIF during acute asthma may result in inadequate drug delivery to the lungs. Our aim was to measure the inspiratory flow in relation to inspiratory resistance during acute asthma in children presenting to the emergency room. School-age (range, 6-18 years) children were referred to the emergency room for acute asthma. PIF measurements were performed by In-Check Dial trade mark device with simulated airflow resistances equivalent to Turbuhaler, Diskus, and free flow. Percent change in PIF between remission and acute asthma (%Delta) was correlated with percent change in clinical score (CS) and percent change in spirometry in children <9 and >9 years old. Thirty-three children (21 males) participated. PIF with simulated Turbuhaler resistance was significantly lower than with simulated Diskus resistance in both acute and remission states (P < 0.0001). PIF with simulated Turbuhaler resistance increased from 62.1 +/- 15.3 (acute) to 74.4 +/- 16.5 l/min (remission, P < 0.0001), while

with Diskus it rose from 72.6 +/- 20.5 to 91.1 +/- 18.9 l/min (P < 0.0001). Turbuhaler %Delta PIF correlated with %Delta FEV(1) (P = 0.01) and with %Delta CS (P = 0.0001). A lesser degree of correlation was observed while using Diskus resistance and in children above 9 years old. During acute asthmatic attacks, PIF is reduced; this reduction is particularly prominent in young children who use a high-resistance device. However, the PIF generated is generally within the values considered compatible with adequate lung deposition with both Diskus and Turbuhaler.

Benzarti M. et al. [Skin test reactivity to seven aeroallergens in a Sousse area population sample]. *Tunis Med.* 2002; 80(8) : 450-4.p **Abstract:** INTRODUCTION: Allergy skin tests are an important tool in the diagnosis of allergy diseases. They are useful in epidemiologic studies. OBJECTIVES: The aim of our study is to estimate the prevalence of the skin sensitivity in a sample of unselected population and to study the relationship between skin test reactivity and clinical manifestations. PATIENTS AND METHODS: During 9 months, we undertake skin prick-test in 500 subjects. Our population was recruited in the blood sample room of the biochemistry laboratory of the University Hospital of Sousse. Seven aeroallergen was tested: Dermatophagoides pteronyssinus (DPT), Dermatophagoides farinae (DF), Pollens of Graminees, Olive-tree, Partetaure, Cockroach and Candidine. A positive and a negative control tests were made. RESULTS: 34% of the population was sensitized to one or more aeroallergens. In the litterature this prevalence vary from 9 to 55.5% according to the methodology applied. In our study the skin reactivity does not change with sex (p = 0.26) but was high in subjects aged between 15 and 35 years. 21.8% were sensitized to house dust mites (DPT, DF) and 18.2% to pollens (Olive-tree, Graminees, Parietaire). Skin reactivity was more common when subjects had personal atopic history (p < 0.003) and/or had actual allergic symptoms particularly rhinitis and asthma (p < 0.006). CONCLUSION: Skin reactivity to common aeroallergens is frequent in the general population, particularly in symptomatic subjects affected by rhinitis and/or allergic asthma. This skin sensitization is the result of genetic and environmental interaction, but skin sensitization does not mean allergy.

Berg J. et al. Identification of preschool children with asthma from low-income families in Los Angeles, CA. *Ann Allergy Asthma Immunol.* 2004; 93(5) : 465-71.p **Abstract:** BACKGROUND: Few studies have addressed asthma screening in the preschool age group. Early asthma recognition and intervention in preschool children may reduce costs related to unscheduled medical care and missed school and work. OBJECTIVE: To facilitate an early recognition and referral process for asthma in a preschool education program in Los Angeles, CA. METHODS: We administered a 7-question survey to parents and guardians of children aged 12 months to 6 years in the prekindergarten program of a large school district in Southern California. English and Spanish survey questions addressed health care use, school absenteeism, and asthma symptoms. Postsurvey reports to parents recommended clinical evaluation of children who had probable asthma. RESULTS: Of the 609 surveys returned from 8 centers (> or = 80% survey return rate), 12% were positive for probable asthma and only 5.4% of these cases had been previously diagnosed. Of the 12% found to have a high probability of asthma, 3 independent factors were associated with a lower likelihood of prior asthma diagnosis: Hispanic descent; Spanish speaking; and medicine use 2 or more times per week for symptoms such as cough, chest tightness, trouble breathing, or wheezing. Symptoms at play, during the day, and at night were noted in 35% to 44% of the preschoolers. Cough was the most frequently reported symptom (71.9%, n = 424). CONCLUSIONS: A school-based screening process in an early education program can help identify preschool children with a high probability of asthma and offer a basis for early recognition and intervention.

Berg J. et al. Latino children with asthma: rates and risks for medical care utilization. *J Asthma.* 2004; 41(2) : 147-57.p **Abstract:** Latino families have been reported to underutilize health care services compared with families from other ethnic backgrounds. As part of a community trial in a low income Latino population designed to decrease environmental tobacco smoke (ETS) exposure in children with asthma in San Diego, we examined unscheduled medical care for asthma. Latino families (N = 193) reported information about medical care use for their children during the past 12 months. About 23% were hospitalized, 45% used the emergency department, and 60% used urgent care services. About 8.5% of families had two or more hospitalizations in 12 months. Most families were insured by Medicaid or had no insurance. Significant risk factors for a child's hospitalization were age (under age six), failure to use a controller medication, and a parental report of the child's health status as being poor. Risk factors for emergency department use were age (under age six) and male gender. These findings indicate that low-income Latino families with young children with asthma lack the medical resources necessary for good asthma control. Quality and monitored health care with optimization of asthma management could reduce costly acute care services.

Berger W.E. et al. A patient satisfaction survey comparing levalbuterol with racemic albuterol in children. *Allergy Asthma Proc.* 2004; 25(6) : 437-44.p **Abstract:** Patient preference studies provide important data on the impact of asthma symptoms and the effects of medication on patients' quality of life and functional activity levels. Such studies are lacking in the evaluation of short-acting beta2-agonist treatment for asthma, especially for racemic albuterol. The introduction in 1999 of levalbuterol, the (R)-isomer of racemic albuterol, has provided the opportunity to assess patient preference between racemic albuterol and levalbuterol. Studies with levalbuterol, 1.25 mg, indicated greater bronchodilation than and comparable beta2-mediated side effects to the standard 2.5-mg dose of racemic albuterol, while lower doses of levalbuterol (0.63 mg) provided comparable bronchodilation with reduced beta2-mediated side effects in patients with asthma. This study evaluated treatment satisfaction by the caregivers of children with asthma who currently use and/or have used either levalbuterol (n = 66) or racemic albuterol (n = 76). Twenty-minute-long telephone surveys were administered to caregivers, asking them to rate satisfaction with their child's asthma treatment and provide reasons for satisfaction and dissatisfaction. Significantly more caregivers administering levalbuterol (92%) were "extremely" or "very satisfied" with therapy versus those who currently administered racemic albuterol (51%; p = 0.001). Symptom relief was graded 8.7 (out of 10) for levalbuterol treatment versus 7.5 for racemic albuterol (p = 0.001). Although these differences, in part, may have been influenced by some of the study limitations (e.g., open-label, non-placebo-controlled and nonrandomized design, and potential caregiver recall bias), the statistically significant differences consistently favored levalbuterol and are consistent with results obtained from other clinical studies. The efficacy, dosing flexibility, and improved side effect profile of levalbuterol were the sources of greatest satisfaction for parents/caregivers in the levalbuterol group. This study supports the conclusion that the majority of caregivers of children with asthma who have experience with both levalbuterol and racemic albuterol prefer levalbuterol over racemic albuterol.

Berger W.E. et al. Safety of budesonide inhalation suspension in infants aged six to twelve months with mild to moderate persistent asthma or recurrent wheeze. *J Pediatr.* 2005; 146(1) : 91-5.p **Abstract:** OBJECTIVE: To compare the safety of budesonide inhalation suspension (BIS) with placebo in infants 6 to 12 months of age with mild to moderate persistent asthma or recurrent wheeze. STUDY DESIGN: In this multicenter, randomized, double-blinded, parallel-group, placebo-controlled study, 141 patients received 0.5 mg BIS (n = 48), 1.0 mg BIS (n = 44), or placebo (n = 49) once daily for 12 weeks. The primary variable was adrenal function, based on

cosyntropin-stimulated plasma cortisol levels. Spontaneous adverse events and clinical laboratory findings also were monitored. RESULTS: Overall, the types and frequencies of adverse events reported during the study were comparable across treatment groups. The response to cosyntropin stimulation was similar across treatment groups, with no significant difference between BIS treatment and placebo. CONCLUSIONS: The safety profile of BIS was similar to that of placebo, with no suppressive effect on adrenal function in patients 6 to 12 months of age with mild to moderate persistent asthma or recurrent wheeze.

Bergmann R.L. et al. *Breastfeeding duration is a risk factor for atopic eczema.* Clin Exp Allergy. 2002; 32(2) : 205-9.p Abstract: BACKGROUND: The results of numerous studies on the influence of breastfeeding in the prevention of atopic disorders are often contradictory. One of the most important problems is confounding by other lifestyle factors. OBJECTIVE: The aim of the present study was to analyse the effect of any breastfeeding duration on the prevalence of atopic eczema in the first seven years of life taking into account other risk factors. METHODS: In an observational birth cohort study 1314 infants born in 1990 were followed-up for seven years. At 3, 6, 12, 18, 24 months and every year thereafter, parents were interviewed and filled in questionnaires, children were examined and blood was taken for in vitro allergy tests. Generalized Estimation Equations (GEE)-models were used to model risk factors for the prevalence of atopic eczema and for confounder adjustment RESULTS: Breastfeeding was carried out for longer if at least one parent had eczema, the mother was older, did not smoke in pregnancy, and the family had a high social status. The prevalence of atopic eczema in the first seven years increased with each year of age (OR 1.05; 95% CI 1.01-1.09 for each year), with each additional month of breastfeeding (1.03; 1.00-1.06 for each additional month), with a history of parental atopic eczema (2.06; 1.38-3.08), and if other atopic signs and symptoms appeared, especially specific sensitization (1.53; 1.25-1.88), and asthma (1.41; 1.07-1.85). Although breastfeeding should be recommended for all infants, it does not prevent eczema in children with a genetic risk. CONCLUSION: Parental eczema is the major risk factor for eczema. But in this study, each month of breastfeeding also increased the risk.

Berkhof J. et al. *The effectiveness of anti-leukotriene agents in childhood asthma: evidence to guide clinical practice.* Pediatr Nurs. 2003; 29(1) : 60-2.p

Berkman N. et al. *The effect of montelukast on bronchial provocation tests and exhaled nitric oxide levels in asthmatic patients.* Isr Med Assoc J. 2003; 5(11) : 778-81.p Abstract: BACKGROUND: Leukotriene antagonist therapy in asthmatic patients alleviates symptoms and improves exercise tolerance, however the effect of these drugs on bronchial provocation tests and exhaled nitric oxide levels are less clearly established. OBJECTIVE: To determine the effect of montelukast treatment on airway hyperresponsiveness to exercise, methacholine and adenosine-5'-monophosphate and on exhaled nitric oxide levels in steroid-naïve asthmatics. METHODS: Following a 2 week run-in period, 20 mild to moderate asthmatics were enrolled in an open label 6 week trial of oral montelukast-sodium therapy. Bronchial hyperreactivity (exercise, methacholine and adenosine-5'-monophosphate challenges) and exhaled nitric oxide levels were measured before and after the 6 week period. RESULTS: Montelukast treatment resulted in a significant improvement in exercise tolerance: median delta FEV1 20.0% (range 0-50) prior to treatment vs. 15.0% (range 0-50) post-treatment (P = 0.029). A significant difference was also observed for exhaled NO following therapy: median NO 16.0 ppb (range 7-41) vs. 13.0 (range 4.8-26) (P = 0.016). No change was seen in baseline lung function tests (FEV1, MEF50) or in the bronchial responsiveness (PC20) for methacholine and adenosine-5'-monophosphate. CONCLUSIONS: This study demonstrates that the leukotriene antagonist montelukast-sodium reduces bronchial hyperreactivity in response to exercise and reduces

exhaled nitric oxide levels but has little effect on bronchial responsiveness to methacholine and adenosine challenges.

Bernard A. et al. *Lung hyperpermeability and asthma prevalence in schoolchildren: unexpected associations with the attendance at indoor chlorinated swimming pools.* Occup Environ Med. 2003; 60(6) : 385-94.p Abstract: AIMS: To study whether exposure to nitrogen trichloride in indoor chlorinated pools may affect the respiratory epithelium of children and increase the risk of some lung diseases such as asthma. METHODS: In 226 healthy children, serum surfactant associated proteins A and B (SP-A and SP-B), 16 kDa Clara cell protein (CC16), and IgE were measured. Lung specific proteins were measured in the serum of 16 children and 13 adults before and after exposure to NCI(3) in an indoor chlorinated pool. Relations between pool attendance and asthma prevalence were studied in 1881 children. Asthma was screened with the exercise induced bronchoconstriction test (EIB). RESULTS: Pool attendance was the most consistent predictor of lung epithelium permeability. A positive dose-effect relation was found with cumulated pool attendance and serum SP-A and SP-B. Serum IgE was unrelated to pool attendance, but correlated positively with lung hyperpermeability as assessed by serum SP-B. Changes in serum levels of lung proteins were reproduced in children and adults attending an indoor pool. Serum SP-A and SP-B were already significantly increased after one hour on the pool side without swimming. Positive EIB and total asthma prevalence were significantly correlated with cumulated pool attendance indices. CONCLUSIONS: Regular attendance at chlorinated pools by young children is associated with an exposure dependent increase in lung epithelium permeability and increase in the risk of developing asthma, especially in association with other risk factors. We therefore postulate that the increasing exposure of children to chlorination products in indoor pools might be an important cause of the rising incidence of childhood asthma and allergic diseases in industrialised countries. Further epidemiological studies should be undertaken to test this hypothesis.

Bernardini R. et al. *Cross-reactivity between IgE-binding proteins from Anisakis simplex and Dermatophagoides pteronyssinus.* Int J Immunopathol Pharmacol. 2005; 18(4) : 671-5.p Abstract: An association was found between Anisakis simplex (As) and Dermatophagoides pteronyssinus (Dp) sensitization. One recent study shows a cross-reactivity between As and Dp and tropomyosin (tr) is suspected as being one of the proteins responsible of this cross-reaction. The aim of our study was: 1) to confirm the cross-reactivity between Dp and As; 2) to determine the importance of tr in this cross reaction. SDS-PAGE analysis of Dp and As (metabolic and somatic) extracts was carried out. Then an IgE immunoblotting test using serum from a patient who had specific IgE only to Dp and As and immunoblotting inhibition experiments using Dp extract and tr as inhibitors were performed. We found that patients serum reacted: 1) against larval As antigens with a molecular weight (mw) of 25 kilodalton (kD) and a mw > than 100 kD, 2) against various metabolic As antigens with a mw > than 100 kD, a mw ranging approximately from 35 to 50 kD, and a mw around 20 kD, and 3) against Dp proteins with mw between 35 and 55 kD. Preincubation of patient's serum with Dp extract caused the disappearance of reactivity against antigens with a mw > than 100 kD in both larval and metabolic As extracts and against proteins with mw ranging approximately from 35 to 50 kD in the metabolic As extract. Preincubation of patients serum with As extract caused the disappearance of reactivity against antigens with mw between 35 and 55 kD in the Dp extract. Pre-incubation of patients serum with tr did not induce any change in the immunoblotting profile. The results show that 1) cross-reactive components between Dp and As are some proteins with a mw ranging approximately from 35 to 50 kD and with a mw > than 100 kD, and 2) tr is not involved in cross-reactivity between As and Dp.

Bernsen R.M. et al. *Perinatal characteristics and obstetric complications as risk factors for asthma, allergy and eczema at the age of 6 years.* Clin Exp Allergy. 2005; 35(9) : 1135-40.p Abstract: BACKGROUND: Considerable effort has been put into identifying early determinants for atopic disorders. Many studies have evaluated the role of fetal development and obstetric complications. However, the results are not unequivocal. STUDY OBJECTIVE: To assess the relationship between perinatal characteristics and obstetric complications, and the presence of reported current asthma, allergy and eczema at the age of 6 years in the framework of a previously conducted study. METHOD: Seven hundred families in the Netherlands with index children born in 1988-1990 were retrospectively selected. Data were extracted from the Municipal Health Service's records of health examinations of these children and their siblings. These examinations were carried out at the age of 6 years. The records contained data on reported atopic disorders and perinatal characteristics. RESULTS: Gestational age was inversely related to the risk of asthma (P for trend: 0.03). Children with low birth weight tended to have a lower risk of any allergy, albeit not significant (P=0.07). However, no link was found between neonatal head circumference and atopic disorders. The ratio of neonatal head circumference to birth weight was positively associated with the risk of atopic disorders, especially with the risk of asthma (odds ratio (OR)=1.87; 95% confidence interval (CI(95%))=[1.11, 3.15]). Vacuum extraction was a risk factor for allergy (OR=1.84, CI(95%)=[1.03, 3.28]), but not for asthma. Induced labour was positively associated with the risk of inhalant allergy (OR=2.22, CI(95%)=[1.09, 4.51]) and, to a lesser extent, asthma (OR=1.72, CI(95%)=[0.95, 3.10]). For caesarean section and forcipal extraction there were no such relationships. CONCLUSIONS: Prematurity is a risk factor for asthma reported at 6 years. A high ratio of head circumference to birth weight is a risk factor for any atopic disorder. Vacuum extraction was associated with a higher risk of allergy, and induced labour is a risk factor for inhalant allergy. All results should be viewed with the possibility of residual confounding.

Bertel F. et al. [Conjunctival provocation test with *Dermatophagoides pteronyssinus* in the diagnosis of allergic conjunctivitis from house mites]. J Fr Ophtalmol. 2001; 24(6) : 581-9.p Abstract: INTRODUCTION: Perennial conjunctivitis due to house dust mites is the most frequent form of allergic conjunctivitis in urban environments. However, its diagnosis remains difficult for ophthalmologists. In this study, we evaluated a conjunctival provocation test (CPT) using standardized extracts of *Dermatophagoides pteronyssinus* (Dpt) and compared it to the diagnostic methods commonly performed in allergology: prick tests with dust and house dust mites and specific and IgE assay. MATERIALS AND METHODS: We performed a CPT on 60 volunteer patients, between the ages of 8 and 64 years, corresponding to 30 patients sensitized to house dust mites with the presence of specific IgE and chronic conjunctivitis, 21 patients not sensitized to house dust mites but presenting features of chronic conjunctivitis, and 9 asymptomatic patients. A house dust mite desensitizing treatment was not an exclusion criterion for a number of allergic patients. CPTs were prepared from Dpt allergenic extracts (Laboratoires Stallergenes, Antony, France) with 5 progressive concentrations by dilution in a nonphenolic physiological solution: 1.2 RI, 3.7 RI, 11 RI, 33 RI, and 100 RI. CPTs were performed in only one eye and asymmetry of the ocular response was evaluated by the cumulative clinical score of Abelson Chambers and Smith. The correlation between the 2 diagnostic tests was established by calculating the Cohen correlation coefficient or kappa. We also evaluated the sensitivity and diagnostic specificity for each test. RESULTS: The statistical correlation between specific IgE and the other allergological tests in for allergic conjunctivitis to house dust mites was 0.93 for the CPT, 0.46 for the prick test to Dpt, and 0.33 for the prick test to dust. The diagnostic sensitivities and specificities for each test were 90% and 100% for the CPT, 60% and 70% for the prick test to dust, 70% and 76% for prick test to Dpt, respectively. Beyond an antigenic cut-off value of 11 RI, we also observed greater

hypersensitivity reactions for patients with lacrimal IgE or elevated specific IgE levels. CONCLUSION: The results obtained with the CPT confirm its high antigenic quality. It is a particularly useful, rapid, and perfectly safe clinical test. It is the only test able to establish a relationship between ocular manifestations and specific I(8)E.

Berti I. et al. *Treatment of mild asthma.* N Engl J Med. 2005; 353(4) : 424-7; author reply 424-7.p

Berti L.C. et al. *Comparison of health status of children using a school-based health center for comprehensive care.* J Pediatr Health Care. 2001; 15(5) : 244-50.p Abstract: OBJECTIVE: Our objective was to compare health problems and medical coverage of homeless and housed children who used a school-based health center (SBHC) for comprehensive care. METHODS: Medical charts of homeless children (n = 76) and housed children (n = 232) seen for comprehensive care at an SBHC in New York City during the 1998-99 school year were systematically reviewed and compared. RESULTS: Controlled for ethnicity and medical coverage, homeless children were 2.5 times as likely (P <.001) to have health problems and 3 times as likely (P <.001) to have severe health problems as housed children. The most common health problems identified in the homeless population were asthma (33%), vision (13%), mental health (9%), and acute problems (8%). Lack of medical coverage was evident in 58% of homeless children, compared with 15% of housed children (P <.001). CONCLUSION: Study findings identify homeless children as being at increased risk for health problems and lack of medical coverage. These findings support use of an SBHC for comprehensive care by underserved segments of the population and a need for increased vigilance on the part of health care providers caring for homeless children.

Betz C.L. *Healthy people 2010: a sequel.* J Pediatr Nurs. 2003; 18(4) : 223-4.p

Beydon N. et al. *Pulmonary function tests in preschool children with asthma.* Am J Respir Crit Care Med. 2003; 168(6) : 640-4.p Abstract: Pulmonary function tests are seldom performed in preschool children with asthma. The aim of this multicenter study was to compare pulmonary function in 74 preschool children with asthma (height of 90-130 cm) and 84 healthy control subjects. Functional residual capacity (helium dilution technique) and expiratory interrupter resistance (interrupter technique) were measured. As compared with control children, children with asthma had a significantly higher resistance (0.77 +/- 0.20 vs. 0.92 +/- 0.22 kPa. L-1. second, p < 0.001) and significantly lower specific expiratory interrupter conductance (p < 0.005) values. Resistance values were significantly higher in children with asthma with than without symptoms on exertion (p < 0.05). The effect of bronchodilator administration, expressed as the percentage of baseline and predicted resistance values, was significantly greater in children with asthma than in control subjects (-18.6 +/- 13.6% vs. -11.2 +/- 15.2%, p <= 0.001, and -23.2 +/- 19.2% vs. -12.6 +/- 17.8%, p < 0.001), respectively. A 35% decrease in resistance after bronchodilation expressed as the percentage of predicted values had a likelihood ratio of 3 for separating the bronchodilator response in children with asthma from that in healthy control subjects. Pulmonary function tests that do not require active cooperation may help in the management and follow-up of preschool children with asthma who are unable to perform forced expiratory maneuvers.

Bhargava D. et al. *Tonsillar actinomycosis: a clinicopathological study.* Acta Trop. 2001; 80(2) : 163-8.p Abstract: Actinomycosis has been known to involve virtually every anatomic site in the body. Although actinomycosis has been identified in resected tonsils, its possible role in adeno-tonsillar disease has received little attention. A

clinicopathological study of 302 patients who had adeno-tonsillar surgery is presented. Tonsillar actinomycosis was present in 86 (28.5%) patients. The statistical analysis revealed a significant association ($P < 0.0001$) of actinomycosis and tonsillar hypertrophy (56.8%) compared to only 10.3% in the recurrent tonsillitis group. A statistically significant association ($P < 0.0001$) of tonsillar actinomycosis and sickle cell anaemia, beta thalassaemia, bronchial asthma and beta haemolytic streptococcal infections was also seen. This data supports a predisposition of the above conditions to tonsillar actinomycosis and adeno-tonsillar hypertrophy and a possible etiopathologic role of this organism in adeno-tonsillar hypertrophy and disease. Although the clinical association of actinomycosis and tonsillar hypertrophy and beta haemolytic streptococcal infection has been described before the association of actinomycosis with sickle cell anaemia, beta thalassaemia and bronchial asthma is being observed for the first time in literature.

Bheekie A. et al. *Peak expiratory flow rate and symptom self-monitoring of asthma initiated from community pharmacies.* J Clin Pharm Ther. 2001; 26(4) : 287-96.p Abstract: OBJECTIVE: To compare the use of patient-performed peak expiratory flow (PEFR) and symptom monitoring as asthma self-management tools initiated from community pharmacies. DESIGN AND SETTING: 110 patients over 6 years of age were recruited from five private-sector community pharmacies. Patients were identified from pharmacist recall as having 'asthma'. Information on the frequency of their asthma symptoms, medication use, level of physical activity, school or work attendance and lung function was obtained using a questionnaire to classify patients as either mild, moderate or severe. Each patient was alternately assigned to either the symptom or PEFR monitoring procedure in the order they were recruited. Patients performing symptom monitoring used a visual analogue scale to assess symptoms, whereas those in the PEFR monitoring group assessed symptoms and used a pocket-size peak flow meter to measure lung function. Both self-monitoring groups were required to adhere to an individualized management plan based on guideline recommendations and to record their monitored data in a diary card for 2 months. Data from the diary cards were reviewed, collated, transcribed and analysed using the Student t and Mann-Whitney tests. OUTCOME MEASURES: The average monthly frequency of appropriate patient responses determined from their adherence to the self-management plan was used to compare the usefulness of symptom and PEFR self-monitoring. In particular, appropriate use of medication and need for medical consultation was compared. RESULTS: 21 symptom and 40 PEFR-assigned patients completed 2 months' monitoring. The average monthly frequency of appropriate responses in patients using PEFR (0.76) was significantly higher than that of patients using symptom monitoring (0.53, $P < 0.006$). Patients applying symptom monitoring had a higher monthly frequency (0.39) of inappropriate medication use compared to the PEFR group (0.14). Furthermore, the patients' mean daily symptom scores (2.85) were significantly lower than that estimated by the researcher (4.12, $P < 0.03$). For all three asthma severity groups a higher monthly average of appropriate responses was observed in patients using PEFR monitoring compared to those who used symptom monitoring. CONCLUSION: PEFR self-monitoring proved to be a more useful asthma tool than symptom self-monitoring. Patients applying symptom monitoring tend to underestimate the severity of their condition and use medication inappropriately. Active involvement of community pharmacists in facilitating and reinforcing out-patient self-monitoring would help to optimize asthma management.

Bibakis I. et al. *Childhood atopy and allergic disease and skin test responses to environmental mycobacteria in rural Crete: a cross-sectional survey.* Clin Exp Allergy. 2005; 35(5) : 624-9.p Abstract: BACKGROUND: Through its powerful immunoregulatory effects, infection with atypical mycobacteria may exert a protective effect on the development of childhood allergic disease. OBJECTIVE: To examine the relationship between childhood atopy or allergic disease

and previous infection with four species of atypical mycobacteria. METHODS: Eight hundred and six children aged 8-18 years and living in rural Crete--most of whom had had previous BCG immunization--underwent skin prick testing with 10 aeroallergens; their parents completed a standardized questionnaire relating to allergic disease. No less than 8 weeks later each child underwent intradermal skin tests with 0.1 mL solutions of four selected mycobacterial reagents (Aviumin C, Gordonin, Chelonin and Ranin I). RESULTS: Twenty-three percent of children were atopic on skin prick testing; far fewer had symptoms of asthma (5%) or hayfever in conjunction with a positive prick test to pollens (2%). Eighty percent of children had positive skin responses to one or more mycobacterial species. Among all children--and those with a BCG scar--there was no association between atopy or allergic symptoms and mycobacterial skin responses; among the few children without a BCG scar however those with positive mycobacterial responses were less likely to be atopic or to report allergic symptoms; these differences were not statistically significant. CONCLUSIONS: Our findings, in a population of BCG-immunized children, do not lend support to the suggestion that infection with atypical mycobacteria is protective against childhood allergic disease.

Bibi H. et al. *The relationship between asthma and obesity in children: is it real or a case of over diagnosis?* J Asthma. 2004; 41(4) : 403-10.p Abstract: OBJECTIVE: To determine whether obesity among children is associated with an increased incidence of asthma. DESIGN AND METHOD: Five thousand nine hundred eighty-four children participated in a lung health study in the Ashkelon region, Israel. A lung health questionnaire was completed and they underwent spirometry. Body mass index (BMI) was then calculated for each child. RESULTS: Three hundred two children (5.05%) were above the 95th percentile for BMI and considered obese. Obese children tended to wheeze more than the non-obese children 14.5% vs. 10.5%, respectively ($p < 0.038$). Asthma (physician diagnosis) was diagnosed more often among obese children than non-obese 7.2% vs. 3.9%, respectively ($p < 0.008$). Inhaler use was more prevalent among obese children than non-obese 15.9% vs. 8.8%, respectively ($p < 0.001$). Bronchial hyperreactivity was significantly greater among the non-obese asthmatic children compared with their obese counterparts, 352 (51.4%) vs. 10 (27.8%), respectively ($p < 0.001$). Chest symptoms and asthma were more frequent in obese than non-obese boys. CONCLUSION: Asthma, wheezing, and inhaler use were more common in obese children than in non-obese children. Symptoms were more prevalent among obese boys. Increasing BMI among children is a risk factor for asthma, which may in reality be obesity-related chest symptoms that mimic asthma.

Bibi H. et al. *Comparison of positive allergy skin tests among asthmatic children from rural and urban areas living within small geographic area.* Ann Allergy Asthma Immunol. 2002; 88(4) : 416-20.p Abstract: BACKGROUND: Evidence of increased asthma and allergic response among urban versus rural residents has been reported. OBJECTIVE: To evaluate the prevalence of allergic response among asthmatic children from urban and rural areas living within close proximity. METHODS: In all, 448 asthmatic children from urban (363) and rural (85) areas were studied. The study group consisted of 234 9-year-olds and 214 12-year-olds. A health questionnaire was completed on each child who subsequently underwent allergic skin prick tests (SPTs). RESULTS: There was significantly more positive SPT response to house-dust mite, mold, cat, and cypress among asthmatic children from urban areas compared with children living in rural areas: 58.3% versus 37.6%, 46.1% versus 31.8%, 17.45 versus 5.9%, and 26.2% versus 15.3%, respectively. Positive SPT for indoor allergens were significantly greater among asthmatic urban residents than asthmatic rural residents: 63.3% versus 45.5%, respectively ($P < 0.02$). Positive SPT response to all the allergens checked was higher among the 12-year-old age group when compared with the 9-year-olds, 34.6% versus 22.7%, respectively ($P = 0.05$). CONCLUSIONS: Allergic response

measured by SPT is significantly more common among asthmatic children from urban areas as opposed to rural, even though both areas are within small distance of one another. Further, asthmatic children living in urban areas demonstrated more allergic response to both indoor and outdoor allergens. The allergic response tends to increase with increased age in both urban and rural asthmatic children.

Biggart E. et al. *Antiasthmatic drug delivery in children.* Paediatr Drugs. 2002; 4(2) : 85-93.p **Abstract:** Asthma therapy can be administered to children via a number of routes, including oral, inhaled (via a multiplicity of devices), rectal, intravenous, subcutaneous, and intramuscular. The inhaled route is used most often. This can reduce, but never eliminate, systemic absorption. Swallowed aerosolized medication is subject to hepatic first-pass metabolism, but this metabolic route is bypassed by the drug impacting on the airway, including the pharynx. Although there are a large number of studies from a laboratory setting about drug deposition characteristics, there is very little evidence from community-based studies about what families think actually works well in the everyday treatment of the child. However, it is clear that altering the inhaler device can result in marked changes in the dose administered, and any such change should be part of a review of the dose of prescribed medication. Nebulizers are being used much less frequently, and in particular, all but the most severe exacerbations can be treated at least as effectively with equivalent dosages of beta(2)-adrenoceptor agonists from a large volume spacer.

Birkisson I.F. et al. *Genetic approaches to assessing evidence for a T helper type 1 cytokine defect in adult asthma.* Am J Respir Crit Care Med. 2004; 169(9) : 1007-13.p **Abstract:** Recent evidence suggests that deficiency in the Th1 cytokine pathway may underlie the susceptibility to allergic asthma. This study examined whether (1) single-nucleotide polymorphisms exist in the promoter region of the two interleukin (IL)-12 subunit genes in patients with asthma; (2) messenger RNA and protein expressions of signal transducers and activators of transcription, IL-12, IFN-gamma, and their receptors are altered in asthma; and (3) linkage to genes in the Th1 pathway is present in families with asthma in Iceland. The promoter regions of the IL-12 subunit genes were sequenced in 94 patients with asthma and 94 control subjects without asthma. Linkage was examined in 169 families that included over 570 patients with asthma and 950 of their unaffected relatives. The results demonstrate no evidence of linkage to microsatellite markers in close association with genes within the Th1 pathway, and no polymorphism was detected in the promoter regions of the two IL-12 subunit genes in the cohort with asthma patients. Moreover, we found no differences in the messenger RNA or protein expression signals of genes in the IL-12 pathway between the patients and control subjects. We conclude that decrease in Th1 type cytokine response is unlikely to present a primary event in asthma.

Bisgaard H. et al. *Cost-effectiveness of fluticasone propionate administered via metered-dose inhaler plus babyhaler spacer in the treatment of asthma in preschool-aged children.* Chest. 2001; 120(6) : 1835-42.p **Abstract:** **STUDY OBJECTIVES:** To evaluate the cost-effectiveness of inhaled fluticasone propionate (FP) in children aged 12 to 47 months with asthma symptoms. **DESIGN:** A retrospective economic analysis conducted from the perspective of the Danish health-care system, based on clinical data from a 12-week study. **SETTING:** Thirty-three outpatient centers in nine countries. **PATIENTS:** Two hundred thirty-seven children aged 12 to 47 months with documented history of recurrent wheeze or asthma symptoms. **INTERVENTIONS:** Two dosages of FP, 100 microg/d and 200 microg/d, and placebo administered in two divided doses via a metered-dose inhaler and a Babyhaler (Glaxo Wellcome; Middlesex, UK) spacer device. **MEASUREMENTS:** Effectiveness in terms of asthma exacerbations, control of cough and wheeze symptoms, symptom-free days, overall direct costs of asthma

management in Danish kroner at 1999 prices, and mean and incremental cost-effectiveness ratios. **RESULTS:** FP, 200 microg/d, was significantly more effective than placebo treatment in terms of the proportion of exacerbation-free patients (73.7% vs 59.8%; $p = 0.025$) and patients experiencing a $> \text{ or } = 25\%$ improvement in cough symptoms (57.9% vs 39.0%; $p = 0.018$). The costs per exacerbation-free patient, per patient with a $> \text{ or } = 25\%$ improvement in cough and wheeze symptoms from baseline, and per symptom-free day were lower in the FP groups than in the placebo group. The incremental cost-effectiveness ratios for these end points indicated that the additional benefits of FP, 200 microg/d, were achieved at a lower overall cost compared with placebo treatment. **CONCLUSIONS:** From the perspective of the Danish health-care system, FP, 100 microg bid, administered via the Babyhaler inhalation device was cost-effective relative to standard therapy with bronchodilators alone.

Bjor O. et al. *A retrospective population based trend analysis on hospital admissions for lower respiratory illness among Swedish children from 1987 to 2000.* BMC Public Health. 2003; 3 : 22.p **Abstract:** **BACKGROUND:** Data relating to hospital admissions of very young children for wheezing illness have been conflicting. Our primary aim was to assess whether a previous increase in hospital admissions for lower respiratory illness had continued in young Swedish children. We have included re-admissions in our analyses in order to evaluate the burden of lower respiratory illness in very young children. We have also assessed whether changes in the labelling of symptoms have affected the time trend. **METHODS:** A retrospective, population based study was conducted to assess the time trend in admissions and re-admissions for lower respiratory illness. Data were obtained from the Swedish Hospital Discharge Register for all children with a first hospital admission before nine years of age, a total of 109,176 children. The register covers more than 98% of all hospital admissions in Sweden. The coding of diagnoses was based on ICD-9 from 1987 to 1996 and ICD-10 from 1997. **RESULTS:** The first admission rates declined significantly in children with a first admission after two years of age. However, an increasing admission trend was observed in children aged less than one year and 35% of first admissions occurred in this age group. The annual increase was 3.8% (95% CI 1.3-6.3) in boys and 5.0% (95% CI 2.4-7.6) in girls. A diagnostic shift appeared to occur when ICD-10 was introduced in 1997. The asthma and pneumonia admission rate in children aged less than one year levelled off, whereas the increase in admissions for bronchitis continued. The re-admission rates for asthma decreased and the probability of re-admission was higher in boys. National drug statistics demonstrated a substantial increase in the delivery of inhaled steroids to all age groups but most prescriptions occurred to children aged one year or more. **CONCLUSION:** Hospital admissions for lower respiratory illness are still increasing in children aged < 1 year. Our findings are in line with other recent studies suggesting a change in the responsiveness to viral infections in very young children, but changes in admission criteria cannot be excluded. An increased use of inhaled steroids may have contributed to decreasing re-admission rates.

Blackhall K. et al. *Ionisers for chronic asthma.* Cochrane Database Syst Rev. 2003; (3) : CD002986.p **Abstract:** **BACKGROUND:** Previous reports have shown that ion content in the air may have an effect on respiratory function. Results from studies which test the efficacy of air ionisers to reduce asthma symptoms are often inconclusive and their use as a treatment for asthma remains debatable. **OBJECTIVES:** We conducted a systematic review of the available evidence to determine the effectiveness of positive and negative ion generators in people with asthma. **SEARCH STRATEGY:** We searched the Cochrane Airways Group Asthma trials register (January 1966 to March 2003), Cochrane Central Register of Controlled Trials (Cochrane Library issue 2, 2003) as well as The Alternative Medicine Database AMED (1985 to March 2003). **SELECTION CRITERIA:** Randomised controlled trials (parallel or crossover design studies) comparing ionisers with

dummy ionisers (being negative or positive ion emitters), in children or adults with chronic asthma. DATA COLLECTION AND ANALYSIS: Two reviewers independently assessed titles and abstracts of studies and assessed trial quality. Study quality was determined using two methods: The Cochrane approach to allocation concealment and the five point Jadad scale. MAIN RESULTS: Six studies were selected for inclusion (106 participants). No results were combined as the studies were all of a crossover design. EFFECTS OF NEGATIVE ION GENERATORS (five studies) No study reported a significant difference in lung function between ionised and control air (morning Peak expiratory flow (PEF) - three studies; forced expiratory flow in one second (FEV1) - one study). There were no significant differences in symptoms or beta-2 agonist usage between ionised and control air in three studies. EFFECTS OF POSITIVE ION GENERATORS (one study) This study demonstrated that although positively ionised air was associated with a larger fall in FEV1 with exercise, this did not reach statistical significance. Baseline FEV1 was not demonstrated to be significantly different between treatment groups. REVIEWER'S CONCLUSIONS: Based on the evidence currently available from randomised controlled trials, a recommendation cannot be given for the use of room air ionisers to reduce symptoms in patients with chronic asthma.

Blackwell D.L. et al. *Summary health statistics for U.S. children: National Health Interview Survey, 1999.* Vital Health Stat 10. 2003; (210) : 1-50.p **Abstract:** OBJECTIVES: This report presents statistics from the 1999 National Health Interview Survey (NHIS) on selected health measures for children under 18 years of age, classified by sex, age, race/ethnicity, family structure, parent's education, family income, poverty status, health insurance coverage, place of residence, region, and current health status. The topics covered are asthma, allergies, learning disability, attention deficit disorder, use of medication, respondent-assessed health status, school-loss days, usual place of medical care, time since last contact with a health care professional, selected health care risk factors, and time since last dental contact. SOURCE OF DATA: The NHIS is a multistage probability sample survey conducted annually by interviewers of the U.S. Census Bureau for the National Center for Health Statistics, Centers for Disease Control and Prevention, and is representative of the civilian noninstitutionalized population of the United States. Basic information is collected during face-to-face interviews with adults present at the time of interview. Information about children is collected about one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. SELECTED HIGHLIGHTS: In 1999 most U.S. children under 18 years of age enjoyed excellent or very good health (83%). However, 12% of children had no health insurance coverage, and 6% of children had no usual place of medical care. Eleven percent of children had ever been diagnosed with asthma. An estimated 7% of children 3-17 years of age had a learning disability, and an estimated 6% of children had Attention Deficit Disorder (ADD). Lastly, 9% of children in single mother families had two or more visits to an emergency room in the past year, compared with 4% of children in two parent families.

Blackwell D.L. et al. *Summary health statistics for U.S. children: National Health Interview Survey, 2000.* Vital Health Stat 10. 2003; (213) : 1-48.p **Abstract:** OBJECTIVES: This report presents statistics from the 2000 National Health Interview Survey on selected health measures for children under 18 years of age, classified by sex, age, race, Hispanic origin, family structure, parent's education, family income, poverty status, health insurance coverage, residence, region, and health status. The topics covered are asthma, allergies, learning disability, Attention Deficit Hyperactivity Disorder (ADHD), prescription medication, respondent-assessed health status, school-loss days, usual place of health care, time since last contact with a health care professional, unmet dental need, time since last dental contact, and selected measures of health care access. SOURCE OF DATA: The NHIS is a multistage probability sample survey

conducted annually by interviewers of the U.S. Census Bureau for the National Center for Health Statistics, Centers for Disease Control and Prevention, and is representative of the civilian noninstitutionalized population of the United States. Data are collected during face-to-face interviews with adults present at the interview. Information about children is collected for one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. SELECTED HIGHLIGHTS: In 2000 most U.S. children under 18 years of age enjoyed excellent or very good health (83%). However, 12% had no health insurance coverage, and 6% had no usual place of health care. Twelve percent of children had ever been diagnosed with asthma. Eight percent of children 3-17 years of age had a learning disability, and 7% of children in this age group had ADHD. Lastly, 11% of children in single-mother families had two or more visits to an emergency room in the past year compared with 6% in two-parent families.

Blaisdell C.J. et al. *Using seasonal variations in asthma hospitalizations in children to predict hospitalization frequency.* J Asthma. 2002; 39(7) : 567-75.p **Abstract:** Asthma hospitalization rates have increased in the United States since 1980. The exposure risk of many environmental factors, which contribute to respiratory disease, vary throughout the year. The objective of this study was to investigate the seasonal variation of pediatric asthma hospitalizations and predict hospitalization frequency. This was a longitudinal analysis of all pediatric asthma hospitalizations in the state of Maryland by age, gender, race, and residence using non-confidential discharge data sets from 1986 to 1999. Of the 631,422 pediatric hospitalizations in the state of Maryland during the years 1986-1999, 45,924 (7%) had a primary admission diagnosis of asthma. Frequency of hospitalization for asthma was lowest in the summer in all age groups, and highest in the fall. Seasonal variation in severe asthma episodes was least striking in children aged 15-18. This was in contrast to non-asthma admissions, which were highest in winter in preschool children, but relatively flat in school- and teenaged children. Using neural network modeling, weekly asthma hospitalizations could be predicted with an R2 between 0.71 and 0.8. Temporal trends in asthma hospitalizations were seen in each age group, gender, race, and location. The seasonal variability in asthma hospitalizations suggests that acute asthma is influenced by variables beyond socioeconomic factors and adherence to medical regimens. Strategies to combat exacerbations of asthma should take into consideration seasonal effects on a population. In addition, temporal trends examined over many years can be used to predict frequency of severe asthma episodes in a population.

Blais M.S. *Antihistamines: treatment selection criteria for pediatric seasonal allergic rhinitis.* Allergy Asthma Proc. 2005; 26(2) : 95-102.p **Abstract:** Given the absolute numbers of children suffering from seasonal allergic rhinitis (SAR) and the fact that this number is rising, there is an unquestionable need for safe and effective treatments for the disease. The limited seriousness of the symptoms of SAR belies their true impact: the disease can have a profound effect on children's quality of life and impair learning performance. Furthermore, SAR has been linked to a number of comorbid conditions and forms part of the "allergic march" to more serious diseases such as asthma. Antihistamines are administered to relieve the symptoms of SAR, but they do not represent a homogeneous group. For example, older-generation antihistamines are associated with side effects such as impaired psychomotor performance. Newer-generation antihistamines must be evaluated individually based on their proven efficacy and safety so as to tailor treatment to each child's needs. Effective and safe treatment of SAR, with an antihistamine that does not cause sedation, should improve children's quality of life and could prevent the development of more serious conditions, thus reducing morbidity and possible future health care expenditure.

Blaiss M.S. *Pediatric asthma disease management programs--do they work?* *Ann Allergy Asthma Immunol.* 2003; 90(3) : 282-3.p

Blandon Vijil V. et al. *Quality of life in pediatric patients with asthma with or without obesity: a pilot study.* *Allergol Immunopathol (Madr).* 2004; 32(5) : 259-64.p Abstract: **BACKGROUND:** In addition to the increased incidence of asthma, obesity in asthmatic children is also on the rise. Several studies have been performed to determine whether obesity could be a risk factor for asthma, but this association has not been demonstrated in all patients. The Pediatric Asthma Quality of Life Questionnaire (PAQLQ) is a standardized and validated tool for use in the pediatric population, which evaluates the effect of asthma on patients' daily activities. **METHODS AND RESULTS:** To determine the effect of obesity and overweight on quality of life, the PAQLQ was applied to 100 pediatric patients with intermittent asthma and mild persistent asthma and obesity, overweight and normal weight. The results of the three dimensions evaluated in the questionnaire (emotions, symptoms and limitation of activities) showed significant differences in quality of life in the obese asthmatic group only ($p < 0.000$). No differences were found when the groups with and without overweight were compared. **CONCLUSIONS:** The PAQLQ revealed a significant difference in the quality of life in obese asthmatic patients. Overweight and normal weight had no effect quality of life.

Bloch J.R. *Camp nursing: can children with asthma safely attend a regular outdoor day camp?* *Pediatr Nurs.* 2001; 27(5) : 463-8.p Abstract: Although specialty camps are available nationwide for children with asthma, many families prefer to have their children attend regular camps. A retrospective descriptive study was undertaken to evaluate the needs of 156 children, ages 3-16 years, with asthma who attended a large, outdoor, nonspecialty, day camp in a suburban wooded setting. Findings indicate that 10.9% ($n = 17$) received scheduled daily asthma medication, and 12.2% ($n = 19$) required PRN asthma medication while attending camp. Twenty-one children (13.5%) presented, at least once, to the camp nursing office with respiratory complaints. Of a total of 35 visits to the camp nursing office for acute asthma problems, 20% ($n = 7$) required the child to leave camp. Nurses can encourage parents to learn about camp facilities and policies to enable them to carefully evaluate safety when considering a camp for their child with asthma.

Bloom B. et al. *Summary health statistics for U.S. children: National Health Interview Survey, 2001.* *Vital Health Stat 10.* 2003; (216) : 1-54.p Abstract: **OBJECTIVES:** This report presents statistics from the 2001 National Health Interview Survey (NHIS) on selected health measures for children under 18 years of age, classified by sex, age, race, Hispanic origin, family structure, parent's education, family income, poverty status, health insurance coverage, residence, region, and health status. The topics covered are asthma, allergies, learning disability, Attention Deficit Hyperactivity Disorder (ADHD), prescription medication, respondent-assessed health status, school-loss days, usual place of health care, time since last contact with a health care professional, unmet dental need, time since last dental contact, and selected measures of health care access. **SOURCE OF DATA:** The NHIS is a multistage probability sample survey conducted annually by interviewers of the U.S. Census Bureau for the Centers for Disease Control and Prevention, National Center for Health Statistics, and is representative of the civilian noninstitutionalized population of the United States. Data are collected during face-to-face interviews with adults present at the interview. Information about children is collected for one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. **SELECTED HIGHLIGHTS:** In 2001, most U.S. children under 18 years of age enjoyed excellent or very good health (84%). However, 10% had no health insurance coverage, and 5% had no usual place of health care. Thirteen percent of children had ever been diagnosed with asthma. Eight percent of children 3-17 years of age had a learning disability,

and 6% of children had ADHD. Lastly, 11% of children in single-mother families had two or more visits to an emergency room in the past year compared with 6% of children in two-parent families.

Bloom B. et al. *Summary health statistics for U.S. children: National Health Interview Survey, 2004.* *Vital Health Stat 10.* 2006; (227) : 1-85.p Abstract: **OBJECTIVES:** This report presents both age-adjusted and unadjusted statistics from the 2004 National Health Interview Survey (NHIS) on selected health measures for children under 18 years of age, classified by sex, age, race, Hispanic origin, family structure, parent's education, family income, poverty status, health insurance coverage, place of residence, region, and current health status. The topics covered are asthma, allergies, learning disability and Attention Deficit Hyperactivity Disorder (ADHD), prescription medication use, respondent-assessed health status, school-loss days, usual place of health care, time since last contact with a health care professional, selected measures of health care access and utilization, and dental care. **SOURCE OF DATA:** The NHIS is a multistage probability sample survey conducted annually by interviewers of the U. S. Census Bureau for the Centers for Disease Control and Prevention's National Center for Health Statistics and is representative of the civilian noninstitutionalized population of the United States. Data are collected for all family members during face-to-face interviews with adults present at the time of interview. Additional information about children is collected for one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. **SELECTED HIGHLIGHTS:** In 2004, most U.S. children under 18 years of age had excellent or very good health (82%). However, 9% of children had no health insurance coverage, and 5% of children had no usual place of health care. Twelve percent of children had ever been diagnosed with asthma. An estimated 8% of children 3-17 years of age had a learning disability, and an estimated 7% of children had ADHD.

Bloom B. et al. *Summary health statistics for U.S. children: National Health Interview Survey, 1997.* *Vital Health Stat 10.* 2002; (203) : 1-46.p Abstract: **OBJECTIVE:** This report presents statistics from the 1997 National Health Interview Survey on selected health measures for sample children under 18 years of age, classified by sex, age, race/ethnicity, family structure, parent's education, family income, poverty status, health insurance coverage, place of residence, region, and current health status. The topics covered are asthma, allergies, learning disability, Attention Deficit Disorder, use of medication, respondent- assessed health status, school-loss days, usual source of medical care, time since last contact with a health care professional, selected health care risk factors, and time since last dental contact. **SOURCE OF DATA:** The NHIS is a multistage probability sample survey conducted annually by interviewers of the U. S. Census Bureau for the National Center for Health Statistics, Centers for Disease Control and Prevention, and is representative of the civilian noninstitutionalized population of the United States. Data are collected during face-to-face interviews with adults present at the time of interview. Information about children is collected for one sample child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. **HIGHLIGHTS:** In 1997, most U.S. children under 18 years of age enjoyed excellent or very good health (82%). However, 13% of children had no health insurance coverage, and 6% of children had no usual place of medical care. The percent of children with unmet medical need was twice as high in single-mother families (4%) as in two-parent families (2%). Eleven percent of children had ever been diagnosed with asthma. An estimated 8% of children 3-17 years of age had a learning disability, and an estimated 6% of children had Attention Deficit Disorder.

Boelens J.J. *Breastfeeding, atopy, and asthma.* *Lancet.* 2003; 361(9352) : 174-5; author reply 175-6.p

- Boesen I.** *Asthmatic bronchitis in children. Prognosis for 162 cases, observed 6-11 years. 1953.* Acta Paediatr. 2003; 92(12) : 1490.p
- Bokulic R.E.** *Screening for exercise-induced asthma.* J Pediatr . 2002; 141(3) : 306-8.p
- Bollinger M.E. et al.** *The impact of food allergy on the daily activities of children and their families.* Ann Allergy Asthma Immunol. 2006; 96(3) : 415-21.p **Abstract:** **BACKGROUND:** Food allergy affects a significant number of children, and its management requires considerable time and vigilance. **OBJECTIVE:** To determine the impact of food allergy on the daily activities of food allergic children and their families. **METHODS:** Caregivers of food allergic children from a university-based allergy practice completed a questionnaire that evaluated their perception of the impact of their child's food allergy on family activities. **RESULTS:** Of the 87 families who completed the study, more than 60% of caregivers reported that food allergy significantly affected meal preparation and 49% or more indicated that food allergy affected family social activities. Forty-one percent of parents reported a significant impact on their stress levels and 34% reported that food allergy had an impact on school attendance, with 10% choosing to home school their children because of food allergy. The number of food allergies had a significant impact on activity scores, but the existence of comorbid conditions such as asthma and atopic dermatitis did not significantly affect the results. **CONCLUSIONS:** Food allergy has a significant effect on activities of families of food allergic children. Further study is needed to determine more detailed effects of food allergy on parent-child interactions and development.
- Bollinger M.E. et al.** *Contamination of nebulizer equipment with cockroach allergen: there's a bug in the system!* Ann Allergy Asthma Immunol. 2004; 92(4) : 475-7.p **Abstract:** **BACKGROUND:** Physicians often have anecdotal reports of patients describing increased asthma symptoms after the use of nebulizers; however, there are few published reports of nebulizer-associated exacerbations. **OBJECTIVE:** To present 2 cases of asthmatic children who experienced a life-threatening exacerbation of their symptoms after nebulizer use. **METHODS:** Case 2's nebulizer was tested for cockroach allergen by washing the medication reservoir with 2 mL of sterile filtered 1% phosphate-buffered saline, 0.05% bovine serum albumin, and Tween 20 overnight with rotation. The patient's sealed albuterol nebulizer medication was used as a control. The control albuterol and test solutions were analyzed for *Blattella germanica* 1 and 2 allergens using a monoclonal antibody-based immunoenzymetric assay. **RESULTS:** The reservoir from case 2 was found to have measurable levels of both Bla g 1 and Bla g 2. The control albuterol solution had no measurable cockroach allergen. An insect found in the nebulizer box of case 2 was identified as an infantile German cockroach. **CONCLUSIONS:** Nebulizer use provides an opportunity for antigen exposure directly to small airways, which may lead to severe allergic reactions in patients using contaminated equipment.
- Bonilla S. et al.** *School absenteeism in children with asthma in a Los Angeles inner city school.* J Pediatr. 2005; 147(6) : 802-6.p **Abstract:** **OBJECTIVE:** To investigate the pattern of school absenteeism in asthmatic children within a Los Angeles inner city school. **STUDY DESIGN:** Five hundred twenty-eight students of predominant Hispanic ethnicity, from a Los Angeles inner city school were divided into 3 groups: known asthma, high probability of asthma, and low probability of asthma using a previously validated instrument. Attendance records of these students were analyzed to determine total and respiratory absences over a year. School records were compared to the corresponding answers on 513 surveys to determine the accuracy of parental responses in regard to their children's absenteeism. **RESULTS:** Children with known asthma missed on average 2 more days of school than children with low probability of asthma and high probability of asthma. This was only significant in the younger age groups. Survey responses were found to have a 45.6% agreement with school attendance records. Underestimation occurred more often when school-recorded absentee rates were highest. Overestimation occurred more by parents of children with known asthma or a high probability of asthma. **CONCLUSION:** In a Los Angeles inner city population, younger children with known asthma miss more days of school than those with no asthma. Survey-reported absenteeism is less accurate than school attendance records.
- Boogaard R. et al.** *Tracheomalacia and bronchomalacia in children: incidence and patient characteristics.* Chest. 2005; 128(5) : 3391-7.p **Abstract:** **OBJECTIVE:** Congenital airway malacia is one of the few causes of irreversible airways obstruction in children, but the incidence in the general population is unknown. Severe airway malacia or malacia associated with specific syndromes is usually recognized and diagnosed early in infancy, but information about clinical features of children with primary malacia, often diagnosed only later in childhood, is scarce. **METHODS:** We analyzed all flexible bronchoscopies performed between 1997 and 2004 in the Sophia Children's Hospital, summarized clinical features of children with primary airway malacia, estimated the incidence of primary airway malacia, and calculated the predictive value of a clinical diagnosis of airway malacia by pediatric pulmonologists. **RESULTS:** In a total of 512 bronchoscopies, airway malacia was diagnosed in 160 children (94 males) at a median age of 4.0 years (range, 0 to 17 years). Airway malacia was classified as primary in 136 children and secondary in 24 children. The incidence of primary airway malacia was estimated to be at least 1 in 2,100. When pediatric pulmonologists expected to find airway malacia (based on symptoms, history, and lung function) prior to bronchoscopy, this was correct in 74% of the cases. In 52% of the airway malacia diagnoses, the diagnosis was not suspected prior to bronchoscopy. Presenting clinical features of children with airway malacia were variable and atypical, showing considerable overlap with features of allergic asthma. Peak expiratory flow was more reduced than FEV(1). **CONCLUSION:** Primary airway malacia is not rare in the general population, with an estimated incidence of at least 1 in 2,100 children. Airway malacia is difficult to recognize based on clinical features that show overlap with those of more common pulmonary diseases. We recommend bronchoscopy in patients with impaired exercise tolerance, recurrent lower airways infection, and therapy-resistant, irreversible, and/or atypical asthma to rule out airway malacia.
- Booker R.** *Do patients think that dry powder inhalers can be used interchangeably?* Int J Clin Pract Suppl. 2005; (149) : 30-2.p **Abstract:** As recognised in management guidelines, patients are the most important group of people in any prescribing decision. Despite their importance, few studies have asked what patients think about being switched between different inhalers. This paper reports two such studies, one involving interviews of a sample of patients and the other consisting of a quantitative survey of patients across five countries. In the qualitative study, four of the five patients interviewed reported that they would be confused, worried and unhappy about a switch in their dry powder inhaler and would revisit their physician to be shown how to use the inhaler or to ask for a new prescription for their old inhaler. In the quantitative survey of 499 patients with asthma, more than half (51%) were opposed to their current dry powder inhaler being replaced by a substitute device, with 83% reporting concerns. There was considerable concern about training in use of the new device and confusion about the need for change. Almost a quarter of patients (23%) would want training, and 23% of patients thought they would need information about the new inhaler. From limited information, it appears that patients would be concerned about switching of their existing dry powder inhaler for another, with the potential for confusion, need for additional consultations and need for training in the new device.

Boquete M. et al. *Factors influencing the clinical picture and the differential sensitization to house dust mites and storage mites.* J Investig Allergol Clin Immunol. 2000; 10(4) : 229-34.p **Abstract:** Sensitization to house dust mites and storage mites has been studied in a number of papers, but several environmental factors and clinical conditions that differently affect sensitization to these mites are still controversial. The purpose of this study was to determine the influence of climatic conditions, occupation and patient age in the differential sensitization to house dust and storage mites, and also to search for possible different symptoms caused by each group of mites. Eighty patients sensitized to mites but not to other inhalant allergens were studied by case history and by skin prick test and serum IgE to Dermatophagoides pteronyssinus. Dermatophagoides farinae, Lepidoglyphus destructor and Tyrophagus putrescentiae. Home conditions, including content of the allergens Der p 1, Der f 1, Lep d 2 and Tp, were determined for all patients. Human activities, such as farming or similar occupations, and humidity are conditions for preferential sensitization to storage mites, while we found no difference between living in rural or urban areas. Mean age for the onset of sensitization was 6.7 years for house dust mites and 18.7 years for storage mites. Conjunctivitis was more frequent in patients allergic to storage mites, whereas perioral syndrome (itching of the tongue and swelling of the lips) was only seen in patients sensitized to T. putrescentiae. We concluded that climatic and damp conditions and human activity, but not urban or rural living environments, influence the differential sensitization to house dust mites and storage mites.

Borish L. et al. *Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma.* Ann Allergy Asthma Immunol. 2005; 95(3) : 247-53.p **Abstract:** BACKGROUND: Limited data are available on levels of IgE in large cohorts of patients with severe or difficult-to-treat asthma. OBJECTIVE: To examine IgE levels and disease in patients from The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study. METHODS: From January 2001 to October 2001, 4,923 patients were screened for inclusion in the study. Of these, 4,756 patients 6 years or older with severe or difficult-to-treat asthma were enrolled and completed a baseline study visit. Total serum IgE levels were measured at the baseline visit and are summarized by geometric means. RESULTS: The mean total IgE level of the population is 106.6 IU/mL (95% confidence interval, 101.5-112.0 IU/mL). Children (6-12 years old) and adolescents (13-17 years old) have higher mean IgE levels than adults (> or =18 years old) (P < .001). Males have a higher mean IgE level than females (P < .001). IgE levels are higher among nonwhite patients than white patients (P < .001). Current smokers have higher IgE levels than past smokers or never smokers (P < .001). Among children, patients with severe asthma have a higher mean IgE level (280.2 IU/mL) than patients with moderate (145.8 IU/mL) or mild (137.8 IU/mL) asthma (P < .001). Among adults, patients with childhood-onset asthma have higher IgE levels (124.3 IU/mL [n = 1,348]) than patients with adult-onset asthma (65.7 IU/mL [n = 1,956]) (P < .001). CONCLUSION: In patients with severe or difficult-to-treat asthma from the TENOR study, higher total IgE levels were observed in males, children, smokers, nonwhite racial/ethnic groups, and adults with childhood-onset disease. In addition, IgE levels are associated with asthma severity among younger patients.

Bornehag C.G. et al. *'Dampness' at home and its association with airway, nose, and skin symptoms among 10,851 preschool children in Sweden: a cross-sectional study.* Indoor Air. 2005; 15 Suppl 10 : 48-55.p **Abstract:** There is convincing epidemiological evidence that 'dampness' in buildings is associated with respiratory effects. In order to identify health-relevant exposures in buildings with 'dampness', the study 'Dampness in Buildings and Health' (DBH) was initiated. In the first step of the study, cross-sectional data on home

characteristics including 'dampness' problems, and symptoms in airway, nose, and skin among 10,851 children (1-6 years), were collected by means of a questionnaire to the parents. The prevalence of wheezing during the last 12 months was 18.9% and doctor-diagnosed asthma 5.4%. Rhinitis during the last 12 months was reported for 11.1% of the children and eczema during the last 12 months 18.7%. Gender, allergic symptoms among parents, and age of the child were associated with symptoms. Water leakage was reported in 17.8% of the buildings, condensation on windows in 14.3%, and detached flooring materials in 8.3%. Visible mould or damp spots were reported in only 1.5% of the buildings. The four 'dampness' indices were associated to higher prevalence of symptoms in both crude and adjusted analysis. Furthermore, it was found that the combination of water leakage in the home and PVC as flooring material in the child's or parent's bedroom was associated to higher prevalence of symptoms among children. However, the interpretation of this finding is unclear. The combination of water leakage and PVC may be a proxy, for example, reconstruction because of water damages. PRACTICAL IMPLICATIONS: The study have showed that moisture-related problems in buildings are a risk factor for asthma and allergic symptoms among preschool children. The recommendation to the general public is to remediate damp buildings.

Bornehag C.G. et al. *Dampness in buildings and health (DBH): Report from an ongoing epidemiological investigation on the association between indoor environmental factors and health effects among children in Sweden.* Indoor Air. 2004; 14 Suppl 7 : 59-66.p **Abstract:** With the aim of identifying health-relevant exposures in buildings, an epidemiological study "Dampness in Buildings and Health" (DBH) started in the year 2000 in Sweden. The health focus of the study is on asthma and allergic symptoms among small children and their parents. The first step in the study was an epidemiological cross-sectional questionnaire on housing and health involving 14,077 preschool children in the county of Varmland in Sweden (March-April 2000). Self-reported moisture-related problems in the building were strongly associated with asthma, allergic symptoms, and airway infections among children and adults. Other factors associated with symptoms among the children were allergic heredity, smoking in the family, male sex, urban living, short breast feeding, pet keeping, daycare attendance, non-farming life and some food habits. The second step in the study was a nested case-control study including 198 children with symptoms and 202 healthy controls. A detailed clinical examination by physicians in parallel with extensive inspections and measurements in the subjects' homes were conducted from October 2001 to April 2002. The influence of selection bias in case-control studies has been studied, and questionnaires on self-reported symptoms and building characteristics have been validated. Identified risk factors for allergic symptoms are, e.g., inspector-observed dampness, a low ventilation rate, endotoxin, Penicillium and phthalates in dust. In the third phase, a 5-year follow-up study will be carried out during 2005. The same questionnaire as used in DBH-phase 1 will be distributed to the 10,852 children/parents who responded to the first questionnaire in 2000. Finally, in a fourth phase, controlled experimental studies in climate chambers and in vitro tests regarding findings from DBH-Phase 2 are planned to be conducted during 2004-08. PRACTICAL IMPLICATIONS: Asthma and allergies among small children are associated with a number of risk factors in the indoor environment. In investigations of building-related health problems many factors have to be considered, including "dampness" emissions from building materials, and ventilation rates.

Bornehag C.G. et al. *Potential selection biases.* Environ Health Perspect. 2005; 113(3) : A152-3.p

Borok G. *Sinusitis and foods.* S Afr Med J. 2002; 92(9) : 668.p

- Borrelli B. et al.** *Motivating parents of kids with asthma to quit smoking: the PAQS project.* Health Educ Res. 2002; 17(5) : 659-69.p Abstract: The Parents of Asthmatics Quit Smoking (PAQS) project contrasts two theory-based smoking cessation interventions for parents of children with asthma, and compares mechanisms of behavior change within and across theoretical perspectives. We hypothesize that enhancing the perception of risk to self and child will motivate smoking cessation more than standard approaches that emphasize building self-efficacy and coping skills for quitting in a population that is largely not motivated to quit smoking. Smokers (n = 288) and their asthmatic children who receive nurse-delivered in-home asthma education (as part of the insurance carrier's standard of care) are randomized into one of two treatment conditions: (1) the Behavioral Action Model (BAM), in which nurses emphasize goal setting and skill building to enhance self-efficacy to quit smoking, or 2) the Precaution Adoption Model (PAM), in which nurses tailor the intervention to the smoker's readiness to quit and incorporate biomarker feedback [i.e. level of carbon monoxide exposure to the smoker and level of environmental tobacco smoke (ETS) exposure to the child] in order to increase risk perception in smokers. In both conditions, smokers who are ready to quit receive the nicotine patch. Analyses will examine (1) quit rates, ETS level and motivation to quit as the primary dependent variables, (2) mediators of behavior change between and within conditions, and (3) relations between parent smoking outcomes and child asthma morbidity (i.e. ER visits and asthma symptoms) post-treatment. Results will help tailor interventions to this population, and identify mechanisms of behavior change that result in adaptive health outcomes for smokers and their children who have asthma.
- Borres M.P. et al.** *Asthma and allergies at school--a Swedish national position paper.* Allergy. 2002; 57(5) : 454-7.p Abstract: The marked rise in allergies during the past decade has been increasingly perceptible for school personnel. A quarter of Swedish parents of children with allergies are unsatisfied with the school environment and how the schools are organized around their children. The Association of School Physicians has, together with six other medical, teaching and patient organizations, developed written guidelines for the management of asthma and allergies in Swedish schools. The aim was to regulate the responsibility of the school and its personnel for students with asthma and allergies, and to strengthen safety arrangements within schools. A secondary aim was to describe how the curriculum, teaching equipment, excursions, and other school activities, could be arranged appropriately and safely for students with asthma and allergies. Five-hundred copies of the document were circulated to all of Sweden's municipalities, county councils and pediatric departments. There was general agreement regarding the schools' responsibility that no child should risk becoming ill or having exacerbation of symptoms due to conditions at school. Recommendations regarding smoking on school premises and the use of perfumes were criticised. The strength of this document is that all organizations actively involved with schools have agreed upon these recommendations. This document serves to suggest a minimum level of activities thus ensuring that even students with asthma and allergies will receive appropriate schooling.
- Botkin J.R. et al.** *Salmeterol and inhaled corticosteroids in patients with persistent asthma.* JAMA. 2001; 286(24) : 3075; author reply 3077-8.p
- Bottini N. et al.** *Genetic polymorphism and TH1/TH2 orientation.* Int Arch Allergy Immunol. 2005; 138(4) : 328-33.p Abstract: BACKGROUND: It is likely that besides developmental and environmental factors, genetic factors also play an important role in Th1/Th2 orientation and susceptibility to related disorders. Thus, for each genetic factor involved one would expect an opposite pattern of susceptibility towards Th1- and Th2-associated diseases. METHODS: We report a comparative analysis of the pattern of association of four genetic polymorphisms with bronchial asthma (Th2 disease) and Crohn's disease (CD; Th1 disease). The study population included 291 Roman children with bronchial asthma and 72 adult Romans with CD, and haptoglobin, adenosine deaminase (ADA), acid phosphatase locus 1 (ACPI) and MN phenotypes were determined. RESULTS: Compared with controls from the same population, the pattern of phenotype association observed in bronchial asthma is exactly opposite to that observed in CD. The analysis of pairwise gametic type distribution for ACPI, ADA and MN polymorphisms has shown that the pattern of differences between bronchial asthma and controls is opposite to that observed between CD and controls. CONCLUSIONS: The pattern of differences between bronchial asthma versus CD is compatible with the hypothesis that some of the genetic systems considered contribute to Th1/Th2 orientation.
- Bottini N. et al.** *Cooperative effect of adenosine deaminase and ABO-secretor genetic complex on susceptibility to childhood asthma.* Eur Respir J. 2002; 20(6) : 1613-5.p
- Bottini N. et al.** *Atopic and nonatopic asthma in children.* J Asthma. 2005; 42(1) : 25-8.p Abstract: In 155 asthmatic children we have studied the relationship between prick test positivity and a set of genetic factors previously found to be associated with bronchial asthma. Among these factors, MN system (p = 0.009) and age at onset of symptoms (p = 0.05) are the most important variables separating prick test negative from prick test positive children. MN and age at onset influence independently prick test positivity pointing to an additive effect of the two variables. M phenotype appears correlated positively with an increased susceptibility to nonallergic asthma in all age groups, whereas N phenotype appears correlated positively with age at onset but in allergic asthma only. The MN system codifies for glycoprotein A, a sialoglycoprotein that represents a major ligand for several bacteria and viruses that recognize the N-acetylneuraminic acid present in this protein. The present data suggest that genetic variability in this system might influence bacterial and viral competition and mucosal damage influencing susceptibility to asthmatic reactions in absence of IgE hyperproduction.
- Bottini N. et al.** *Adaptation to past malarial endemia and susceptibility to common diseases in modern populations: a study of adenosine deaminase and MN blood group genetic polymorphisms.* Am J Phys Anthropol. 2005; 128(1) : 194-8.p Abstract: We carried out a study of adenosine deaminase (ADA) and MN blood group genetic polymorphisms in relation to past malarial morbidity in Sardinia and in relation to susceptibility to allergic asthma (a Th2 disorder) and Crohn's disease (a Th1 disorder) in the population of Rome. Eight hundred and eight schoolchildren, aged 7-14 years from 14 Sardinian villages located in the central area of the island, were considered. One hundred and twenty-two children with allergic asthma and 39 adult patients with Crohn's disease from the population of Rome were also studied. The data suggest an interaction between the two systems concerning resistance/susceptibility, both to malaria and to the diseases considered. In Sardinia, the frequency of the *L(M)/ADA*2 gametic type is negatively correlated with past malarial endemia, suggesting an increased susceptibility to malaria leading to its decrease in areas with high malarial endemia. In Rome, this gametic type is correlated negatively to allergic asthma and positively to Crohn's disease, suggesting a protective effect against allergic asthma and increased susceptibility to Crohn's disease.
- Bousquet J. et al.** *Clinical studies in asthmatics with a new non-extra fine HFA formulation of beclomethasone dipropionate (BDP Modulite).* Respir Med. 2002; 96 Suppl D : S17-27.p Abstract: The main objective of the clinical development programme for BDP Modulite, a new non-extra fine formulation of beclomethasone dipropionate

(BDP) in hydrofluoroalkane (HFA), has been to demonstrate therapeutic equivalence compared with standard BDP chlorofluorocarbon (CFC) products at the recommended posology (delivered dose and patient population). A total of 1158 asthmatic patients were included in five clinical studies and 658 patients were treated with BDP Modulite. Four studies were undertaken in mild or moderate-to-severe asthmatic adults, while one study was carried out in children. The duration of treatment was 12 weeks in three studies and 6 weeks in the other two studies. A range of doses of BDP Modulite from 200 micrograms bid up to 1500 micrograms bid was evaluated against CFC comparators. The primary efficacy variable in all studies was morning PEFR while secondary variables included other lung function parameters, symptom scores and salbutamol use. All studies demonstrated equivalence of efficacy for morning PEFR for BDP Modulite versus BDP-CFC when compared on a microgram for microgram basis. The secondary outcome variables also consistently support similar efficacy of the two products. The safety and tolerability profile for BDP Modulite was similar to BDP-CFC; the incidence of adverse events was comparable between treatments and plasma and urinary cortisol were generally unchanged in patients receiving 1000 micrograms day⁻¹ for 6-12 weeks. In conclusion, the results of the clinical studies with BDP Modulite show that this new HFA formulation allows a seamless transition to CFC-free BDP, thus simplifying the changeover.

Boutin-Forzano S. et al. *Visits to the emergency room for asthma attacks and short-term variations in air pollution. A case-crossover study.* *Respiration.* 2004; 71(2) : 134-7.p Abstract: BACKGROUND: The 'case-crossover' design is a strategy fitted to studying transient effects of intermittent exposure on acute-onset disease occurring shortly after exposure. It has the important advantage of eliminating most confounding variables, allowing a stronger causality inference. OBJECTIVES: The objective of the study was to evaluate the relationships between emergency room (ER) visits for asthma attacks and gaseous air pollution changes. METHODS: The study included 549 individuals, 3-49 years old, visiting the ER during 1 year. Exposure to gaseous air pollutants (SO₂, NO₂, O₃) on the same day and up to 4 days before was computed according to the patient's address. The statistical analysis included meteorological data as potential confounding variables. RESULTS: No association could be shown between ER visits and SO₂ or NO₂ levels. In contrast, there was a statistically significant association between ER visits and mean O₃ levels, on the day of admission and also on D -2 and D -3. For an increase of 10 microg/m³, the risk of requiring an ER admission increased by 6-10%. CONCLUSIONS: Using this new strategy, we confirmed that ozone changes lead to a moderate increase in risk of requiring an ER admission in asthmatic subjects.

Boychuk R.B. et al. *Change in approach and delivery of medical care in children with asthma: results from a multicenter emergency department educational asthma management program.* *Pediatrics.* 2006; 117(4 Pt 2) : S145-51.p Abstract: OBJECTIVES: The Hawaii Child Asthma Research to Elevate Standards (CARES) Program implemented an emergency department (ED)-based education and management program to facilitate National Asthma Education and Prevention Program (NAEPP) guideline understanding among asthmatic children and their families, ED staff, and health care providers. METHODS: The multipronged approach used: (1) 2-phased prospective tracking system of ED asthma patients; (2) ED-based educational intervention for patients/families; and (3) asthma education for ED staff and community-based health care providers. Data were collected across 4 EDs during phase I (October 8, 2002, to October 1, 2003) and phase II (October 1, 2003, to July 8, 2004). Follow-up data were collected by telephone 3 weeks (phase I), and 3 weeks and 3 months (phase II) after the ED encounter. The patient/family intervention was delivered throughout phase II. During phase I, ED and community-based health care professionals developed strategies for building an integrated asthma care system. ED staff training was delivered before phase II.

Continuing medical education for health care providers was delivered before and during the first month of phase II. RESULTS: Tracking data on 706 phase I and 353 phase II patient encounters revealed that the majority of patients with persistent asthma did not use long-term controller medications and did not possess a written asthma action plan. From preintervention to postintervention, the number of patients possessing a written asthma action plan increased from 48 to 322. Of 186 persistent asthmatics, 34 were using controller medications daily, 34 as needed, and 118 not at all. Daily use increased to 80 3 weeks postintervention and to 68 3 months postintervention. CONCLUSION: An ED-based childhood asthma tracking system can serve as a basis for designing and implementing an ED-based educational intervention. ED staff, primary care providers, and others can work together to promote asthma care.

Boyd J.H. et al. *Asthma and acute chest in sickle-cell disease.* *Pediatr Pulmonol.* 2004; 38(3) : 229-32.p Abstract: Our objective was to determine if physician-diagnosed asthma increases the risk of acute chest syndrome (ACS) in children with sickle-cell disease (SCD) hospitalized for pain. Our study design was a retrospective case-control study of all SCD patients, aged 2-21 years, hospitalized for pain during the interval 1999-2000. Medical records of first admissions during the interval were reviewed to determine the presence of ACS during the admission. Cases were defined as patients with ACS, and controls were patients without ACS. Independently, medical records of admissions prior to the study interval were reviewed for evidence of physician-diagnosed asthma. Sixty-three cases with ACS and 76 controls without ACS were identified. No significant differences in gender, age, and hemoglobin phenotype were found. Patients with physician-diagnosed asthma were 4.0 times (95% CI, 1.7, 9.5) more likely to develop ACS during the admission than patients without asthma. Individuals with physician-diagnosed asthma had a longer hospitalization for ACS, i.e., 5.6 days vs. 2.6 days, respectively (P = 0.01). In conclusion, our preliminary data suggest that asthma in children with SCD admitted to the hospital for pain may be a risk factor for ACS and may increase the duration of hospitalization when compared to children with SCD and without asthma.

Boyd R. et al. *Pressurised metered dose inhalers with spacers versus nebulisers for beta-agonist delivery in acute asthma in children in the emergency department.* *Emerg Med J.* 2005; 22(9) : 641-2.p Abstract: OBJECTIVES: Wet nebulisers are widely used for beta-2 agonist delivery in Australasian emergency departments (ED). An increasing body of work suggests that pressurised metered dose inhalers with spacers (pMDI-S) are as effective. This study aims to investigate the effect on admission rates, total time in the ED, and total time in hospital after initiation of routine pMDI-S treatment for mild to moderate asthma in children presenting to the ED. METHODS: Children with a discharge diagnosis of asthma were identified over sequential 3 month time periods. In the first period, wet nebuliser treatment was routine and in the subsequent trial period pMDI-S treatment was instituted as routine. Admissions rates, total time in hospital, and total time in the ED were recorded for each group. RESULTS: Admission rates fell significantly from 31% to 20.6% after routine use of pMDI-S treatment. There was a non-significant trend to an increase in total ED and total hospital times. CONCLUSION: Introduction of routine pMDI-S treatment in the paediatric ED results in a significant drop in admission rates but no significant change in total hospital times or total ED times.

Boyle J.S. et al. *School-based asthma: a study in an African American elementary school.* *J Transcult Nurs.* 2004; 15(3) : 195-206.p Abstract: ISSUES AND PURPOSE: Chronic illnesses, such as asthma experienced by children, are difficult for families and school professionals to manage. This study explored beliefs about asthma and asthma management among schoolchildren, parents, and teachers in an African American school. DESIGN AND METHODS: Focus

groups were conducted with schoolchildren, parents, and teachers. Data were analyzed by content analysis; segments of information were categorized into groups that were later abstracted into themes illustrating beliefs and behaviors about asthma. RESULTS: The children reported fear of not being able to breathe and the limitations of living with asthma. The teachers were concerned that they did not have a sufficient understanding of asthma to manage children's asthma during the school day. Parents described complex lifestyles and the challenges of asthma management.

Braback L. et al. *Early determinants of first hospital admissions for asthma and acute bronchitis among Swedish children.* Acta Paediatr. 2003; 92(1) : 27-33.p **Abstract:** AIM: To assess the changing impact of prenatal and perinatal factors with increasing age on first admissions for asthma and acute bronchitis. METHODS: The Swedish Medical Birth Registry was linked to the National Hospital Discharge Registry for 214,276 Swedish children born in 1987 and 1988. The linkage comprised first admissions for acute bronchitis or asthma from 1987 to 1995. First admissions for gastroenteritis were included to distinguish between factors specific to asthma or bronchitis and non-specific factors related to an increased risk of hospital admission. RESULTS: Admissions for asthma and acute bronchitis before 2 y of age had a close dose-response relationship with maternal smoking, low gestational age, low maternal age and older siblings. Very premature children exposed to more than 9 cigarettes a day in utero ran a 10 times higher risk of hospitalization than postmature children without exposure to maternal smoking. However, the proportion of admissions attributed to maternal smoking was only 4.7% after adjustments for significant covariates. The number of significant determinants declined in children with their first admission for asthma after 2 y of age but male gender and low educational level were independent determinants in all age groups. Older siblings were related to an increased risk of first asthma admission before 2 y of age but a slightly reduced risk of first admission after 2 y of age. CONCLUSION: This study illustrates the varied epidemiology of asthma in different age groups. Maternal smoking was an important determinant for admission before 2 y of age but mainly in combination with other factors. The decline in hospital admissions in early childhood would therefore be small, even after the elimination of maternal smoking, if other significant perinatal and socioeconomic factors were unchanged.

Braganza S. et al. *The use of complementary therapies in inner-city asthmatic children.* J Asthma. 2003; 40(7) : 823-7.p **Abstract:** Use of complementary/alternative medicine (CAM) has been increasing, especially among patients with a chronic illness. Although asthma is the most common chronic illness affecting children in the United States, very little is known about the use of CAM in children with asthma. Our objective was to determine the prevalence and correlates of CAM use among inner-city children with asthma. A cross-sectional survey of parents of children with asthma attending an urban health center was performed. Parents were surveyed regarding CAM use over the past year, perceived efficacy of CAM, severity of child's asthma symptoms and demographic information. Differences in proportions were tested by chi-square or Fisher's exact test as appropriate. Three hundred ten parents participated, of whom 61% were Hispanic and 37% were African American. Parental mean age was 33 years and the mean age of the child was 7.2 years; 89% of parents had treated their child in the past year with some form of CAM. However, only 18% had informed a physician of doing so. The most common forms of CAM used were as follows: prayers (53%), rubs (53%), and massage (45%). Of those who used CAM, 59% perceived it to be at least as effective as pharmacotherapy, and 44% used CAM as first treatment of an asthma attack. Mild and moderate persistent asthmatics had significantly higher rates of CAM use than did mild intermittent and severe persistent asthmatics. We found a very high rate of CAM use among children with asthma in this inner-city population. Most importantly, a very high proportion of parents perceived the therapies to be effective, used them as first

treatment of an acute exacerbation, and did not inform a physician of doing so. These findings have implications for the care of asthmatic children by pediatricians practicing in urban settings.

Brand P.L. [What are the main problems with inhaled treatment in children?]. Rev Pneumol Clin. 2005; 61(Spec no. 2) : 3S25-8.p

Brannan J.D. et al. *The safety and efficacy of inhaled dry powder mannitol as a bronchial provocation test for airway hyperresponsiveness: a phase 3 comparison study with hypertonic (4.5%) saline.* Respir Res. 2005; 6 : 144.p **Abstract:** BACKGROUND: Inhaled mannitol is a new bronchial provocation test (BPT) developed to improve portability and standardisation of osmotic challenge testing. Osmotic challenge tests have an advantage over the traditional methods of measuring airway hyperresponsiveness using methacholine as they demonstrate higher specificity to identify asthma and thus the need for treatment with inhaled corticosteroids (ICS). The safety and the efficacy of mannitol (M) as a BPT to measure airway hyperresponsiveness were compared to hypertonic (4.5%) saline (HS) in people both with and without signs and symptoms of asthma. METHODS: A phase III, multi-centre, open label, operator-blinded, crossover design, randomised trial, with follow-up. Asthmatics and non-asthmatics (6-83 yr) were recruited and 592 subjects completed the study. Mannitol was delivered using a low resistance dry powder inhaler and HS was delivered using an ultrasonic nebuliser. The FEV1 was measured 60 seconds after each dose of mannitol (5,10,20,40,80,160,160,160 mg) and after each exposure to HS (0.5,1.0,2.0,4.0,8.0 minutes). A 15% fall in FEV1 defined a positive test. Adverse events were monitored and diaries kept for 7 days following the tests. RESULTS: Mean pre-test FEV1 (mean +/- SD) was 95.5 +/- 14% predicted. 296 were positive to mannitol (M+) and 322 positive to HS (HS+). A post study physician conducted clinical assessment identified 82.3% asthmatic (44% classified mild) and 17.7% non-asthmatic. Of those M+, 70.1% were taking ICS and of those mannitol negative (M-), 81.1 % were taking ICS. The % fall in FEV1 for mannitol in asthmatics was 21.0% +/- 5.7 and for the non-asthmatics, 5.5% +/- 4.8. The median PD15 M was 148 mg and PD15 HS 6.2 ml. The sensitivity of M to identify HS+ was 80.7% and the specificity 86.7%. The sensitivity of M compared with the clinical assessment was 59.8% and specificity 95.2% and increased to 88.7% and 95.0% respectively when the M- subjects taking ICS were excluded. Cough was common during testing. There were no serious adverse events. The diarised events were similar for mannitol and HS, the most common being headache (17.2%M, 19%HS), pharyngolaryngeal pain (5.1%M, 3%HS), nausea (4.3%M, 3%HS), and cough (2.2%M, 2.4%HS). CONCLUSION: The efficacy and safety of mannitol was demonstrated in non-asthmatic and clinically diagnosed asthmatic adults and children.

Brauer M. et al. *Air pollution from traffic and the development of respiratory infections and asthmatic and allergic symptoms in children.* Am J Respir Crit Care Med. 2002; 166(8) : 1092-8.p **Abstract:** Despite the important contribution of traffic sources to urban air quality, relatively few studies have evaluated the effects of traffic-related air pollution on health, such as its influence on the development of asthma and other childhood respiratory diseases. We examined the relationship between traffic-related air pollution and the development of asthmatic/allergic symptoms and respiratory infections in a birth cohort (n approximately 4,000) study in The Netherlands. A validated model was used to assign outdoor concentrations of traffic-related air pollutants (nitrogen dioxide, particulate matter less than 2.5 micro m in aerodynamic diameter, and "soot") at the home of each subject of the cohort. Questionnaire-derived data on wheezing, dry nighttime cough, ear, nose, and throat infections, skin rash, and physician-diagnosed asthma, bronchitis, influenza, and eczema at 2 years of age were analyzed in relation to air pollutants. Adjusted odds ratios for wheezing, physician-diagnosed asthma, ear/nose/throat infections, and flu/serious colds

indicated positive associations with air pollutants, some of which reached borderline statistical significance. No associations were observed for the other health outcomes analyzed. Sensitivity analyses generally supported these results and suggested somewhat stronger associations with traffic, for asthma that was diagnosed before 1 year of age. These findings are subject to confirmation at older ages, when asthma can be more readily diagnosed.

Brearey S.P. et al. *Key developments in paediatrics.* Practitioner. 2004; 248(1665) : 874, 876, 879 passim.p

Brehaut J.C. et al. *The health of primary caregivers of children with cerebral palsy: how does it compare with that of other Canadian caregivers?* Pediatrics. 2004; 114(2) : e182-91.p Abstract: BACKGROUND: Caring for any child involves considerable resources, but the demands for these resources are often increased when caring for a child with a disability. These demands have implications for the psychologic and physical health of the caregiver (CG). Although a number of recent trends in health care stress the importance of studying and promoting the health of CGs of children with disabilities, the literature in this area exhibits 2 major weaknesses, ie, most studies draw conclusions from relatively small, potentially biased, clinic-based samples and the majority of work has focused on the psychologic health of CGs, whereas little research has been undertaken to study their physical well-being. The goal of this study was to compare the physical and psychologic health of CGs of children with cerebral palsy (CP) with that of the general population of CGs. METHODS: Data on the physical and psychologic health of 468 primary CGs of children with CP, drawn from 18 of 19 publicly funded children's rehabilitation centers in Ontario, Canada, were collected with a self-completed questionnaire and a face-to-face interview. Identical items and scales had been administered previously to nationally representative samples of the Canadian population in 2 large-scale Canadian surveys, ie, the National Population Health Survey (NPHS) and the National Longitudinal Study of Children and Youth (NLSCY). Subsamples of those data, restricted to adult residents of the province of Ontario who were parents, allowed a comparison of our sample of CGs of children with CP with parent samples from both the NLSCY (n = 2414) and the NPHS (n = 5549). OUTCOME MEASURES: Demographic variables included CG age, gender, education, income, and work-related variables. Psychologic health and support variables included social support, family functioning, frequency of contacts, distress, and emotional and cognitive problems. Physical health variables included the number and variety of chronic conditions, vision, hearing, and mobility problems, and experience of pain. RESULTS: CGs of children with CP had lower incomes than did the general population of CGs (proportion with income over 60,000 dollars: CG: 40.9%; NLSCY: 51.4%), despite the absence of any important differences in education between the 2 samples. Results showed that CGs of children with CP were less likely to report working for pay (CG: 66%; NLSCY: 81.2%), less likely to be engaged in full-time work (CG: 67.5%; NLSCY: 73.2%), and more likely to list caring for their families as their main activity (CG: 37.2%; NLSCY: 28.4%). Measures of support showed no difference in reported social support (CG: mean score: 14.5; SD: 3.4; NLSCY: mean score: 14.3; SD: 2.7) or family functioning (CG: mean score: 8.6; SD: 5.6; NLSCY: mean score: 9.0; SD: 4.9) between the 2 samples, although the CG sample did report a statistically greater number of support contacts (CG: mean score: 4.5; SD: 0.7; NPHS: mean score: 4.2; SD: 0.9). Measures of psychologic health showed greater reported distress (CG: mean score: 4.7; SD: 4.4; NPHS: mean score: 2.2; SD: 2.7), chronicity of distress (CG: mean score: 5.5; SD: 1.4; NPHS: mean score: 5.2; SD: 1.1), emotional problems (CG: 25.3% indicating problems; NPHS: 13.7%), and cognitive problems (CG: 38.8%; NPHS: 14.3%) among CGs of children with CP. They also reported a greater likelihood of a variety of physical problems, including back problems (CG: 35.5% reporting the condition; SE: 2.2%; NLSCY: 12.2%; SE: 0.7%), migraine headaches (CG: 24.2%; SE: 2.0%; NLSCY: 11.2%; SE: 0.7%), stomach/intestinal ulcers (CG: 8.4%;

SE: 1.3%; NLSCY: 1.7%; SE: 0.3%), asthma (CG: 15.8%; SE: 1.7%; NLSCY: 6.3%; SE: 0.5%), arthritis/rheumatism (CG: 17.3%; SE: 1.8%; NLSCY: 7.3%; SE: 0.5%), and experience of pain (CG: 28.8%; SE: 2.1%; NPHS: 11.0%; SE: 0.5), as well as a greater overall number of chronic physical conditions (CG: 24.1% reporting no chronic conditions; NLSCY: 55.2%). CONCLUSIONS: Although many families cope well despite the added challenges of caring for a child with a disability, our findings suggest that the demands of their children's disabilities can explain differences in the health status of parents and that parents of children with CP are more likely to have a variety of physical and psychologic health problems. Many of these findings are consistent with a stress process model, in which stress from caregiving can directly or indirectly affect a variety of measures of health, although some of the findings (asthma and arthritis) seem to strain this hypothesis. Alternate interpretations of these findings include the possibility that parents who are in regular contact with the health care system may have more opportunities to discuss and receive attention for their own health concerns than do comparison adults or that the greater number of health issues reported by CGs is related to the nature of our study, perhaps leading these parents to focus on their health and well-being in more depth than is usually feasible in a population survey. CGs of children with CP also had lower incomes, despite the absence of any important differences in education. The findings are consistent with the idea that the financial burden of caring for a child with a disability results in part from a reduced availability of these parents to work for pay. IMPLICATIONS FOR SERVICE PROVIDERS: Physicians and other health care professionals should be aware of the important relationship between child disability and CG health. Family-centered policies and services that explicitly consider CG health are likely to benefit the well-being of both CGs and their families. Future work should address the extent to which the family-centeredness of services, as experienced by CGs, is associated with better health outcomes for parents and their families.

Bremberg S. *Does an increase of low income families affect child health inequalities? A Swedish case study.* J Epidemiol Community Health. 2003; 57(8) : 584-8.p Abstract: STUDY OBJECTIVE: Reduction of health inequalities is a primary public health target in many countries. A change of proportion of low income families might affect child health inequalities. Yet, the importance of family incomes in high income welfare states is not well established. The aim of this study was to investigate the effect of increased percentage of low income families on child health inequalities during an economic recession in Sweden, 1991-1996. DESIGN: Health inequalities for six health indicators were assessed during the period 1991-1996 and during adjacent periods. Relative inequality indices were estimated according to Pamuk and Mackenback. Appraisal of a child's socioeconomic situation was based on social data for the child's residency area. SETTING: The total population of children and adolescents 0-<19 years old living in Stockholm County, Sweden, was studied. Each one year cohort comprised 20 470-25 420 people. MAIN OUTCOME MEASURES: Mortality; rate of low birth weight; days of hospital care for infections, asthma/allergic disorders, and unintentional injuries; and rate of abortions. Main results: Mortality decreased annually by 6.9%. The average relative inequality index for mortality before the recession was 1.40 and was lower during the recession, 1.14. The remaining five health indicators, and the relative inequality index for these indicators, did not differ significantly between the recession years (1991-1996) and adjacent periods. CONCLUSIONS: Relative health inequalities did not change, or decreased, during the recession years. The findings indicate that the connection was weak between child health inequalities and family incomes, within the frame of time and the range of income changes that occurred during the study period.

Brenner J.S. et al. *Asthma and obesity in adolescents: is there an association?* J Asthma. 2001; 38(6) : 509-15.p Abstract: To determine if obesity is more prevalent in adolescents with asthma

compared with nonasthmatic adolescents and to determine if obesity is associated with more severe asthma, we studied 265 adolescent asthmatics 12-21 years of age and 482 nonasthmatic adolescents. The prevalence of obesity in the asthmatic group was 20% compared to 17% in the control group. The prevalence of being at risk of overweight was similar for asthmatics (16%) and controls (15%). The prevalence of obesity in moderate to severe asthmatics (21%) was not different from prevalence of obesity in mild asthmatics (19%) or controls (17%). In this study of primarily African-American urban adolescents, obesity was not associated with asthma or more severe asthma.

Breyse P. et al. *The relationship between housing and health: children at risk.* Environ Health Perspect. 2004; 112(15) : 1583-8.p **Abstract:** In November 2002, the National Center for Healthy Housing convened a 2-day workshop to review the state of knowledge in the field of healthy housing. The workshop, supported with funds from the U.S. Centers for Disease Control and Prevention's National Center for Injury Prevention and Control and National Center for Environmental Health, was unique in that it focused solely on the effect of housing on children's health and the translation of research findings into practical activities in home construction, rehabilitation, and maintenance. Participants included experts and practitioners representing the health, housing, and environmental arenas. Presentations by subject-matter experts covered four key areas: asthma, neurotoxicants, injury, and translational research. Panel discussions followed the presentations, which generated robust dialogue on potential future research opportunities and overall policy gaps. Lack of consensus on standard measurements, incomplete understanding about the interaction of home hazards, inadequate research on the effectiveness of interventions, and insufficient political support limit current efforts to achieve healthy housing. However, change is forthcoming and achievable. Key words: asthma, childhood exposure, environmental toxicants, healthy housing, lead poisoning.

Broad L.M. et al. *Nurse practitioners and traditional healers: an alliance of mutual respect in the art and science of health practices.* Holist Nurs Pract. 2002; 16(2) : 50-7.p **Abstract:** The indigenous people of Hawaii have had difficulty adapting to the Western diet and stressful lifestyle of today's mixed cultural and economic development. This has left a health toll of high rates of diabetes, hypertension, hypercholesterolemia, cardiovascular problems, asthma, and obesity. To promote a healthy lifestyle and promote the U.S. Department of Health and Human Services (DHHS) goal of 100% access to health care and 0% disparity (no one will be denied health care), nurse practitioner/traditional Hawaiian healing clinics have been placed in community settings, which are known to community people and comfortable to access. These clinics provide health care to uninsured and underinsured people in an atmosphere that assures respect for the culture and the health needs. This pilot study examines the perceptions of 30 residents of Hawaii and the type of provider sought. Seventy-five percent of the respondents were generally satisfied with the health care received from both Hawaiian and Western care providers. Back and neck problems and injuries were associated with the use of Hawaiian therapies and appeared to reflect chronic conditions. Western health care is sought for predominantly acute conditions (infections, allergies, and upper respiratory conditions) and for diabetes and hypertension.

Brody J.L. et al. *Voluntary assent in biomedical research with adolescents: a comparison of parent and adolescent views.* Ethics Behav. 2003; 13(1) : 79-95.p **Abstract:** An informed consent and voluntary assent in biomedical research with adolescents is contingent on a variety of factors, including adolescent and parent perceptions of research risk, benefit, and decision-making autonomy. Thirty-seven adolescents with asthma and their parents evaluated a high or low aversion form of a pediatric asthma research vignette and

provided an enrollment decision; their perceptions of family influence over the participation decision; and evaluations of risk, aversion, benefit, and burden of study procedures. Adolescents and their parents agreed on research participation decisions 74% of the time, yet both claimed ultimate responsibility for the participation decision. Both rated most study procedures as significantly more aversive than risky. Parents were more likely to rate aspects of the hypothetical study as beneficial and to provide higher risk ratings for procedures. Disagreements concerning research participation decisions and decision-making autonomy have implications for the exercise of voluntary assent in biomedical research.

Brouwer C.N. et al. *The impact of recurrent acute otitis media on the quality of life of children and their caregivers.* Clin Otolaryngol. 2005; 30(3) : 258-65.p **Abstract:** **OBJECTIVE:** To assess the quality of life of 384 Dutch children aged 1-7 years with recurrent acute otitis media (AOM), and compare it with that of children from four reference populations: (i) children from a general population; (ii) children with mild-to-moderate asthma, (iii) children with mild-to-moderately severe chronic illness, and (iv) US children with persistent or recurrent otitis media. **DESIGN:** Survey. **SETTING:** A general and an academic hospital (study population of children with recurrent AOM, n = 384); general population (n = 225 and 117); primary care (children with asthma, n = 64); community care (children with chronic illness, n = 82); and a general hospital (children with persistent or recurrent otitis media, n = 169). **PARTICIPANTS:** A total of 384 children aged 1-7 years who had experienced at least two episodes of AOM in the preceding year and their caregivers. **MAIN OUTCOME MEASURES:** Generic and disease-specific quality of life as judged by the children's caregivers. Age-adjusted total and subscale scores were compared with those of the reference populations. **RESULTS:** For all generic questionnaires, children with recurrent AOM had poorer scores than children from the general population. Quality of life of children with four or more episodes of AOM in the preceding year was poorer than that of children with two to three episodes. Children with recurrent AOM scored lower on the health-related questionnaire than children with mild-to-moderately severe chronic illness. Quality of life of the present study population was similar to those of children with asthma and US children with chronic otitis media with effusion or recurrent AOM. **CONCLUSION:** Recurrent AOM has a considerable negative impact on the quality of life of children and causes concern to their caregivers. These effects are proportional to the severity of the condition. Professionals involved in the care of children with OM should be aware that OM not only affects physical functioning but also general well-being of the child and its family. These outcomes should therefore be included in the evaluation of the child with otitis media both in the clinical and research setting.

Brown H.M. *A neglected breakthrough in asthma therapy.* Lancet . 2003; 361(9355) : 433-4.p

Brown J.V. et al. *A home visiting asthma education program: challenges to program implementation.* Health Educ Behav. 2005; 32(1) : 42-56.p **Abstract:** This study describes the implementation of a nurse home visiting asthma education program for low-income African American families of young children with asthma. Of 55 families, 71% completed the program consisting of eight lessons. The achievement of learning objectives was predicted by caregiver factors, such as education, presence of father or surrogate father in the household, and safety of the neighborhood, but not by child factors, such as age or severity of asthma as implied by the prescribed asthma medication regimen. Incompatibility between the scheduling needs of the families and the nurse home visitors was a major obstacle in delivering the program on time, despite the flexibility of the nurse home visitors. The authors suggest that future home-based asthma education programs contain a more limited number of home visits but add telephone follow-ups and address the

broader needs of low-income families that most likely function as barriers to program success.

Brown R. et al. *Physician asthma education program improves outcomes for children of low-income families.* Chest. 2004; 126(2) : 369-74.p
Abstract: STUDY OBJECTIVES: To determine whether an interactive physician seminar that has been shown to improve patient/parent satisfaction and to decrease emergency department visits for children with asthma was also effective for those children from low-income families. DESIGN: Seventy-four pediatricians and 637 of their patients were randomized to receive two asthma seminars or no educational programs and were observed for 2 years. SETTING: Physicians in the New York, NY, and Ann Arbor, MI, areas were enrolled, and, on average, 10 patients with asthma per provider were surveyed and observed for 2 years. PATIENTS OR PARTICIPANTS: A total of 637 subjects were enrolled, and 369 subjects remained in the study after 2 years. Of these, 279 had complete medical and survey information. INTERVENTIONS: Physicians were randomized, and then a random sample of their patients was enrolled and surveyed regarding the physician's communication style, the child's asthma symptoms, medical needs, and asthma care. Low income was defined as annual income of < 20,000 dollars. MEASUREMENTS AND RESULTS: The families of 36 children (13%) had an income of < 20,000 dollars, and they were treated by 23 physicians. Low-income children in the treatment group tended to have higher levels of use of controller medications, to receive a written asthma action plan, and to miss fewer days of school, although these differences were not statistically significant compared to low-income children in the control group. However, low-income treatment group children were significantly less likely to be admitted to an emergency department (annual rate, 0.208 vs 1.441, respectively) or to a hospital (annual rate, 0 vs 0.029, respectively) for asthma care compared to children in the control group. CONCLUSIONS: The educational program for physicians improved asthma outcomes for their low-income patients. Provider interventions targeted to these high-risk patients may diminish hospital and emergency department asthma care.

Brown V. et al. *T cell cytokine profiles in childhood asthma.* Thorax. 2003; 58(4) : 311-6.p
Abstract: BACKGROUND: An imbalance of T cell subsets in asthma with a predominance of Th2 type cells has been proposed. The aim of this study was simultaneously to detect surface markers and intracellular production of cytokines in T cells from the airways of children with and without asthma. METHODS: Bronchoalveolar lavage (BAL) fluid was obtained by wedging a suction catheter into the distal airway immediately before elective surgery. Cells were stimulated with phorbol 12-myristate 13-acetate (PMA) and ionomycin and intracytoplasmic cytokine retention was achieved using monensin. The cells were stained with the relevant antibodies and analysed by flow cytometry. RESULTS: No statistical difference was observed between children with atopic asthma, atopic non-asthmatic subjects, and normal controls in the percentage of CD3+ cells producing interleukin (IL)-2 or IL-4. Interferon (IFN)gamma+ T cells were, however, present in a much higher percentage than either IL-2 or IL-4 positive cells. The percentage of IFNgamma+ T cells was significantly increased in subjects with atopic asthma (median 71.3%, interquartile range (IQR) 65.1-82.2, n=13) compared with both atopic non-asthmatic subjects (51.9%, IQR 37.2-70.3, n=12), p<0.05 and normal controls (58.1%, IQR 36.1-66.1, n=23), p<0.01. CONCLUSIONS: These findings indicate that IFNgamma producing T cells are more abundant in the airways of children with atopic asthma than in atopic non-asthmatic subjects and controls. The proinflammatory activities of IFNgamma may play an important role in the pathogenesis of childhood asthma and may suggest that asthma is not simply a Th2 driven response.

Browne G.J. et al. *The benefits of using clinical pathways for managing acute paediatric illness in an emergency department.* J Qual Clin

Pract. 2001; 21(3) : 50-5.p
Abstract: The aim of this study was to provide an evaluation of the overall effectiveness of using a number of clinical pathways in treating common acute paediatric conditions in an emergency department. This was a before and after study conducted on the effectiveness of three clinical pathways (gastroenteritis, asthma, and croup) in the emergency department of the Children's Hospital at Westmead, conducted over two separate yearly periods January to December 1996 and January to December 1999 representing before and after the introduction of clinical pathways in the emergency department. The main outcomes of the effectiveness of the pathways, namely admission to an in-patient bed, length of hospital stay and re-presentation after discharge from the ED were compared. Other outcomes of interest such as parental satisfaction and patient waiting times were also presented. Any deviation from a key clinical pathway process was reported. A total of 2854 children were managed by a clinical pathway compared to 2680 children managed before clinical pathways were introduced. The admission rate was reduced by threefold (9.1% compared to 23.6%) with a twofold reduction in length of hospital stay (32.7 h compared to 17.5 h). In 3.6% of children using a clinical pathway an unscheduled medical visit or re-presentation to the emergency department occurred after discharge, compared to 4.9% before the use of clinical pathways. No adverse events were reported in these children. In 76 cases deviation from a clinical pathway process was reported. High parental satisfaction was reported for clinical pathways throughout the study. Clinical pathways in this emergency department allowed rapid stabilisation of children, reducing admission rate, with a shortened length of hospital stay and few patients re-presenting after discharge and were well accepted by parents.

Bryant-Stephens T. et al. *Community asthma education program for parents of urban asthmatic children.* J Natl Med Assoc. 2004; 96(7) : 954-60.p
Abstract: OBJECTIVES: To demonstrate the effectiveness of community asthma education provided by peers in the urban community. METHOD: A convenience sample of 267 self-referred, primarily African-American parents or primary caregivers of asthmatic children aged 18 months to 16 years completed a five-session education program. Program efficacy was evaluated at baseline, immediately postinstruction, and at three-, six-, and 12 months retention. Outcomes included three questionnaires measuring asthma self-management knowledge, control and quality of life. RESULTS: Immediately following program completion, participants demonstrated improvements in asthma knowledge (13% increased proportion correct, p < 0.01), ability to control their child's asthma (16% increased score, p < 0.01), and asthma quality of life (7% increased score, p < 0.01). Retention of knowledge with steady improvement of control and quality of life was observed up to one year postinstruction, as compared with immediate postprogram scores (p = 0.09 and 0.05, respectively). CONCLUSIONS: A community-based asthma educational program for caregivers should be an important component of childhood asthma management. The complexities of asthma management are best taught in educational programs that are easily accessible, provide a comfortable environment for participants, and are taught by peers.

Buchvald F. et al. *Exhaled nitric oxide predicts exercise-induced bronchoconstriction in asthmatic school children.* Chest. 2005; 128(4) : 1964-7.p
Abstract: BACKGROUND: Exercise-induced bronchoconstriction (EIB) is of particular importance in children with asthma. It is an important measure of asthma control and should be monitored by exercise testing. However, exercise testing puts a large demand on health-care resources and is therefore not widely used in routine monitoring of pediatric asthma control. The fractional concentration of exhaled nitric oxide (FeNO) also reflects uncontrolled asthma. We hypothesized that FeNO may be used for prescreening of asthmatic children to exclude those with good asthma control unlikely to have EIB, thereby reducing the need for exercise testing. OBJECTIVE: The aim of this study was to estimate

the value of FeNO as a predictor of EIB in asthmatic children. METHODS: Stable outpatient asthmatic school children performed standard exercise challenge tests and measurement of FeNO. RESULTS: FeNO and response to a standardized submaximal exercise test on the treadmill were measured in 111 school children with asthma. EIB could be excluded with a probability of 90% in asthmatic children with FeNO levels < 20 parts per billion (ppb) without current inhaled corticosteroid treatment, and < 12 ppb in children with current inhaled corticosteroid treatment. CONCLUSION: Measurement of FeNO is a simple, and time- and resource-efficient tool that may be used to screen for EIB testing and therefore optimizes the resources for exercise testing in pediatric asthma monitoring.

Buckeridge D.L. et al. *Effect of motor vehicle emissions on respiratory health in an urban area.* Environ Health Perspect. 2002; 110(3) : 293-300.p **Abstract** : Motor vehicles emit particulate matter < 2.5 microm in diameter (PM(2.5)), and as a result, PM(2.5) concentrations tend to be elevated near busy streets. Studies of the relationship between motor vehicle emissions and respiratory health are generally limited by difficulties in exposure assessment. We developed a refined exposure model and implemented it using a geographic information system to estimate the average daily census enumeration area (EA) exposure to PM(2.5). Southeast Toronto, the study area, includes 334 EAs and covers 16 km(2) of urban area. We used hospital admission diagnostic codes from 1990 to 1992 to measure respiratory and genitourinary conditions. We assessed the effect of EA exposure on hospital admissions using a Poisson mixed-effects model and examined the spatial distributions of variables. Exposure to PM(2.5) has a significant effect on admission rates for a subset of respiratory diagnoses (asthma, bronchitis, chronic obstructive pulmonary disease, pneumonia, upper respiratory tract infection), with a relative risk of 1.24 (95% confidence interval, 1.05-1.45) for a log(10) increase in exposure. We noted a weaker effect of exposure on hospitalization for all respiratory conditions, and no effect on hospitalization for nonrespiratory conditions.

Buckmaster A. et al. *Reduce the rads: a quality assurance project on reducing unnecessary chest X-rays in children with asthma.* J Paediatr Child Health. 2005; 41(3) : 107-11.p **Abstract**: OBJECTIVES: To quantify and then reduce the number of unnecessary chest X-rays (CXR) being performed on children presenting with asthma. METHODS: A retrospective review of case notes of all children, aged 1-15 years, who presented with asthma and had a CXR performed. The setting was two General Hospitals that see all children presenting to an emergency department in the region. The period of review was before and after the development and implementation of a simple guide for staff, with an education programme, outlining when CXR were deemed unnecessary (known asthmatic, primary diagnosis asthma, improving with treatment, pneumothorax not suspected, and not in Intensive Care Unit). RESULTS: In the 12 months prior to the education programme, 466 children presented with asthma: 260 had a CXR, of which 211 (81.1%) were unnecessary. During the 6 month period following implementation of the programme 197 presented with asthma: 72 had a CXR, of which 56 (78%) were deemed unnecessary. However the percentage of all children presenting with asthma who had an unnecessary CXR fell from 45.3% (211/466) to 28.4% (56/197); P = 0.00005. There was also a decrease in the admission rate from 46% before to 31% after the period of education. CONCLUSION: This study determined that an unacceptably high rate of unnecessary CXR was being ordered in children presenting to hospital with asthma. It also showed how a clinically and statistically significant reduction in the overall number of CXR could be achieved, through a simple and easy to implement educational programme. Further measures are needed in addition to ongoing education in order to improve on this achievement.

Buckner E.B. et al. *Knowledge, resilience, and effectiveness of education in a young teen asthma camp.* Pediatr Nurs. 2005; 31(3) : 201-7, 210.p **Abstract**: A young teen asthma camp was developed as a 3-day residential experience in a traditional camp setting offering activities such as swimming, canoeing, horseback riding, ropes, course crafts, and games. The overall purpose, goals and plans for the camp experience were developed by a team of nurse educators, nurse practitioners, clinicians (nurses and physicians) with experience in asthma management, and camp directors. Feasibility and outcomes were measured for the camp using materials in the Power Breathing Program for teens developed by the Asthma and Allergy Foundation of America (AAFA) and questionnaires developed by the Consortium of Children's Asthma Camps.

Buetow S. et al. *Reasons for poor understanding of when and how to access GP care for childhood asthma in Auckland, New Zealand.* Fam Pract. 2002; 19(4) : 319-25.p **Abstract**: BACKGROUND: Attempts to explain why some patients lack the understanding needed to access GP care for childhood asthma are uncommon and have tended to be based on reported statistical associations. OBJECTIVES: The aims of this study were to describe and account for poor patient understanding of when and how to access GP care for childhood asthma in Auckland, New Zealand. METHODS: A general inductive approach was used to analyse 29 semi-structured, personal interviews, during March-May 2001, with Auckland key informants selected through maximum variation sampling. Informant checking and the literature supported the text analysis by two independent researchers. RESULTS: Key informants reported wide variations in the extent to which guardians and asthmatic children understand when and how to access GP services. Two sets of barriers to patient understanding were identified. The first limits the willingness of people to seek understanding and the second limits their ability to understand, even if they want to understand. CONCLUSIONS: Use of qualitative methodology was able to reveal barriers to patient understanding. Strategies operating at the GP and system levels were identified to help overcome these barriers.

Buetow S. et al. *Attendance for general practitioner asthma care by children with moderate to severe asthma in Auckland, New Zealand.* Soc Sci Med. 2004; 59(9) : 1831-42.p **Abstract**: Attendance for general practitioner (GP) care of childhood asthma varies widely in New Zealand (NZ). There is little current research to account for the variations, although groups such as Maori and Pacific peoples have traditionally faced barriers to accessing GP care. This paper aims to describe and account for attendance levels for GP asthma care among 6-9 year-olds with moderate to severe asthma in Auckland, NZ. During 2002, randomly selected schools identified all 6-9 year-olds with possible breathing problems. Completion of a questionnaire by each parent/guardian indicated which children had moderate to severe asthma, and what characteristics influenced their access to GP asthma care. A multilevel, negative binomial regression model (NBRM) was fitted to account for the number of reported GP visits for asthma, with adjustment for clustering within schools. Twenty-six schools (89.7 percent) identified 931 children with possible breathing problems. Useable questionnaires were returned to schools by 455 children (48.9 percent). Results indicated 209 children with moderate to severe asthma, almost one in every three reportedly making 5 or more GP visits for asthma in the previous year. Maori, Pacific and Asian children were disproportionately represented among these 'high attendees'. Low attendees (0-2 visits) were mainly NZ Europeans. The NBRM (n=155) showed that expected visits were increased by perceived need, ill-health, asthma severity and, in particular, Maori and Pacific child ethnicity. It may be that Maori and Pacific children no longer face significant barriers to accessing GP asthma care. However, more likely is that barriers apply only to accessing routine, preventative care, leading to poor asthma control, exacerbations requiring acute care, and paradoxically an increase in GP visits. That barriers may increase total numbers of visits challenges the assumption, for all health systems, that access can be

defined in terms of barriers that must be overcome to obtain health care.

Bufe A. et al. *Atopic phenotype in children is associated with decreased virus-induced interferon-alpha release.* *Int Arch Allergy Immunol.* 2002; 127(1) : 82-8.p **Abstract:** BACKGROUND: Interferon-alpha (IFN-alpha) production in humans is an early event in the nonspecific cellular response to viruses and mediates a wide range of antiviral and immunoregulatory activities. Little is known about the role of IFN-alpha in allergic disease. METHODS: In the present study, we performed a retrospective comparative analysis of 88 children with and without an atopic phenotype for virus-induced IFN-alpha production in blood cultures. RESULTS: We were able to demonstrate that patients with allergic asthma (aA) produced significantly lower amounts of virus-induced IFN-alpha than healthy children and patients with nonallergic asthma (naA). Furthermore, the number of eosinophils in atopic children as a marker for allergic inflammation correlated negatively with the IFN-alpha level in blood cultures. Additionally, we found differences between aA and naA patients with respect to the capacity to produce IFN-gamma. Although atopy is thought to be associated with a Th2 cytokine response, in our study, IFN-gamma release was not reduced in the allergic children. In contrast, patients with allergic rhinitis showed a significant increase in IFN-gamma release compared to naA patients. CONCLUSIONS: In our study, an early atopic phenotype was related to a reduction in virus induced IFN-alpha release from blood cultures. Thus, after further prospective evaluation, the IFN-alpha level may serve as an additional in vitro marker for the definition of atopy in children.

Buford T.A. *School-age children with asthma and their parents: relationships with health care providers.* *Issues Compr Pediatr Nurs.* 2005; 28(3) : 153-62.p **Abstract:** Health care providers, including nurses, physicians, and other personnel, are key figures who design and implement plans of care to help families manage childhood asthma, yet families' perceptions of relationships with these professionals has received limited study. Child and parent perspectives about relationships with their health care providers emerged as themes in a study that explored responsibility sharing between school-age children with asthma and their parents (Buford, 2004). Fourteen school-age children with asthma and 14 of their parents from 11 families participated in the study. Parents and, to a lesser extent, children, described aspects of their relationships with their health care providers that were supports or barriers to asthma management. Implications for nurses and other health care providers stem from these data and include the importance for health care providers to educate themselves and their patients about state-of-the-art asthma care. Education should be directed to both parents and their children. In addition, parents need to receive education about how to coach their children because the children depend on them for information and direction. Finally, nurses and other health care providers need to listen to parents and value their input about their children's conditions.

Buford T.A. *Transfer of asthma management responsibility from parents to their school-age children.* *J Pediatr Nurs.* 2004; 19(1) : 3-12.p **Abstract:** This study used grounded theory to explore the process of transfer of responsibility for asthma management from parents to their school-age children. Interviews were conducted with 11 mothers, 2 fathers, 1 grandmother, and their 14 children who were between 8 and 13 years old. Responses revealed that transfer of responsibility within families is a complex, uneven process that occurs over years and involves identifiable stages and transitions. The Theoretical Model for Parent-Child Transfer of Asthma Responsibility emerged from the data. The central concept underlying the process was controlling the situation. Specific cues stimulated changes in parent-child responsibility.

Buhl R. et al. *The anti-IgE antibody omalizumab improves asthma-related quality of life in patients with allergic asthma.* *Eur Respir J.* 2002; 20(5) : 1088-94.p **Abstract:** The aim of the present study was to determine the effect of treatment with omalizumab, an anti-immunoglobulin E antibody, on asthma-related quality of life (AQoL) in patients with moderate-to-severe allergic asthma. A total of 546 patients with allergic asthma were randomised to double-blind subcutaneous treatment with either placebo or omalizumab for 52 weeks. A constant beclomethasone dipropionate dose was maintained during the first 16 weeks (steroid-stable phase). This was followed by a 12-week steroid-reduction phase. The core study was followed by a 24-week double-blind extension phase. AQoL was evaluated at baseline and at the end of the steroid-stable (week 16), steroid-reduction (week 28) and extension phases (week 52) using the Juniper Asthma Quality of Life Questionnaire (AQLQ). Baseline AQLQ scores were comparable for the two treatment groups. Relative to placebo, omalizumab-treated patients demonstrated statistically significant improvements from baseline across all four AQLQ domains, as well as overall AQoL score, at weeks 16 (except environmental exposure), 28 and 52. Patients on omalizumab were also more likely to achieve clinically significant improvements in AQoL during the course of the study. Overall, almost 70% of patients and investigators rated treatment with omalizumab as "excellent/good", compared with approximately 40% of placebo recipients. Clinical studies show that omalizumab enhances disease control whilst reducing corticosteroid consumption in patients with allergic asthma. The results of the present study show that these changes are paralleled by improvements in asthma-related quality of life that are meaningful to such patients.

Bukstein D.A. et al. *A comparison of asthma-related expenditures for patients started on montelukast versus fluticasone propionate as monotherapy.* *Clin Ther.* 2001; 23(9) : 1589-600.p **Abstract:** BACKGROUND: The prevalence of asthma is increasing, and this chronic condition imposes a substantial economic burden worldwide. It is not known whether newer therapies, such as leukotriene receptor antagonists (LTRAs), can ease this burden. OBJECTIVE: This analysis examined the association between choice of first-line asthma control therapy and health care resource utilization and expenditures in patients with mild asthma. METHODS: A retrospective cohort analysis of claims data for patients who started therapy with fluticasone propionate or montelukast between January 1, 1997, and February 28, 1999, was performed, adjusting for baseline differences. RESULTS: Data from 343 patients (229 fluticasone; 114 montelukast) were analyzed. Patients starting therapy with fluticasone were significantly older (33.3 vs 27.6 years; $P = 0.015$) and significantly less likely than patients starting therapy with montelukast to have been started on control therapy by an asthma specialist (52.0% vs 69.3%; $P = 0.007$). There were no significant differences in mean changes in total asthma-related health care expenditures, oral steroid and antibiotic prescriptions, hospitalizations, or emergent care visits. The mean increase in total asthma-related pharmacy expenses was significantly greater for patients who were prescribed montelukast than for those prescribed fluticasone ($P < 0.001$). Treatment adherence was better in patients prescribed montelukast versus fluticasone (5.1 vs 3.1 prescriptions filled per year, respectively; $P < 0.001$). Montelukast patients had a significantly lower increase in the number of beta-agonist prescriptions filled per year than fluticasone patients (0.19 vs 0.66; $P = 0.03$). In the subsequent year, 4% (10/229) of fluticasone patients added or switched to an LTRA. No montelukast patients added to or switched control therapy. CONCLUSION: The mean change in total asthma-related health care expenditures was not significantly different in patients started on fluticasone propionate versus montelukast. Montelukast patients had better adherence to their treatment regimen and required fewer beta-agonist prescriptions, which is an indicator of asthma control and possibly therapeutic effectiveness.

- Bukstein D.A. et al.** "Real-world" effectiveness of daily controller medicine in children with mild persistent asthma. *Ann Allergy Asthma Immunol.* 2003; 90(5) : 543-9.p Abstract: BACKGROUND: Unmeasured confounders and selection bias can significantly influence the results of retrospective observational analyses of asthma therapy. OBJECTIVE: To evaluate the efficacy of oral montelukast and inhaled fluticasone propionate in a randomized, prospective 12-month "real-world" observational analysis of children with mild persistent asthma. METHODS: Children (n = 104) between 6 and 15 years of age with mild asthma as determined by forced expiratory volume in 1 second, symptoms, and evaluation by an experienced pediatric allergist or pulmonologist, who were not currently receiving controller therapy, were randomly assigned to fluticasone or montelukast on an alternating basis. Subjects were asked to complete a questionnaire at 6 and 12 months; otherwise, medical care was identical to that of similar managed care patients. Outcome parameters were evaluated after 12 months by claims database analysis. An acute asthma attack requiring emergent care was the primary outcome parameter. Measures of adherence, symptoms, and asthma control, as measured by the pediatric Asthma Therapy Assessment Questionnaire, were secondary outcome parameters. RESULTS: Demographics, spirometry, symptoms at enrollment, emergent care visits, asthma hospitalizations, routine office visits, and symptoms at study completion were not significantly different between study groups. Adherence, as evaluated by the number of controller fills, was significantly ($P = 0.0003$) better for montelukast (7.65 +/- 3.01) than fluticasone (5.46 +/- 3.01). Similar numbers of subjects in each study group required beta-agonists and oral prednisone. CONCLUSIONS: These results suggest that oral montelukast and inhaled fluticasone have similar real-world efficacies in the treatment of children with mild asthma, possibly as a result of the significantly better adherence with oral montelukast therapy compared with inhaled fluticasone.
- Bullinger M. et al.** *Quality of life in children and families with bleeding disorders.* *J Pediatr Hematol Oncol.* 2003; 25 Suppl 1 : S64-7.p Abstract: Quality of life (QoL) in children and adolescents with bleeding disorders and their families is a relatively new topic. It is important to understand more about QoL in this patient population to evaluate and if necessary to improve the care patients receive. To achieve this aim, a questionnaire to assess patients' QoL in hemophilia was developed and psychometrically tested. Three hundred twenty hemophiliac children and adolescents from six European countries and their families were asked to fill out a questionnaire regarding different aspects of their well-being and functioning, as well as their views on hemophilia care. Generic QoL questionnaires showed that children with hemophilia have a higher QoL than other patients with chronic disease, such as asthma/atopic dermatitis and obesity. Several determinants affected patients' QoL (e.g., number of bleeds, social support). Parents' and children's assessments differed with regard to social and emotional aspects of QoL. The study showed that variations in QoL can be explained by clinical and psychosocial factors and suggested that QoL can be assessed and enhanced both by medical and non-medical (e.g., psychological) interventions.
- Bundy D.G. et al.** *Interpreting subgroup analyses: is a school-based asthma treatment program's effect modified by secondhand smoke exposure?* *Arch Pediatr Adolesc Med.* 2004; 158(5) : 469-71.p
- Burkhart P.V. et al.** *Children's adherence to recommended asthma self-management.* *Pediatr Nurs.* 2002; 28(4) : 409-14.p Abstract: PURPOSE: Adherence to peak expiratory flow rate monitoring by children with asthma was evaluated, and a behavioral strategy to enhance adherence to daily monitoring was tested. DESIGN AND METHODS: Forty-two 7- through 11-year-old children with persistent asthma were recruited into a 5-week randomized, controlled clinical trial. Adherence data were collected electronically by PeakLog and the self-report Asthma Diary. RESULTS: Adherence declined over time. At week 5, intervention group adherence (Median = 79%) was higher than the usual care group adherence (Median = 64%), but the difference was not statistically significant. The effect size did suggest that differences between groups were present. CONCLUSIONS: Even small improvements in adherence to asthma treatment may be clinically significant in light of the alarming increases in asthma morbidity and mortality. Contingency management shows promise for improving adherence outcomes. Future research should engage larger sample sizes and increase the number and intensity of sessions to teach behavioral strategies.
- Burkhart P.V. et al.** *Self-concept and health locus of control: factors related to children's adherence to recommended asthma regimen.* *Pediatr Nurs.* 2005; 31(5) : 404-9.p Abstract: PURPOSE: To determine the relationships of adherence to daily peak expiratory flow rate (PEFR) monitoring, recommended for asthma self-management, with self-concept and health locus of control in a sample of 42 children, ages 7 through 11. DESIGN/METHODS: Secondary analysis was conducted on data collected as part of our 5-week randomized, controlled asthma self-management clinical trial. During the study, the Piers-Harris Children's Self-Concept Scale (PHCSC) and Children's Health Locus of Control Scale (CHLOC) were administered at baseline (Week 1) and Week 5 for comparison, while adherence to electronically-measured peak flow monitor (PFM) was evaluated during Week 5. RESULTS: Adherence was positively correlated with higher self-concept ($r(s) = .33, p = .03$) and internal health locus of control ($r(s) = .30, p = .05$). Adherence to PFM and the intellectual and anxiety subscales of the PHCSC also were positively associated ($r(s) = .38, p = .01$, in both cases). CONCLUSIONS: Children who have a positive self-concept, particularly in the areas of intellect and anxiety, are more adherent to their recommended asthma regimen. Similarly, those who perceive their ability to control their health more positively adhere better to daily PEFR monitoring. These results suggest that children's adherence interventions may need to include components aimed at enhancing self-concept and health locus of control.
- Burkhart P.V. et al.** *An evaluation of children's metered-dose inhaler technique for asthma medications.* *Nurs Clin North Am.* 2005; 40(1) : 167-82.p Abstract: Regardless of the medication delivery system, health care providers need to teach accurate medication administration techniques to their patients, educate them about the particular nuances of the prescribed delivery system (eg, proper storage), and reinforce these issues at each health encounter. A single instruction session is not sufficient to maintain appropriate inhaler techniques for patients who require continued use. Providing written steps for the administration technique is helpful so that the patient can refer to them later when using the medication. The National Heart, Lung, and Blood Institute's "Practical Guide for the Diagnosis and Management of Asthma" recommends that practitioners follow these steps for effective inhaler technique training when first prescribing an inhaler: 1. Teach patients the steps and give written instruction handouts. 2. Demonstrate how to use the inhaler step-by-step. 3. Ask patients to demonstrate how to use the inhaler. Let the patient refer to the handout on the first training. Then use the handout as a checklist to assess the patient's future technique. 4. Provide feedback to patients about what they did right and what they need to improve. Have patients demonstrate their technique again, if necessary. The last two steps should be performed (ie, demonstration and providing feedback on what patients did right and what they need to improve) at every subsequent visit. If the patient makes multiple errors, it is advisable to focus on improving one or two key steps at a time. With improvements in drug delivery come challenges, necessitating that practitioners stay current with new medication administration techniques. Teaching and reinforcing accurate technique at each health care encounter are critical to help ensure medication efficacy for patients with asthma. Since one fifth of children in the study performed incorrect medication technique

even after education, checklists of steps for the correct use of inhalation devices, such as those provided in this article, should be given to patients for home use and for use by clinicians to evaluate patient technique at each health encounter.

Burkhart P.V. et al. *Children's self-reports of characteristics of their asthma episodes.* J Asthma. 2003; 40(8) : 909-16.p Abstract: Our purpose was to examine school-age children's self-reports of characteristics of their asthma episodes including the precipitating events, symptoms experienced during the episodes, and interventions used to resolve the episodes. Children's self-reports of their asthma episodes were assessed over a 6-week period for 42 children with persistent asthma who participated in a randomized, controlled clinical trial to evaluate the efficacy of an asthma self-management program on adherence to recommended daily peak expiratory flow rate monitoring. Children were instructed to answer the following questions on the Asthma Report Form each time they experienced an asthma episode: 1) What were you doing; 2) How did you feel; and 3) What did you do to help your breathing? Of the children, 71% experienced at least one asthma episode during the 6 weeks. There were a total of 206 episodes. Physical activity (51%) was the most cited trigger, cough alone or combined with other symptoms (84%) was the predominant symptom, and rescue asthma medication (59%) was identified most often as the intervention used by the children to resolve the asthma episode. Children's self-reports provided valuable information about their asthma episodes. The finding that most of the children experienced at least one asthma episode during the 6-week period underscores the importance of family education on how to handle asthma episodes effectively at home. Because physical activity was cited most often as a trigger for asthma episodes, families should receive education on preventive steps for averting an asthma episode prior to the child engaging in physical activity.

Burr M.L. et al. *Asthma prevalence in 1973, 1988 and 2003.* Thorax. 2006; 61(4) : 296-9.p Abstract: BACKGROUND: A study was undertaken to see whether the prevalence of asthma has changed since a survey was conducted in 1988, using the same methods that showed an increase during the previous 15 years. METHODS: A survey of 12 year old children was conducted in schools in South Wales where surveys had taken place in 1973 and 1988. The survey comprised a parentally completed questionnaire and an exercise challenge test, performed when no bronchodilator had been recently used. RESULTS: In 1973, 1988, and 2003, questionnaires were obtained for 817, 965 and 1148 children, respectively; the exercise test was performed by 812, 960 and 1019 children, respectively. The prevalence of reported wheeze in the last year rose during each 15 year period (9.8%, 15.2%, 19.7%), with an even steeper rise in reported asthma ever (5.5%, 12.0%, 27.3%). There was a continued increase in wheeze attributed to running, in terms of all children (5.8%, 10.5%, 16.0%) and also as the proportion of those with a history of wheeze (34.1%, 47.0%, 57.3%). The use of inhaled corticosteroids (not available in 1973) increased fourfold between 1988 and 2003. The prevalence of exercise induced bronchoconstriction rose between 1973 and 1988 but had declined by 2003. CONCLUSIONS: The rise in the prevalence of asthmatic symptoms has continued since 1988. This appears to conflict with a reported recent decline, unless asthma prevalence peaked in the 1990s. The decline in exercise induced bronchoconstriction is probably attributable to better control of the disease as more children are now using inhaled corticosteroids as preventive treatment.

Bush A. *Classification of phenotypes.* Pediatr Pulmonol Suppl. 2004; 26 : 30-3.p

Bush A. *Treatment options of asthma in infancy.* Pediatr Pulmonol Suppl. 2004; 26 : 20-2.p

Busse W.W. et al. *Is interleukin-10 a "10" in virus-provoked asthma?* Am J Respir Crit Care Med. 2005; 172(4) : 405-6.p

Butterfoss F.D. et al. *Health planning that magnifies the community's voice: allies against asthma.* Health Educ Behav. 2005; 32(1) : 113-28.p Abstract: Allies Against Asthma, a working group of the Consortium for Infant and Child Health (CINCH), conducted a comprehensive asthma needs assessment in Hampton Roads, Virginia, in 2001. Results from extant data and parent surveys indicated that asthma prevalence was high (15% to 18%), 45% to 50% of children received primary care for asthma in the emergency department, 30% had been recently hospitalized, and most children were not adequately medicated. Focus groups revealed inadequate asthma education, low income, lack of resources and consistent care, disparities in insurance coverage, and noncompliance with national asthma guidelines. An integrated community asthma action plan was developed and funded. Members were satisfied with the planning process--88% felt the plan reflected the needs assessment, and 86% agreed the plan would effectively improve asthma management. Interventions commenced in January 2002. The inclusive process that led to these interventions will ensure that the project is successful and sustainable.

Butz A.M. et al. *Factors associated with preventive asthma care in inner-city children.* Clin Pediatr (Phila). 2004; 43(8) : 709-19.p Abstract: The goal of this cross-sectional study was to determine if the caregiver's quality of life was associated with the child receiving appropriate preventive asthma care (2 or more preventive asthma care visits per year) in a sample of inner-city children with moderate to severe persistent asthma. Our findings confirm that children with moderate to severe persistent asthma are not receiving adequate preventive asthma care despite experiencing frequent asthma symptoms. Having a recent emergency department (ED) visit and increased number of school absences due to asthma were the strongest factors associated with these children receiving guideline-based preventive asthma care. However, for a subgroup of children without recent ED care, we found that low caregiver education level, increased school absences, and decreased caregiver's quality of life, albeit a trend, were associated with the child's receiving adequate preventive asthma care. This suggests that in a subgroup of children receiving adequate preventive care, other issues beyond basic asthma management may need to be addressed.

Butz A.M. et al. *Home-based asthma self-management education for inner city children.* Public Health Nurs. 2005; 22(3) : 189-99.p Abstract: Optimal home self-management in young children with asthma includes accurate symptom identification followed by timely and appropriate treatment. The objective of this study was to evaluate a home-based asthma educational intervention targeting symptom identification for parents of children with asthma. Two hundred twenty-one children with asthma were enrolled into an ongoing home-based clinical trial and randomized into either a standard asthma education (SAE) or a symptom/nebulizer education intervention (SNEI). Data included home visit records and parent's self-report on questionnaires. Symptom identification and self-management skills significantly improved from preintervention to postintervention for parents in both groups with the exception of checking medications for expiration dates and the frequency of cleaning nebulizer device and equipment. However, significantly more parents of children in the SNEI group reported treating cough symptoms as compared with the SAE group ($p = 0.05$). Of concern is that only 38% of all parents reported having an asthma action plan in the home. A targeted home-based asthma education intervention can be effective for improving symptom identification and appropriate use of medications in children with asthma. Home asthma educational programs should address accurate symptom identification and a demonstration of asthma medication delivery devices.

Cabana M.D. *Improving care for asthma.* J Pediatr. 2005; 147(3) : 411-2; author reply 412-3.p

Cabana M.D. et al. *Variation in pediatric asthma quality improvement programs by managed care plans.* Am J Med Qual. 2005; 20(4) : 204-9.p **Abstract:** Although asthma quality improvement (QI) programs are common, little is known about the scope and content of QI initiatives in managed care arrangements. The authors conducted a cross-sectional survey of all managed care plans in Michigan serving the pediatric Medicaid population. Using semi-structured interviews, they assessed the comprehensiveness of the asthma QI program regarding provider, allied health professional, pharmacy, and member services. Although all QI initiatives included some type of physician-directed component and patient-directed components, only half included allied health professionals and one quarter included pharmacy-directed components. Interactive physician continuing medical education was associated with plans whose members were concentrated in only 1 or 2 counties. The authors noted wide variation in content, format, inclusion of incentives, inclusion of other health professionals, and outcome goals. The variation in QI approaches by each of the managed care organizations suggests that there is a dearth of information on appropriate and cost-effective methods to improve pediatric asthma quality at the plan level.

Cabana M.D. et al. *Pediatrician self-efficacy for counseling parents of asthmatic children to quit smoking.* Pediatrics. 2004; 113(1 Pt 1) : 78-81.p **Abstract:** **BACKGROUND:** Although environmental tobacco smoke is a common trigger for asthma exacerbations in children, pediatricians infrequently counsel parents who smoke to quit. High physician self-efficacy, or self-confidence, in the ability to counsel parents about smoking cessation is associated with increased physician screening and counseling on this topic. However, it is not clear which factors are associated with high physician self-efficacy for counseling, such as previous training in smoking-cessation counseling or number of years in pediatric practice. **OBJECTIVE:** To identify factors associated with high levels of physician self-efficacy for 4 skills associated with smoking-cessation counseling. **DESIGN:** Cross-sectional survey. **PARTICIPANTS:** A national random sample of 829 primary care pediatricians. **RESULTS:** The response rate was 55% (457 of 829). The percentage of physicians with high levels of self-efficacy for screening parents and screening patients to identify smokers was 87% and 84%, respectively. The percentage of physicians with high levels of self-efficacy for counseling parents and patients was 59% for both groups. The presence of previous training in smoking-cessation counseling was associated with high levels of self-efficacy for all 4 skills including inquiring about an asthma patient's smoking status (odds ratio [OR]: 3.91; 95% confidence interval [CI]: 1.63, 9.37); inquiring about a parent's smoking status (OR: 2.51; 95% CI: 1.09, 5.75); counseling a patient to quit smoking (OR: 5.30; 95% CI: 3.02, 9.31); and counseling a parent to quit (OR: 4.96; 95% CI: 2.85, 8.61). Years since completion of residency were not associated with high self-efficacy. **CONCLUSIONS:** These findings suggest that formal training in smoking cessation has a significant impact on physician self-efficacy related to smoking cessation throughout a physician's career.

Cabana M.D. et al. *Parental management of asthma triggers within a child's environment.* J Allergy Clin Immunol. 2004; 114(2) : 352-7.p **Abstract:** **BACKGROUND:** Control of environmental precipitants of asthma is an important component of self-management. **OBJECTIVE:** To assess the type and frequency of attempts by families to control environmental precipitants of symptoms and their degree of consistency with current guidelines.

METHODS: We analyzed data from a nationwide sample of 896 children (2-12 years) with asthma. We collected data on insurance, race, sex, income, asthma education exposure, and severity. Parents were asked open-ended questions about their child's asthma triggers and what, if any, actions they took to control these triggers. **RESULTS:** We completed interviews with the parents of 896 of 1077 (83%) eligible patients. Patients had a mean age of 7.2 years, 65% were boys, 13% had Medicaid insurance, 12% were African American, and 31% had persistent asthma. Eighty percent (717/896) of parents could identify at least 1 asthma trigger (mean, 2.2; range, 0-9). Eighty-two percent (582/717) of these parents had attempted an environmental control measure. Of 1788 actions initiated, 916 (51%) were unlikely to be beneficial on the basis of current guidelines. No specific demographic characteristic predicted which parents were more or less likely to institute environmental controls. **CONCLUSION:** In our sample, more than half (51%) of the environmental actions initiated were not specifically endorsed by current guidelines. Improving awareness about recognized methods to address triggers may help families use more effective measures. Clinicians should not assume that they can predict which families will be more or less likely to attempt environmental control, but should provide education regarding effective environmental measures for all families with potentially modifiable asthma triggers.

Cabana M.D. et al. *Limits of the HEDIS criteria in determining asthma severity for children.* Pediatrics. 2004; 114(4) : 1049-55.p **Abstract:** **OBJECTIVE:** Although the Health Plan Employer Data Information Set (HEDIS) is a common method for evaluating the quality of asthma care, its accuracy in characterizing persistent asthma in children is unknown. The objective of this study was to compare the assessment of asthma severity (persistent vs nonpersistent asthma) using the HEDIS criteria versus clinical criteria using National Heart, Lung, and Blood Institute (NHLBI) guidelines. **METHODS:** In a cross-sectional study, we analyzed baseline data from interviews with the parents of 896 children who had asthma and participated in a randomized controlled trial. Patients had an active clinical diagnosis of asthma, were between 2 and 12 years of age, and had no other pulmonary diseases. Patients had persistent asthma by parent report according to the HEDIS criteria when, within the last year, they had 1 asthma inpatient admission or emergency department visit or 4 asthma medication dispensing events, or 4 outpatient asthma visits and at least 2 asthma medication dispensing events. Patients had persistent asthma by parent report according to the NHLBI criteria when, within the last 2 months, they had nighttime asthma symptoms >2 nights/mo or daytime asthma symptoms >2 days/wk. We calculated the sensitivity of each HEDIS criterion, separately and then combined, using the NHLBI criteria as a gold standard. **RESULTS:** On the basis of HEDIS criteria, 656 (73%) patients had persistent asthma, compared with 338 (38%) using NHLBI criteria. Although the HEDIS criteria for persistent asthma were fairly sensitive (0.89), they were not very specific (0.70). For children without daily controller medications (n = 346), the sensitivity was even lower (0.45), but the specificity was similar (0.68). We found that the test characteristics were fairly consistent across different age group strata (2-4, 5-9, and 10-12 years of age). **CONCLUSIONS:** HEDIS criteria used to determine the quality of asthma care should be interpreted with caution. Although the criteria for persistent disease-used to determine which children require daily controller medications-are fairly sensitive, they are not very specific and include children who may not require such medications.

Cabanans R. et al. *Importance of albumin in cross-reactivity among cat, dog and horse allergens.* J Investig Allergol Clin Immunol. 2000; 10(2) : 71-7.p **Abstract:** Different allergenic proteins have been involved in cross-reactivity among animals. Albumins seem to be cross-sensitizing allergenic components. The aim of this study was to assess the importance of albumin as a cross-reactive allergen in patients sensitized to cat, dog and horse. One hundred and seventeen patients sensitized to cat were tested for IgE reactivity using skin

prick tests and RAST assays with cat, dog and horse hair/dander extracts and their purified albumin extracts. RAST-inhibition studies were carried out to assess cross-reactivity among cat, dog and horse and among their purified albumins. It was found that 22% of patients exhibited specific IgE to cat albumin; 41% of patients sensitized to cat were also sensitized to dog and horse. Out of these patients, 21% had IgE to three albumins and 17% to two. Reciprocal inhibitions were observed among cat, dog and horse albumins and also among cat, dog and horse hair/dander extracts, using in the latter experiment sera from patients not sensitized to albumins. IgE binding to horse extract was inhibited 30% by its homologous albumin and IgE binding to cat and dog extracts in almost 15% by their respective albumins. It was concluded that albumins from these three animals share some epitopes that account for the cross-reactivity observed in around one-third of patients sensitized to cat, dog and horse. Nevertheless, more than 50% of specific IgE that cross-reacts among these three animals is directed to allergens other than albumin.

Cabezuelo Huerta G. et al. [Underlying causes of recurrent pneumonia].

An Pediatr (Barc). 2005; 63(5) : 409-12.p Abstract: OBJECTIVE: To determine the relative frequency and describe the predisposing causes of recurrent pneumonia in infants and children aged between 1 month and 14 years. METHODS: We retrospectively reviewed the medical records of a tertiary care pediatric hospital covering a 10-year period, from January 1994 through December 2003. Children with cystic fibrosis were not included in the analysis. Recurrent pneumonia was defined as at least two pneumonia episodes in a 1 year period or at least three episodes over a lifetime. RESULTS: Of 1644 children hospitalized with pneumonia, 106 (6.4 %) met the criteria for recurrent pneumonia. An underlying cause was identified in 92 patients (86.7 %). Of these, the underlying cause was diagnosed prior to pneumonia in 67 (72.8 %), during the first episode in 12 (13 %) and during recurrence in 13 (14.1 %). Underlying causes included asthma in 28 patients (30.4 %), congenital cardiac defects in 27 patients (29.3 %), aspiration syndrome in 25 patients (27.1 %), immune disorder in nine patients (9.7 %), pulmonary anomalies in two patients (2.1 %), and anhidrotic ectodermal dysplasia in one patient (1 %). CONCLUSIONS: Recurrent pneumonia occurred in 6.4 % of all children hospitalized for pneumonia. The underlying cause was identified in 86.7 % of the children. The most common causes were asthma, congenital cardiac defects, and aspiration syndrome.

Cairo C. et al. Analysis of circulating gammadelta T cells in children

affected by IgE-associated and non-IgE-associated allergic atopic eczema/dermatitis syndrome. Clin Exp Immunol. 2005; 141(1) : 116-21.p Abstract: Recent studies have suggested that not only alphabeta(+) T cells, but also the less common gammadelta(+) T cells may play a role as effectors and immunoregulatory cells in the development and perpetuation of allergic inflammation. The objective of this study was to focus on the role of gammadelta(+) T cells in atopic dermatitis (AD), a chronic relapsing inflammatory disease of the skin, often associated with allergic bronchial asthma. The present study employed flow cytometric analysis to compare numbers and phenotypic characteristics of gammadelta(+) T cells in the peripheral blood of children with atopic dermatitis and age-matched healthy controls. The percentage of circulating Vgamma 9Vdelta2(+) T lymphocytes was significantly increased in AD patients with respect to the age-matched controls, with a positive correlation with clinical score severity. The prevalent phenotype in both AD patients and controls was CD45RO(+), with no differences observed in the percentage of Vdelta2(+) CD45RO(+) between these groups. Conversely, memory CD45RO(+) CD62L(+) Vdelta2(+) lymphocytes were significantly lower in AD patients. Furthermore, naive circulating Vdelta2(+) T lymphocytes were significantly lower in AD children than in age-matched controls. No correlation was observed between circulating Vgamma 9Vdelta2(+) expansion and IgE serum levels. It was concluded that an association exists between the levels of circulating gammadelta(+) T lymphocytes and atopic

dermatitis, with a positive correlation with clinical score but no link with IgE serum levels. The pathophysiological role of gammadelta T lymphocytes in atopic dermatitis awaits further investigation.

Calhoun W.J. et al. Asthma variability in patients previously treated with

beta2-agonists alone. J Allergy Clin Immunol. 2003; 112(6) : 1088-94.p Abstract: BACKGROUND: According to national asthma guidelines, asthma severity can be classified as intermittent, mild, moderate, or severe on the basis of lung function, symptoms, nighttime awakenings, and exacerbations. Although it is widely believed that patients might not remain consistently in any given severity category over time, few studies have examined this directly. OBJECTIVE: We sought to assess the variability in disease severity-control among patients with persistent asthma who have not yet received an asthma maintenance treatment. METHODS: We performed an analysis of asthma severity-control over time in placebo-treated patients (n = 85) from 2 randomized, double-blind, 12-week clinical trials in patients with asthma previously receiving beta(2)-agonists alone. Asthma severity-control was assessed on the basis of morning percent predicted peak expiratory flow, albuterol use, and symptoms. RESULTS: At baseline, all patients met the criteria for moderate or severe persistent asthma (mean FEV(1) of 64% of predicted value or albuterol use and symptoms on 4.7 and 6.0 days per week, respectively). The mean percentage of treatment weeks that patients met all criteria for intermittent, mild, moderate, and severe asthma were 9%, 14%, 71%, and 6%, respectively. On the basis of morning peak expiratory flow, patients were classified as having intermittent-mild, moderate, or severe disease on 52%, 41%, and 7% of days, respectively. With regard to days per week with albuterol use or asthma symptoms, patients spent 59% and 45% of weeks, respectively, in the intermittent and mild categories. CONCLUSION: Asthma control cannot be adequately assessed in many patients by using discrete point-in-time assessments of lung function, short-acting beta-agonist use, or asthma symptoms. This might lead to underestimation of disease severity and contribute to inadequate therapy and, ultimately, asthma morbidity.

Callahan C.W. et al. Bronchiectasis in children: orphan disease or persistent problem? Pediatr Pulmonol. 2002; 33(6) : 492-6.p

Abstract: More than a decade ago, bronchiectasis unrelated to cystic fibrosis was termed an "orphan disease", because it had become an uncommon clinical entity among children in the developed world. Bronchiectasis is more common among children in lower socioeconomic classes and in developing countries, presumably due to more frequent and recurrent respiratory infections, environmental airway irritants, poor immunization rates, and malnutrition. Reports from the Southern Pacific and from Alaska Native children reveal persistently high rates of childhood bronchiectasis. Better epidemiologic data throughout the world are needed to reassess the importance of this condition. The pathophysiology includes airway inflammation, mucus production, and regional airway obstruction, yet the reasons why some children develop bronchiectasis while other do not is unclear. The coexistence of asthma with bronchiectasis is associated with more severe disease, yet the impact of asthma therapy in children with both disorders has not been studied. Similarly, the pattern of antibiotic use for children with bronchiectasis varies by region with little data to justify one particular approach. It may be that public health measures aimed at improving living conditions for children and prevention of respiratory infections with antiviral vaccines will have more impact on childhood bronchiectasis than medical treatments in the future.

Callais F. et al. Questionnaire or objective assessment for studying exposure to tobacco smoke among asthmatic and healthy children: The French VESTA Study. Prev Med. 2003; 36(1) : 108-13.p

Abstract: BACKGROUND: The underreporting of environmental tobacco smoke (ETS) exposure by parents of study children may depend on the instrument used and population studied, underlining

the need for questionnaire validation in specific study settings. This study explores the validity of parent-reported ETS exposure in a French multicenter study on asthma. **METHODS:** The study population was composed of 313 children ages 4 to 14 years. Exposure to ETS was evaluated both by questionnaires on recent ETS exposure and by assessment of urinary cotinine by an enzyme immunoassay. **RESULTS:** According to parents' reports, about one-third of children were exposed to ETS within the past 2 days before cotinine measurement, and on average 14.9 +/- 15.4 cigarette-equivalent were smoked in their homes. The mean urinary cotinine was 435 +/- 530 nmol/mol creatinine and increased with the reported number of cigarette-equivalents smoked at home but it did not differ between children registered as being exposed to 1-10 cigarettes and children registered as unexposed. Agreement between questionnaire and urinary cotinine was moderate to poor according to our correlation coefficient (0.22) and kappa coefficient (0.09). **CONCLUSION:** These results show that our questionnaire is not discriminating enough to distinguish between nonexposure and mild exposure, but reveals gradients of higher exposure.

Callery P. et al. *Qualitative study of young people's and parents' beliefs about childhood asthma.* Br J Gen Pract. 2003; 53(488) : 185-90.p
Abstract: **BACKGROUND:** Asthma continues to be a common childhood chronic illness managed principally in primary care. Self-management requires co-ordinated efforts of young people, carers and health professionals. Non-compliance occurs even when parents are supervising care, suggesting that decisions are made on the basis of beliefs that contrast with professional advice. Health professionals therefore need to understand the views of parents (or other carers) and patients to promote good self-management. Little attention has been given to carers' and young people's perspectives on asthma. **AIM:** To gain insights into the beliefs of a group of 25 young people aged nine to 16 years old and their carers about asthma and its management. **DESIGN OF STUDY:** Qualitative study using conversational-style interviews. **SETTING:** Generally deprived urban areas of Greater Manchester. **METHOD:** Interviews were conducted with 25 young people with asthma and separately with their carers. The interviews were analysed using the principles and procedures of grounded theory. **RESULTS:** Carers reported assessing asthma symptoms through observed effects on the child and other family members, including emotions and behaviours that disrupted family life. Young people emphasised the effect of asthma on their everyday lives and in particular the extent to which they appeared different to their peers. Some young people reported continuing symptoms and restrictions of activity that differed widely from the reports of their carers. **CONCLUSION:** Differences between young people's and carers' criteria for assessment suggest explanations for some 'non-compliant' behaviour. Carers' assessment of asthma severity through the absence of acute attacks is consistent with managing asthma as intermittent acute episodes. Professionals should take account of differences between young people's, carers' and professionals' perceptions of asthma.

Calvert J. et al. *Effect of body mass on exercise-induced bronchospasm and atopy in African children.* J Allergy Clin Immunol. 2005; 116(4) : 773-9.p
Abstract: **BACKGROUND:** Sensitization to allergen is common in rural populations in less affluent countries, but atopic disease is less frequent than in richer countries. Variables explaining this dichotomy may provide insight into underlying mechanisms of atopic diseases like asthma. **OBJECTIVE:** To test whether risk of exercise-induced bronchospasm (EIB) in urbanized African populations is increased in association with greater skin sensitivity or increased body mass. **METHODS:** A total of 3322 children were enrolled in a prevalence survey of EIB in urban and rural South Africa. Children responding positively to an exercise challenge and a random sample of children responding negatively were recruited into a case-control study (393 controls, 380 cases). Subjects were investigated by using allergen skin prick testing, anthropometry, and assay of IgE. Stools were analyzed for parasite

infestation. **RESULTS:** The prevalence of EIB was higher in urban (14.9%) than rural (8.9%) areas ($P < .0001$). The difference in risk of EIB between urban and rural subjects was associated with atopy (odds ratio [OR] for upper tertile of skin wheal diameter, 2.65; 95% CI, 1.43-4.89; $P < .0001$), increasing weight (OR for upper tertile of body mass index [BMI], 2.17; 95% CI, 1.45-3.26; $P = .001$), and affluence. Increasing BMI was also associated with a greater strength of association between specific IgE and the corresponding skin test (Dermatophagoides pteronyssinus, OR for a positive skin test result in presence of specific IgE: heavier subjects, OR, 34.6; 95% CI, 0.9-109.3; $P < .0001$; lighter subjects, OR, 8.05; 95% CI, 2.74-23.6; $P < .001$). **CONCLUSION:** Increases in BMI of rural children in subsistence economies may lead to an increased prevalence of atopic disease. This observation merits further investigation in prospective studies.

Campbell N. et al. *Anesthetic management of a parturient with Ehlers Danlos syndrome type IV.* Can J Anaesth. 2002; 49(5) : 493-6.p
Abstract: **PURPOSE:** To describe the anesthetic management of a parturient with Ehlers Danlos syndrome (EDS) type IV. **Clinical features:** A 29-yr-old pregnant woman with EDS type IV was seen in the Obstetric Anesthesia Pre-assessment Clinic at 30 weeks gestation. She had a history of vertebral artery dissection, resulting in a transient neurological deficit at 22 yr of age. She had a normal vaginal delivery with continuous epidural analgesia for the delivery of her first child at 27 yr of age, before the diagnosis of EDS was made. Recent fibroblast culture demonstrated the production of abnormal procollagen type III, which is pathognomonic for EDS type IV. The patient and obstetrician preferred a repeat vaginal birth with instrumental delivery in the second stage. Analgesia for labour and delivery was provided with a continuous epidural infusion of ropivacaine and fentanyl. She delivered a healthy female infant with the use of outlet forceps, without complications. **CONCLUSION:** A pre-delivery, multidisciplinary, individualized management plan is required in patients with EDS, a rare disease with variable clinical features. In the case described, continuous epidural analgesia was effective and associated with excellent maternal and fetal outcomes.

Can D. et al. *Immediate adverse reactions to immunotherapy.* J Investig Allergol Clin Immunol. 2003; 13(3) : 177-80.p
Abstract: **BACKGROUND:** Immunotherapy, which has been used since the beginning of this century, has potential adverse reactions. The purpose of this study was to evaluate immediate local and systemic reactions to allergen immunotherapy and to compare rates of adverse reactions to aluminum-adsorbed versus calcium-adsorbed allergen vaccines. **METHODS:** 108 cases (38 girls and 70 boys) were given allergen immunotherapy between 1997 and 2001. The following data were recorded for each patient: primary disease being treated (allergic rhinitis, asthma, or allergic rhinitis and asthma), allergic sensitivities (dust mite or grass pollen), number of injections, the stage of immunotherapy (buildup or maintenance), dilution of allergen vaccine, and type of allergen vaccine (calcium- or aluminum-adsorbed). Adverse reactions were classified as systemic or local. Local reactions were classified as hyperemia and induration less than 5 cm, more than 5 cm, itching, and pain. **RESULTS:** 4783 injections were evaluated in 108 subjects with allergic rhinitis (44%), asthma (40%), allergic asthma, and rhinitis (16%). Frequency of immediate systemic reaction was 0.13%. Frequency of immediate local reactions were: hyperemia and induration less than 5 cm 3%, greater than 5 cm 0.16%, local itching 0.15%, and local pain 0.2%. There was no significant difference in systemic and local reactions between calcium- and aluminum-adsorbed vaccines. Immediate local reactions were more frequent during maintenance therapy compared to buildup. Subjects were more likely to have local reactions during maintenance therapy if they had allergic rhinitis ($p < 0.05$) or were receiving grass pollen vaccine ($p < 0.01$). **CONCLUSION:** Immediate adverse reactions were uncommon when given to children with asthma and allergic rhinitis. Aluminium- and calcium-adsorbed

allergen vaccines showed similar rates of systemic and local reactions.

Candelaria P.V. et al. *Association between asthma-related phenotypes and the CC16 A38G polymorphism in an unselected population of young adult Danes.* *Immunogenetics.* 2005; 57(1-2) : 25-32.p
Abstract: The gene for Clara cell 16-kDa (CC16) protein is a promising candidate for asthma susceptibility. The CC16 38A allele has been associated with decreased CC16 plasma levels and increased incidence of asthma in Australian children. To date these results have not been replicated in adults. Therefore, potential links between CC16 A38G, asthma and atopy were investigated in an unselected population of young adult Danes. Four hundred sixty-four Danes, aged 19-29 years, from Copenhagen participated in an asthma and allergy phenotype-genotype study. Genotyping was done by Sau96I restriction digestion of PCR products spanning the A38G polymorphism. Potential A38G genotype and asthma-related phenotype associations were investigated using regression analysis, adjusting for potential confounders where appropriate. Adults with the 38AA genotype had higher odds of current asthma (OR 3.2, $P=0.013$) and ever asthma (OR 2.2, $P=0.045$) compared with those with the 38GG genotype. Adjusting for atopy had minimal effect on this relationship. A positive linear trend was evident between the 38A allele and atopic dermatitis (OR 1.67, $P=0.02$). No associations were found between the A38G polymorphism and rhinitis, atopy, forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), airway responsiveness (AR) to histamine or peripheral blood eosinophil level (PBEL). An atopy-independent association between CC16 38AA and asthma prevalence was identified, suggesting the CC16 38A allele predisposes to adult asthma independent of Th1/Th2 processes. This finding is consistent with previous studies in children, but is the first reported association between CC16 A38G and asthma in adults. CC16 38A also displayed a positive linear trend with atopic dermatitis.

Cantani A. et al. *Epidemiology of passive smoke: a prospective study in 589 children.* *Eur Rev Med Pharmacol Sci.* 2005; 9(1) : 23-30.p
Abstract: **BACKGROUND:** Several studies have found that in children of smoking parents there is an increased incidence of respiratory illnesses and diminished pulmonary function. In infants of smoking atopic parents IgE levels are higher, atopic symptoms start earlier, and children are more likely to wheeze if the mother smokes than if she does not. Maternal smoking of 0.5 packs or more/day was identified as a risk for asthma developing in the 1st year of life. Among the environmental measures of our prevention program there is an absolute prohibition of smoking in the house of a "at risk" baby. **MATERIALS AND METHODS:** We have studied 289 atopic children, 169 males and 120 females, aged 3.5 to 7.5 years, attending our Division because affected by respiratory allergy. We have asked their parents if they smoked and if there were smoking relatives in their homes, independently of the number or the packs of cigarette smoked. The parents of 300 children comparable for age and sex visiting our outpatient clinic for non respiratory disease served as controls. **RESULTS:** Smokers were 175 fathers and 109 mothers of the asthmatic children and 153 fathers and 89 mothers of the controls. **DISCUSSION:** Analysis of data shows that passive smoking is significantly associated with the development of asthma in atopic children, and that males are more at risk than females. We stress that a high number of asthmatic children have atopic, and asthmatic parents. Cigarette smoke is not only a triggering factor of respiratory allergy in babies at risk of atopy, but especially an additional genetic factor, since asthma can be more easily provoked if an atopic parent smokes (more if both parents smoke), and even in children of not atopic, smoking parents.

Cap P. et al. *Gas chromatography/mass spectrometry analysis of exhaled leukotrienes in asthmatic patients.* *Thorax.* 2004; 59(6) : 465-70.p
Abstract: **BACKGROUND:** Leukotriene-like immunoreactivity has

been detected in exhaled breath condensate (EBC), but definitive evidence for the presence of leukotrienes (LTs) in this biological fluid is not available. A study was undertaken to determine whether LTC₄(4), LTD₄(4), LTE₄(4), and LTB₄(4) are measurable in EBC by gas chromatography/mass spectrometry and to quantify exhaled LTs in adults and children with asthma and in control subjects. **METHODS:** Twenty eight adults and 33 children with mild to moderate persistent asthma treated with inhaled corticosteroids and age matched healthy controls (50 adults and 50 children) were studied. LTB₄(4), LTC₄(4), LTD₄(4), and LTE₄(4) in EBC were measured by gas chromatography/mass spectrometry. **RESULTS:** LTD₄(4), LTE₄(4), and LTB₄(4) were detectable in all samples. Concentrations of LTC₄(4) in EBC were either close to or below the detection limit of 1 pg/ml. Median exhaled LTD₄(4), LTE₄(4), and LTB₄(4) concentrations in asthmatic adults were increased 4.1-fold ($p<0.001$), 1.8-fold ($p<0.01$), and 2.6-fold ($p<0.001$), respectively, compared with values in healthy adults. Median exhaled LTD₄(4), LTE₄(4), and LTB₄(4) concentrations in asthmatic children were increased 2.8-fold ($p<0.001$), 1.3-fold ($p<0.001$), and 1.6-fold ($p<0.001$), respectively, compared with those in healthy children. In patients with asthma there was a correlation between exhaled LTD₄(4) and LTE₄(4) in both adults ($r = 0.87$, $p<0.0001$) and children ($r = 0.78$, $p<0.0001$). **CONCLUSIONS:** Gas chromatography/mass spectrometry can be used to accurately quantify exhaled LTs which are increased in asthmatic adults and children compared with controls.

Cardona I. et al. *A pilot survey of beta2-agonist inhaler availability for children with asthma during organized sporting events.* *Ann Allergy Asthma Immunol.* 2004; 92(3) : 340-3.p
Abstract: **BACKGROUND:** One of the main stimuli that cause asthma exacerbations in children is physical activity, and exercise-induced bronchospasm (EIB) occurs in most asthmatic patients. **OBJECTIVE:** To investigate the level of preparedness for a potential EIB event in suburban children involved in recreational sports. **METHODS:** A cross-sectional study, focusing on children 12 years and younger, who participated in Little League baseball or soccer in Lower Merion Township, PA, was conducted by clinical survey. The survey was performed during a face-to-face encounter with the parent or caretaker of the child. **RESULTS:** Five hundred seventy-nine children 12 years and younger were surveyed. The parents or caretakers of 80 reported a history of asthma, indicating a prevalence of 14%. Only 18 (22%) of these children with asthma were reported to have a rescue medicine readily available. The 95% confidence interval was 14.22% to 33.47%, indicating that we can be 95% certain that the true population with rescue medication lies between 14% and 33%. **CONCLUSIONS:** Despite having been diagnosed as having asthma, more than 75% of children surveyed were unprepared for an EIB event. Measures should be explored to improve the quality of care of asthmatic children involved in community sports. We also propose that it may be beneficial for first-aid kits to include a beta2-agonist bronchodilator.

Cardwell C.R. et al. *A meta-analysis of the association between childhood type 1 diabetes and atopic disease.* *Diabetes Care.* 2003; 26(9) : 2568-74.p
Abstract: **OBJECTIVE:** To review the published literature and perform a meta-analysis summarizing the evidence in support of an inverse association between type 1 diabetes and the atopic disorders: asthma, eczema, and allergic rhinitis in children. **RESEARCH DESIGN AND METHODS:** MEDLINE, Web of Science, and PubMed were searched to identify relevant studies. These were assessed on quality criteria, and odds ratios (ORs) and 95% CIs were calculated for each study from the reported prevalences of atopy in children with diabetes and in control children. Meta-analysis was then used to derive a combined OR and test for heterogeneity in findings between studies. **RESULTS:** Twenty-five studies were identified. Heterogeneity in the findings from different studies was evident but was considerably reduced when the asthma and rhinitis analyses were restricted to those studies judged to be of adequate design. The meta-analysis revealed an

inverse association between asthma and type 1 diabetes, but the finding only attained significance when analysis was restricted to the studies of adequate design (OR 0.82, 95% CI 0.68-0.99). In this subset an association of similar magnitude was observed between eczema and type 1 diabetes (0.82, 0.62-1.10) although this failed to attain statistical significance, and heterogeneity between studies was still present. There was little evidence of an association between rhinitis and type 1 diabetes (0.97, 0.82-1.16) in this subset of studies. **CONCLUSIONS:** Our analysis suggests that there is a small but significant reduction in the prevalence of asthma in children with type 1 diabetes, but the findings for the other atopic diseases are less conclusive.

Carinanos P. et al. *Pollen allergy related to the area of residence in the city of Cordoba, south-west Spain.* J Environ Monit. 2002; 4(5) : 734-8.p **Abstract:** The aim of this study was to analyse the relationship between the distribution of hay-fever patients in the city of Cordoba, south-western Iberian Peninsula, and the specific atmospheric biological content originating from local sources. Four different districts were established in the metropolitan area of the city, according to vegetational and urbanistic characteristics. Air samples were taken in each area using portable Hirst-type samplers (Lanzoni VPPS 1000) and the spectrum of biological content was defined. Patients attending the Allergy Unit at Cordoba Teaching Hospital in 2000 with allergic rhinitis and/or asthma, and displaying a positive reaction to aeroallergen extracts, were distributed within the areas as a function of their district of residence. Aerobiological results revealed differences in pollen content between areas, in terms of both quantity and number of pollen types recorded. These differences were largely due to proximity to rural areas, prevalence of pollen from typically urban species and the possible effect of urban architecture as a barrier to the dispersal/ concentration of particles and other pollutants. Patients were not uniformly distributed within the city. The majority lived in districts in which pollen from rural species was mixed with pollen from ornamentals. Patients living in typically urban districts displayed a higher prevalence of allergy to pollen from ornamentals. It is concluded that a high degree of exposure to the same environment may influence the development of sensitisation to the particular pollen load associated with that area.

Carl J.C. et al. *Comparison of racemic albuterol and levalbuterol for treatment of acute asthma.* J Pediatr. 2003; 143(6) : 731-6.p **Abstract:** **OBJECTIVE:** To determine whether levalbuterol resulted in fewer hospital admissions than racemic albuterol when used for treatment of acute asthma. **Study design** A randomized, double-blind, controlled trial was conducted in the emergency department (ED) and inpatient asthma care unit of an urban tertiary children's hospital. Children age 1 to 18 years (n=482) provided a total of 547 enrollments. Patients received a nebulized solution of either 2.5 mg racemic albuterol or 1.25 mg levalbuterol every 20 minutes (maximum six doses). Patients admitted to the asthma care unit were treated in a standardized fashion by using the same blinded drug assigned in the ED. Hospitalization rate was the primary outcome. **RESULTS:** Hospitalization rate was significantly lower in the levalbuterol group (36%) than in the racemic albuterol group (45 %, P=.02). The adjusted relative risk of admission in the racemic group compared with the levalbuterol group was 1.25 (95% confidence interval, 1.01-1.57). Hospital length of stay was not significantly shorter in the levalbuterol group (levalbuterol, 44.9 hours; racemic albuterol, 50.3 hours; P=.63). No significant adverse events occurred in either group. **CONCLUSIONS:** Substituting levalbuterol for racemic albuterol in the ED management of acute asthma significantly reduced the number of hospitalizations.

Carlsen K.C. et al. *The efficacy and safety of fluticasone propionate in very young children with persistent asthma symptoms.* Respir Med. 2005; 99(11) : 1393-402.p **Abstract:** We aimed to evaluate the efficacy and safety of fluticasone propionate (FP) in children aged

12-47 months with recurrent/persistent asthma symptoms. One hundred and sixty children (12-47 months) were randomised into this multicentre, double-blind, placebo-controlled, parallel-group study, and treated with either FP (100 microg bd) or placebo (2 puffs bd), both administered by metered-dose-inhaler and Babyhaler for 12 weeks. The primary endpoint was percentage of symptom-free 24h periods. Over weeks 1-12, FP-treated patients had significantly more percentage symptom-free 24-h periods compared with placebo (odds ratio 0.53; 95% CI 0.29-0.95; P = 0.035). Relative to baseline, where all patients were symptomatic for at least 21/28 days of the run-in, the improvement equated to one additional symptom-free 24 h period per week. FP patients also had a significantly higher percentage of 24 h periods with no wheeze or cough, the odds ratio for treatment difference corresponding to two additional wheeze-free and one additional cough-free periods per week. FP was well-tolerated, with similar reported adverse events in both groups. Urinary cortisol-creatinine ratio was slightly decreased among FP patients after 12 weeks, but with no clinical correlates. FP is effective for the treatment of chronic persistent asthma symptoms in very young children.

Carlsen K.H. *Inhaled steroids and local side-effects.* Allergy . 2001; 56(10) : 925-7.p

Carra S. et al. *Budesonide but not nedocromil sodium reduces exhaled nitric oxide levels in asthmatic children.* Respir Med. 2001; 95(9) : 734-9.p **Abstract:** Exhaled nitric oxide (ENO) has been proposed as a marker of airway inflammation in asthma and could be useful to evaluate the response to anti-inflammatory treatment. We investigated the effect of budesonide and nedocromil sodium on ENO levels and lung function in asthmatic children. Twenty stable steroid-naïve asthmatic children were randomized in a single blind, cross-over study to receive inhaled budesonide (group A) or nedocromil sodium (group B) for 6 weeks. ENO was measured with a chemiluminescence analyser at baseline and at the end of each treatment period. Repeated-measures ANOVA was carried out. In asthmatic baseline ENO levels [mean 32.5 ppb, 95% confidence interval (CI) 26.4 to 38.7] were significantly higher compared to reference values (8.7 ppb, 95% CI 8.1 to 9.2, P<0.001). There were no treatment-order effect, no carry-over effect and in both groups the response pattern was the same: budesonide significantly lowered ENO levels from 41.0 ppb to 22.8 ppb in group A (mean, P<0.01) and from 22.6 ppb to 13.0 ppb in group B, (mean, P<0.05), while nedocromil did not reduce ENO values (from 24.4 ppb to 22.6 ppb in group B and from 22.8 ppb to 38.0 ppb in group A, mean, P = NS and P<0.01 respectively). After budesonide treatment ENO values of asthmatics were still significantly higher than in healthy children The baseline values of FEV1 and FEF(25-75) were normal in both groups and no significant changes were observed during the study. In conclusion, our study shows that budesonide, but not nedocromil sodium, significantly reduces ENO levels in stable asthmatic children even in absence of changes in the lung function.

Carranza Rosenzweig J.R. et al. *The relationship between health-related quality of life, lung function and daily symptoms in patients with persistent asthma.* Respir Med. 2004; 98(12) : 1157-65.p **Abstract:** It is generally believed that there is a direct correlation between asthma control and a patient's health-related quality of life (HRQL). Objective and subjective measures of asthma control are used interchangeably. A retrospective analysis from 8994 patients from 27 randomized, controlled clinical trials with persistent asthma was conducted to determine the degree of association which exists between objective (lung function) and subjective (symptoms, quality of life) measures. Assessments were made via forced expiratory volume in 1-second (FEV1), self-reported symptoms and the Asthma Quality of Life Questionnaire (AQLQ) overall scores. Baseline percent predicted FEV1 was weakly correlated with baseline symptom-free days (SFD) and baseline overall AQLQ scores (r=-0.11 and 0.09, respectively; P <0.001). Changes in percent predicted

FEV1 correlated weakly with changes in SFD but was more strongly correlated with changes in overall AQLQ scores ($r=0.26$ and 0.38 , respectively; $P < 0.001$). Additionally, SFD at both baseline and endpoint were moderately correlated with overall AQLQ scores at baseline and endpoint ($r=0.36$ and 0.44 ; $P < 0.001$). This study suggests that the impact of asthma on a patients' HRQL is not fully accounted for by objective measures such as lung function. Thus, HRQL data complements rather than duplicates results from traditional, objective assessments of asthma control.

Carraro S. et al. *Acid-base equilibrium in exhaled breath condensate of allergic asthmatic children.* Allergy. 2005; 60(4) : 476-81.p **Abstract:** BACKGROUND: The dysregulation of airway pH control may have a role in asthma pathophysiology. The measurement of exhaled breath condensate (EBC) pH and ammonia levels may be used as a noninvasive method to study acid-base status in the airway of asthmatics. METHODS: Exhaled breath condensate from 29 allergic stable asthmatic children and 13 healthy controls was collected by cooling exhaled air during tidal breathing. Ammonia was measured by high-performance liquid chromatography with fluorescence detection. pH was measured after deaeration of EBC samples by bubbling with argon. The children also underwent FENO measurement. RESULTS: Both pH and ammonia values in EBC were significantly lower in the asthmatics than in the control group [pH: ICS-treated (median and interquartile range) 7.70 (7.62-7.74), steroid-naive 7.53 (7.41-7.68), controls 7.85 (7.80-7.90), $P < 0.01$ and $P < 0.001$, respectively; ammonia: ICS-treated 476.17 microM (282.50-594.80), steroid-naive 253.24 microM (173.43-416.08), controls 788.30 microM (587.29-1310.39), $P < 0.05$ and $P < 0.001$, respectively]. Both pH and ammonia values were higher in ICS-treated than in steroid-naive asthmatic children. There was a significant correlation between EBC pH and ammonia concentrations. CONCLUSIONS: These data show that EBC pH values of stable asthmatic children are lower compared with those of healthy controls and positively correlated with ammonia concentrations, supporting the hypothesis that airway acidification may have a role in the pathobiology of allergic asthma.

Carroll W.D. et al. *Regional variation of airway hyperresponsiveness in children with asthma.* Respir Med. 2005; 99(4) : 403-7.p **Abstract:** Families with asthmatic children were recruited to take part in a multi-centre collaborative study into the genetics of asthma. Detailed phenotypic information was collected on all family members including: lung function, anthropomorphic measurements, response to methacholine challenge, skin prick testing, serum IgE measurements and a detailed nurse-administered questionnaire. Families were eligible for entry into the study if they had two children with a doctor-diagnosis of asthma. Bennett/Twin nebulisers were supplied to each centre from a single source and these were calibrated to determine gravimetric nebuliser output prior to use. Asthmatic probands from each centre had similar degrees of asthma severity and atopy. There was no significant difference in the sex ratios or ages of the probands or numbers of parents with a history of smoking in the families recruited at each centre. However, there was a significant difference in the number of children with airway hyperresponsiveness, with 90% of the North Staffordshire group but only 60% of the Sheffield group having a PC20 of < 8 mg/ml for methacholine. This difference highlights the difficulty of using families from different centres in genetic and epidemiological studies.

Carter E.R. et al. *Changes in asthma prevalence and impact on health and function in Seattle middle-school children: 1995 vs 2003.* Ann Allergy Asthma Immunol. 2005; 94(6) : 634-9.p **Abstract:** BACKGROUND: The prevalence of asthma has increased during the past several decades but may have stabilized during the last 5 years. It is not known whether the functional and health impact of asthma has decreased during the past decade. OBJECTIVE: To evaluate

changes during a recent 8-year period in the prevalence and health and functional impact of current asthma symptoms in young teenagers. METHODS: In 1995 and 2003, 2,330 and 2,397 middle-school students from Seattle, WA, respectively (median age, 13 years), completed written surveys and answered questions pertaining to 4 wheezing or asthma video scenarios. Children were categorized as having physician-diagnosed current asthma (wheeze in the past year and a physician diagnosis of asthma), undiagnosed current asthma symptoms (wheeze in the past year without a physician diagnosis), or no asthma. Outcome measures were the prevalence of asthma and undiagnosed asthma symptoms and the differences between years in respiratory-associated functional impairment (exercise limitation, missed school, disrupted sleep) and health impact (physician visits, wheeze-limited speech). RESULTS: The prevalence of physician-diagnosed current asthma increased from 1995 to 2003 (3.0% to 6.2%), whereas that for undiagnosed current asthma symptoms decreased (12.0% to 6.2%). The degree of functional and health impairment was similar between the 2 study periods for each subgroup and was highest in the children with physician-diagnosed current asthma. CONCLUSIONS: The prevalence of current asthma symptoms in middle-school children from Seattle decreased slightly between 1995 and 2003, whereas the diagnosis of asthma increased. However, the health and functional impact of asthma did not diminish. Asthma is being diagnosed more often, but many children with asthma are still not achieving good asthma control.

Castro Almarales R.L. et al. *Correlation between skin tests to Dermatophagoides pteronyssinus, Dermatophagoides siboney and Blomia tropicalis in Cuban asthmatics.* Allergol Immunopathol (Madr). 2006; 34(1) : 23-6.p **Abstract:** BACKGROUND: Dermatophagoides pteronyssinus, Dermatophagoides siboney and Blomia tropicalis are the most important allergenic mites in Cuba. The aim of this study was to determine the degree of polysensitization and correlation of the skin prick test (SPT) reaction size to these mites in asthmatic patients. METHODS: A total of 232 adult patients with asthmatic symptoms caused by house dust and positive SPT to at least one mite were included. Standardized allergenic extracts were used in SPT. RESULTS: A total of 88.4% of patients were positive to D. siboney, 87.1% to D. pteronyssinus, and 68.1% to B. tropicalis. Sensitization to Dermatophagoides species was predominant, demonstrated by the fact that 31.9% of patients showed positive SPT to either D. siboney or D. pteronyssinus only, whereas only 5.6% was sensitized solely to B. tropicalis. Nevertheless, most patients (58.6%) were polysensitized to the 3 species. The mean wheal size produced by the different allergens in positive patients was similar (n.s. $p > 0.05$). Reaction size was strongly correlated ($r = 0.71$, $p = 5.3 \times 10^{-09}$) between D. siboney and D. pteronyssinus, whereas no significant correlation was found between D. pteronyssinus or D. siboney and B. tropicalis. CONCLUSIONS: The results of this study support the need to include the 3 allergens in diagnostic panels and for combined allergen-specific immunotherapy.

Castro M. *Near-fatal asthma: what have we learned?* Chest. 2002; 121(5) : 1394-5.p

Castro M. et al. *Risk factors for asthma morbidity and mortality in a large metropolitan city.* J Asthma. 2001; 38(8) : 625-35.p **Abstract:** Morbidity and mortality due to asthma continues to increase despite advances in understanding the pathophysiology and treatment of the disease. We evaluated the potential risk factors for asthma morbidity and mortality in a large metropolitan city (St. Louis, MO) using small area geographic analysis. We found that the risk of hospitalization for children with asthma was 8.4 times greater (95% confidence interval [CI] 7.0-9.9) in lower socioeconomic zip code areas and 5.3 times greater (95% CI 4.7-5.9) in those zip codes with a higher percentage of African Americans. Similarly, the risk of death due to asthma was 6.4 times greater in the lower socioeconomic zip

code areas (95% CI 3.4-12.1). Lower socioeconomic status and African American race are strong risk factors for hospitalization and mortality from asthma. Public policy and healthcare resources need to be organized and directed more efficiently to this population.

Catov J.M. et al. *Asthma home teaching: two evaluation approaches.* Dis Manag. 2005; 8(3) : 178-87.p **Abstract:** The aim of this research was to measure the impact of home-based teaching on reducing asthma admissions and emergency department (ED) visits for Medicaid-managed care patients utilizing two different study design methods. This was an historical-prospective study utilizing health plan administrative data, including membership files and medical claims. We identified 381 patients aged 2-56 with hospitalizations or ED visits for asthma. These high risk asthma members were recruited for a home-based teaching program to prevent future hospitalizations or ED visits. We evaluated program effectiveness using two quasi-experimental research designs: a "one-group pre/post-test design," where enrolled members served as their own control, and a more rigorous "untreated control group design with pre/post test," where results for enrolled members and a similar control group were compared pre/post test. Poisson regression models were used to investigate the dependence of member rates for asthma-related events on program enrollment, age, sex, race, and geographic region. Using the pre/post test design, members enrolled in the home-based teaching program demonstrated statistically significant reductions in hospital admissions and ED visits ($p < 0.001$). The untreated control group design, however, found no association between utilization and enrollment in the home-based teaching program ($p = 0.510$). Small differences were detected for subgroups. A marginally statistically significant impact of the program was found for Whites, but not for Blacks. The quasi-experimental design that utilized an external control group provided an approach that more accurately explained true disease management program impact. In addition, this approach allowed for subgroup analyses to detect opportunities for program improvement.

Cayce K.A. et al. *Healthcare utilization for acute and chronic diseases of young, school-age children in the rural and non-rural setting.* Clin Pediatr (Phila). 2005; 44(6) : 491-8.p **Abstract:** To determine the most frequently diagnosed conditions among rural and non-rural children age 5 to 9 and assess for environmental influences, data from the National Ambulatory Medical Care Survey (1996-2001) were used to examine frequencies of diagnoses in children age 5 to 9. Separately, we examined rural and non-rural outpatient physician visits in weighted multivariate logistic regression models. Overall, the most frequent diagnosis was routine health check, followed by several acute conditions. When analyzed separately, non-rural children were significantly more likely to visit a physician for routine health check ($P = 0.002$), asthma ($P = 0.005$), and acute upper respiratory infection ($P = 0.037$). Rural counterparts were significantly more likely to be seen for attention deficit disorder ($P = 0.000$), otitis media ($P = 0.017$), chronic rhinitis ($P = 0.017$) and influenza ($P = 0.037$). Children age 5 to 9 are healthy overall. When illness occurs, it is usually acute. Rural and non-rural, young, school-aged children exhibit many similarities in healthcare utilization, but differences occur. Most surprising is the difference in the diagnosis frequency of attention deficit disorder.

Celedon J.C. et al. *Antibiotic use in the first year of life and asthma in early childhood.* Clin Exp Allergy. 2004; 34(7) : 1011-6.p **Abstract:** **BACKGROUND:** An association between antibiotic use in early life and asthma in childhood has been reported in five retrospective studies and one longitudinal study. **OBJECTIVE:** To examine the relation between the use of oral antibiotics in the first year of life and asthma in early childhood. **METHODS:** Longitudinal follow-up of 4408 children enrolled in a health maintenance organization (HMO) from birth to the age of 5 years. **RESULTS:** After adjusting for sex and illnesses of the lower respiratory tract

(LRIs), we found a significant association between antibiotic use in the first year of life and asthma between the ages of 1 and 2 years (odds ratio (OR) for 1-2 vs. no courses of antibiotics=1.9, 95% confidence interval (CI)=1.3-2.7; OR for 3-4 vs. no courses of antibiotics=1.6, 95% CI=1.1-2.4; OR for at least 5 vs. no courses of antibiotics=2.1, 95% CI=1.5-3.2). After adjustment for sex and LRIs in the first year of life, there was no significant association between antibiotic use in the first year of life and asthma that was initially diagnosed between the ages of 2 and 5 years and that persisted up to the age of 5 years (OR for 1-2 vs. no courses of antibiotics=1.1, 95% CI=0.8-1.4; OR for 3-4 vs. no courses of antibiotics=1.3, 95% CI=0.9-1.8; OR for at least 5 vs. no courses of antibiotics=1.0, 95% CI=0.7-1.4). **Conclusions** Our findings do not support the hypothesis that antibiotic use in early life is associated with the subsequent development of asthma in childhood but rather suggest that frequent antibiotic use in early life is more common among asthmatic children.

Celedon J.C. et al. *The relationship among markers of allergy, asthma, allergic rhinitis, and eczema in Costa Rica.* Pediatr Allergy Immunol. 2002; 13(2) : 91-7.p **Abstract:** The association between allergy markers and asthma and allergic rhinitis is stronger in countries with a Western lifestyle than in rural areas of Africa and Asia. We examined the relationship among allergy markers, asthma, rhinitis, and eczema in a case-control study of 198 schoolchildren, 10-13 years of age, living in Costa Rica, a Latin American country. The geometric mean total serum immunoglobulin E (IgE) level in subjects with and without asthma was 465.0 and 143.0 IU/ml, respectively (difference = 322 IU/ml, 95% CI = 141.8-616.1 IU/ml, $p < 0.001$), and that in subjects with and without allergic rhinitis was 442.5 and 144.3 IU/ml, respectively (difference = 298.2 IU/ml, 95% CI = 125.7-581.0 IU/ml, $p < 0.001$). After adjusting for age, gender, and skin test reactivity to allergens, we found a linear relationship between serum total IgE level and the log odds ratio (OR) of having asthma. In a multivariate analysis, there was a linear relationship between skin test reactivity to allergens and the log OR of having allergic rhinitis. The OR of having allergic rhinitis was almost three times higher in children who had four positive skin tests than in non-reactors. Skin test reactivity to greater than five aeroallergens was an independent predictor of eczema in a multivariate analysis (OR = 3.1, 95% CI = 1.1-8.4). Although the geometric mean total serum IgE levels of Costa Rican children with either asthma or allergic rhinitis are higher than those of children with asthma or allergic rhinitis in most industrialized countries, the relationship among markers of allergy, asthma, rhinitis, and eczema in Costa Rica is similar to that found in countries with a Western lifestyle and different from that found in rural areas of Asia and Africa.

Celedon J.C. et al. *Ethnicity and skin test reactivity to aeroallergens among asthmatic children in Connecticut.* Chest. 2004; 125(1) : 85-92.p **Abstract:** **OBJECTIVES:** To examine the relationship between ethnicity and sensitization to allergens among children with asthma living in urban and suburban areas of Connecticut. **STUDY DESIGN:** Cross-sectional study. Study population: A total of 791 children with mild-to-severe asthma who received their medical care in the city of Hartford. **RESULTS:** Puerto Rican ethnicity was associated with skin test reactivity (STR) to cockroach (odds ratio [OR], 3.3; 95% confidence interval [CI], 1.7 to 6.4), STR to dust mite (OR, 1.7; 95% CI, 1.2 to 2.4), STR to mixed grass pollen (OR, 1.7; 95% CI, 1.1 to 2.7), and STR to mugwort/sage (OR, 2.4; 95% CI, 1.4 to 4.1). African-American ethnicity was associated with STR to four outdoor allergens (ie, mixed tree pollen [OR, 2.3; 95% CI, 1.3 to 3.9], mixed grass pollen [OR, 2.7; 95% CI, 1.6 to 4.8], mugwort/sage [OR, 3.1; 95% CI, 1.6 to 6.0], and ragweed [OR, 2.1; 95% CI, 1.2 to 3.8]). Among all children, STR to outdoor allergens was strongly associated with the extent of allergen sensitization. As an example, children sensitized to mixed grass pollen had 34.7 times higher odds of having at least four positive skin tests to other allergens than nonsensitized children (95% CI for OR, 15.6 to 77.0).

CONCLUSIONS: Our findings suggest that Puerto Rican ethnicity is associated with an increased risk of sensitization to indoor and outdoor allergens among children with asthma, and that allergy skin testing should be performed more often as part of the management of asthma in African-American children and in Puerto Rican children in the United States.

Ceran O. et al. *The relationship of tonsillar hyperplasia and asthma in a group of asthmatic children.* Int J Pediatr Otorhinolaryngol. 2004; 68(6) : 775-8.p **Abstract:** BACKGROUND: The decline of infections in childhood may contribute to the rising severity and prevalence of atopic disorders in developed countries. With this regard, we examined the relationship of frequent tonsillitis and consequent tonsillar hyperplasia with the development of asthma. METHODS: Sixty-seven asthmatic children (ages 3-14) who had no signs or symptoms of acute tonsillitis were included. The control group consisted of 92 randomly selected children who had no signs or symptoms of asthma or acute tonsillitis. Parents were interviewed about the incidence of tonsillitis diagnosed by physicians and history of tonsillectomy; tonsil sizes were evaluated by oropharyngeal inspection by the same observer using the Brodsky L. Scala. RESULTS: A statistically significant association is found between frequent tonsillitis and consequent tonsillar hyperplasia with the development of asthma. CONCLUSIONS: Our data suggests that recurrent tonsillitis is associated with a decline in the prevalence of asthma by inducing a Th 1 predominant immune response. Our findings are compatible with the hygiene hypothesis.

Cesaroni G. et al. *Individual and area-based indicators of socioeconomic status and childhood asthma.* Eur Respir J. 2003; 22(4) : 619-24.p **Abstract:** The current study evaluated the association between individual and area-based indicators of socioeconomic status and the prevalence, severity, and lifetime hospitalisation for asthma in children. The representative sample of 4,027 children from Rome, aged 6-7 yrs, used for the 1994 ISAAC (International Study on Asthma and Allergies in Childhood) initiative, was selected. Individual and small area indicators of socioeconomic status were used. Individual data on parents' education and on childhood asthma were gathered from self-administered parental questionnaires. Two small-area indicators (socioeconomic status index (SES) and average income in 1994) were derived using information available at the census tract of residence. Logistic regression models were used to estimate the association of parental education and small area indicators with asthma prevalence, severity, and hospitalisation. Parental smoking was considered in the analysis as a potential confounder. Prevalence of physician diagnosis of asthma (11.3%) increased as father's education decreased. Prevalence of severe asthma (1.6%) increased as maternal and paternal educational levels decreased. Lifetime hospitalisation for asthma (2.8%) was strongly associated with both parental education and small-area indicators of social disadvantage, even when considered simultaneously in the same logistic model. Socioeconomic conditions are associated with asthma occurrence, its severity, and hospitalisation. The association was stronger for asthma severity and hospitalisation. Individual indicators correlated better with the outcomes than area-based indicators. However, living in an underprivileged area is a strong independent predictor of hospital admission for asthma.

Cetinkaya F. *Sensitivity to local anaesthetics among asthmatic children.* Int J Paediatr Dent. 2001; 11(6) : 405-8.p **Abstract:** OBJECTIVES: Although true allergic reactions to local anaesthetics are rare in the general population, the importance of the problem among asthmatic children has yet to be documented. SAMPLE AND METHODS: Skin prick, intradermal and incremental challenge tests with lidocain were performed in 157 asthmatic children aged 8-15 years and compared with 72 nonasthmatic children of a similar age. All of the asthmatic subjects were allergic to at least one allergen, most frequently pollens and house dust mites. Prick testing began

with an undiluted solution in patients without a history of allergy and with 1:100 dilution in those with a reaction history. Following negative prick testing, intradermal or incremental challenge tests were performed. RESULTS: A total of 125 patients (80%) had been given local anaesthetics in the past, only three children gave history of an adverse local reaction. At the end of the tests, none of the subjects including controls, were found to have immediate or delayed-type allergy to lidocain. CONCLUSIONS: Local anaesthetic allergy does not seem to be a serious problem among asthmatic children and testing in all asthmatic children is not warranted. Those with an adverse reaction history to local anaesthetics should be tested with these drugs.

Chamberlain L.J. et al. *The crucial role of the vanishing school nurse.* Arch Pediatr Adolesc Med. 2004; 158(11) : 1091; author reply 1091-2.p

Chan A. et al. *Variation in the type I interferon gene cluster on 9p21 influences susceptibility to asthma and atopy.* Genes Immun. 2006; 7(2) : 169-78.p **Abstract:** A genome-wide screen for asthma and atopy susceptibility alleles conducted in the Hutterites, a founder population of European descent, reported evidence of linkage with a short tandem repeat polymorphism (STRP) within the type I interferon (IFN) gene cluster on chromosome 9p21. The goal of this study was to identify variation within the IFN gene cluster that influences susceptibility to asthma and atopic phenotypes. We screened approximately 25 kb of sequence, including the flanking sequence of all 15 functional genes and the single coding exon in 12, in Hutterites representing different IFNA-STRP genotypes. We identified 78 polymorphisms, and genotyped 40 of these (in 14 genes) in a large Hutterite pedigree. Modest associations (0.003<P<0.05) with asthma, bronchial hyper-responsiveness (BHR), and atopy were observed with individual variants or genes, spanning the entire 400 kb region. However, pairwise combinations of haplotypes between genes showed highly significant associations with different phenotypes (P<10(-5)) that were localized to specific pairs of genes or regions of this cluster. These results suggest that variation in multiple genes in the type I IFN cluster on 9p22 contribute to asthma and atopy susceptibility, and that not all genes contribute equally to all phenotypes.

Chan D.S. et al. *Multidisciplinary education and management program for children with asthma.* Am J Health Syst Pharm. 2001; 58(15) : 1413-7.p **Abstract:** A multidisciplinary program for managing asthma in a pediatric population is discussed. A coordinated, multidisciplinary program for managing asthma in children was initiated in November 1997 at a U.S. Army medical center. The program, designed to improve care and decrease hospitalizations for asthma, was pharmacist managed and pulmonologist directed and was implemented by pediatricians. Patient education was provided by a pediatric clinical pharmacist or a nurse case manager; providers also received intensive education. Follow-up occurred at predetermined intervals and included asthma education, discussion of expectations and goals, analysis of metered-dose-inhaler and spacer technique, and assessment of compliance. Between November 1997 and January 1999, 210 inpatients were screened for asthma. One hundred seven were believed to have asthma and received inpatient asthma counseling and teaching. Of these 107 patients, 79 were enrolled in the program and monitored in the ambulatory care setting. Seventy-one (90%) of the 79 program enrollees were not rehospitalized during the ensuing two years. The number of children admitted to the hospital for asthma decreased from 147 in 1997 (a rate of 3.2 per 1000 population) to 93 in 1998 (2.1 per 1000) and to 87 in 1999 (1.9 per 1000). A multidisciplinary approach to the management of children with asthma may reduce hospitalizations of such patients.

- Chan D.S. et al.** *An Internet-based store-and-forward video home telehealth system for improving asthma outcomes in children.* Am J Health Syst Pharm. 2003; 60(19) : 1976-81.p **Abstract:** The adherence and disease-control outcomes associated with the use of an Internet-based store-and-forward video home telehealth system to manage asthma in children were studied. Pediatric patients with persistent asthma were provided with home computers and Internet access and monitored biweekly over the Internet. All patients were seen in the pediatric clinic at 0, 2, 6, 12, and 24 weeks. Half of the patients received asthma education in person and half via an interactive Web site. Adherence measures were assessed by therapeutic and diagnostic monitoring. Therapeutic monitoring included digital videos of patients using their controller medication inhaler. Diagnostic monitoring included an asthma symptom diary and a video of peak flow meter use. Videos were submitted electronically twice a week by using in-home telemonitoring with store-and-forward technology. Feedback was provided electronically to each patient. Disease control was assessed by examining quality of life, utilization of services, rescue-therapy use, symptom control, satisfaction with home telemonitoring, and retention of asthma knowledge. Patients were randomly assigned to an asthma education group (Internet versus office), and the data were analyzed by comparing results for study days 0-90 and 91-180. Ten children participated. A total of 321 videos of inhaler use and 309 videos of peak flow meter use were submitted. Inhaler technique scores improved significantly in the second study period. Submission of diagnostic monitoring videos and asthma diary entries decreased significantly. Peak flow values as a percentage of personal best values increased significantly. Overall, there was no change in quality of life reported by patients. However, the caregivers in the virtual-education group reported an increase in the patients' quality-of-life survey scores. Emergency department visits and hospital admissions for asthma were avoided. Rescue therapy was infrequent. A high rate of satisfaction with home telemonitoring was reported. Internet-based, store-and-forward video assessment of children's use of asthma medications and monitoring tools in their homes appeared effective and well accepted.
- Chan I.H. et al.** *Gene-gene interactions for asthma and plasma total IgE concentration in Chinese children.* J Allergy Clin Immunol. 2006; 117(1) : 127-33.p **Abstract:** BACKGROUND: Asthma is a complex disease resulting from interactions between multiple genes and environmental factors. Study of gene-gene interactions could provide insight into asthma pathophysiology. OBJECTIVE: We investigated the interaction among 12 different loci in 8 candidate genes and asthma and increased plasma total IgE concentrations in 240 Chinese asthmatic subjects and 140 control subjects. METHODS: Genotyping was performed by means of RFLP analysis. Multifactor dimensionality reduction and logistic regression were used to analyze gene-gene interactions. RESULTS: A significant interaction was found between R130Q in the IL-13 gene (IL13) and I50V in the IL-4 receptor alpha gene (IL4RA) on the risk of asthma, with a cross-validation consistency of 10 of 10 and a prediction error of 33.7% (P = .014). The odds ratio of the high-risk to low-risk group was 2.6 (95% CI, 1.4-5.0; P = .004). For increased plasma total IgE concentration, the best 2-locus model consisted of R130Q in IL13 and C-431T in the thymus and activation-regulated chemokine gene (TARC). This model showed a maximum cross-validation consistency of 10 and a minimum prediction error of 36.1% (P = .022). The odds ratio of the high-risk to low-risk group was 3.9 (95% CI, 2.0-7.7; P = .0001). Logistic regression revealed significant interactions between IL13 and IL4RA for asthma (P = .042) and IL13 and TARC for increased total IgE concentration (P = .012). CONCLUSIONS: Our data suggest significant interactions between IL13 and IL4RA for asthma and IL13 and TARC for increased plasma total IgE concentrations in Chinese children.
- Chan K.S. et al.** *How do ethnicity and primary language spoken at home affect management practices and outcomes in children and adolescents with asthma?* Arch Pediatr Adolesc Med. 2005; 159(3) : 283-9.p **Abstract:** BACKGROUND: Lower rates of preventive medication use and higher rates of hospitalization and emergency department use have been documented among Latino children and adolescents with asthma. However, little is known about how language barriers influence asthma management practices and outcomes. OBJECTIVE: To examine the effects of language on asthma management practices and asthma-related outcomes. DESIGN: Cross-sectional survey of asthma management practices, perceived efficacy, asthma knowledge, family functioning, and health-related quality of life in 405 white non-Latino, African American non-Latino, and Latino children and adolescents from English- and Spanish-speaking homes. RESULTS: Latino children and adolescents from Spanish-speaking homes had lower rates of goal setting and peak flow monitoring, poorer asthma knowledge, and greater negative family impact than white children and adolescents (P < .05 for all). Although Latino children and adolescents from English-speaking homes did worse than their non-Latino white peers, the decrements were modest and not statistically significant (P > .16 for all). Management practices and outcomes for non-Latino African American children and adolescents closely approximated those of white children and adolescents. CONCLUSIONS: Language barriers seem to contribute to poorer asthma management practices and knowledge among Latino children and adolescents. Efforts to increase knowledge in this group may enhance asthma self-care and limit the morbidity associated with asthma.
- Chan P.W. et al.** *Ethnicity and asthma symptoms associated with ingestion of fruits.* J Paediatr Child Health. 2002; 38(6) : 622.p
- Chan-Yeung M. et al.** *The Canadian Childhood Asthma Primary Prevention Study: outcomes at 7 years of age.* J Allergy Clin Immunol. 2005; 116(1) : 49-55.p **Abstract:** BACKGROUND: Avoidance of any one of the individual risk factors associated with childhood asthma has not been successful in preventing its development. OBJECTIVE: The purpose of this study is to determine the effectiveness of a multifaceted intervention program for the primary prevention of asthma in high-risk infants at 7 years of age. METHODS: Five hundred forty-five high-risk infants with an immediate family history of asthma and allergies were prospectively randomized into intervention or control groups prenatally. Intervention measures introduced before birth and during the first year of life included avoidance of house dust, pets, and environmental tobacco smoke and encouragement of breast-feeding with delayed introduction of solid foods. Assessment of outcomes at 7 years consisted of examination by pediatric allergists, methacholine inhalation tests, and allergy skin tests. RESULTS: At 7 years, 469 of the 545 children were contacted, and 380 returned for further assessment. The prevalence of pediatric allergist-diagnosed asthma was significantly lower in the intervention group than in the control group (14.9% vs 23.0%; adjusted risk ratio, 0.44; 95% CI, 0.25-0.79). The prevalence of allergic rhinitis, atopic dermatitis, atopy (defined as positive skin test reactions to any common allergen), and bronchial hyperresponsiveness (defined as the provocative concentration of methacholine that induced a 20% decrease in FEV1 from a postsaline value of less than 7.8 mg/mL) were not significantly different between the 2 groups. The prevalence of asthma (defined as wheeze without colds and the presence of bronchial hyperresponsiveness) was also significantly lower in the intervention group compared with the control group (12.9% vs 25.0%; adjusted risk ratio, 0.39; 95% CI, 0.22-0.71). CONCLUSION: The multifaceted intervention program was effective in reducing the prevalence of asthma in high-risk children at 7 years of age.
- Chaney G. et al.** *A new asthma spacer device to improve compliance in children: a pilot study.* Respiriology. 2004; 9(4) : 499-506.p **Abstract:** OBJECTIVE: This pilot study was designed to compare

the acceptance, ease of use, and effects on compliance between currently used spacer devices and the Funhaler--a new small volume spacer device designed to improve adherence to asthma medication in children. **METHODOLOGY:** A matched questionnaire-based survey was conducted by two interviews of each caregiver by the same person. A total of 32 children were randomly recruited from seven clinics spanning widely differing socioeconomic and geographical areas of Perth, Western Australia. Preschool children taking regular inhaled asthma medication using an existing low volume spacer device and aged between 1.5 and 6 years, took part in the pilot study. Parents completed two matched questionnaires. The first questionnaire was completed at the beginning of the study and the second after 2 weeks' use of the Funhaler spacer. Data collected related primarily to ease of use of the devices, child and parental compliance, and treatment attitudes. During the study, parents were also called at random on one occasion to ascertain whether they had attempted to medicate their child the previous day. **RESULTS:** Using the Funhaler incentive spacer device, parents reported significantly more success at medicating their children (22/30 always successful) in comparison to using their existing spacer device (3/30). Parental adherence to prescribed frequency and the delivery technique of children were also improved. The children also showed improved satisfaction and willingness to use the device and parents' attitude towards medicating their children was improved with the Funhaler spacer device. **CONCLUSIONS:** Use of a novel, incentive spacer device (Funhaler) appeared to be associated with increased success and fewer problems in medicating children, improved child and parental adherence, and a more positive attitude towards treatment, suggesting that more extensive long-term efficacy trials with the device are warranted.

Chang A.B. et al. *The relationship between inflammation and dipalmitoyl phosphatidylcholine in induced sputum of children with asthma.* J Asthma. 2003; 40(1) : 63-70.p **Abstract:** **BACKGROUND:** Animal studies have shown elevated surfactant production in response to lung injury. In human airways, the contribution of surfactant to the airway epithelial barrier and importance of eosinophilic inflammation is increasingly appreciated. The relationship between blood and sputum inflammatory indices of childhood asthma to surfactant levels is unknown. In this study we hypothesized that the degree of inflammation influences the level of dipalmitoyl phosphatidylcholine (DPPC) in airways of children with asthma. **METHODS:** Sixteen children with asthma (ages 5.5-16 years) underwent venipuncture, skin prick test, spirometry, hypertonic saline challenge, and induced sputum during a nonacute phase. Sputum (sp) and blood (se) markers of inflammation (eosinophils, neutrophils, eosinophilic cationic protein [ECP]), were related to sputum DPPC levels and several markers of asthma severity (airway hyperresponsiveness, quality of life, FEV1). **RESULTS:** On multiple regression, sp-DPPC significantly correlated to sp-ECP ($r=0.53$, $P=0.0048$). Se-ECP, se-Eo, sp-eosinophils, sp-neutrophils, se-neutrophils, and inhaled steroids dose did not significantly influence sp-DPPC. Exposure to smoke did not influence inflammatory markers. FEV1 and quality of life data did not relate to any blood or sputum variable. A significant association between AHR and se-eosinophils, but not between AHR and se-ECP, sp-eosinophils, or sp-ECP was found. **CONCLUSION:** Elevated DPPC levels occur in the presence of chronic eosinophilic inflammation in airways of children with stable asthma. Whether this represents an inherent lung mechanism for epithelial protection remains to be elucidated.

Chang A.B. et al. *Effect of inspiratory flow on methacholine challenge in children.* J Asthma. 2004; 41(3) : 349-54.p **Abstract:** Regulation of inspiratory flow alters the outcomes of the methacholine (MHC) challenge in adults and cough receptor sensitivity in children. The effect of inspiratory flow on the reproducibility of the MHC challenge in children is unknown. The aim of this study was to evaluate the effect of inspiratory flow alteration on the repeatability of

the MHC challenge in children with and without asthma. Twenty-five children undertook the MHC challenge on three different days by using a dosimeter connected to a setup that allowed regulation of inspiratory flow and pattern. Children were randomized to commence the challenges at 20 or 60 L/min, and the last challenge was performed at 20 L/min. The within-subject standard deviation, 95% range for change, and doubling dose for the differing inspiratory flow (20 vs. 60 L/min) was more than twice that of when inspiratory flow was maintained at 20 L/min for both occasions. The range of the "limits of agreement" of the Bland and Altman plot was smaller when inspiratory flow was constant. For short-term comparative individual studies in children, inspiratory flow should be regulated. Laboratories and research measuring change in airway hyperresponsiveness to MHC should determine and report reproducibility indices of the challenge so airway hyperresponsiveness changes can be interpreted meaningfully.

Chang A.B. et al. *Leukotriene receptor antagonist for prolonged non-specific cough in children.* Cochrane Database Syst Rev. 2006; (2) : CD005602.p **Abstract:** **BACKGROUND:** Non-specific cough is defined as non-productive cough in the absence of identifiable respiratory disease or known aetiology. It is commonly seen in paediatric practice. These children are treated with a variety of therapies including a variety of asthma medications. The leukotriene pathway is reported to be involved in the sensory (neurogenic) pathway, which is a mechanism thought to be involved in the pathogenesis of chronic cough. **OBJECTIVES:** To evaluate the effectiveness of leukotriene receptor antagonist (LTRA) in treating children with prolonged non-specific cough. **SEARCH STRATEGY:** The Cochrane Register of Controlled Trials (CENTRAL), the Cochrane Airways Group Specialised Register, MEDLINE and EMBASE databases were searched by the Cochrane Airways Group. The latest searches were carried out in September 2005. **SELECTION CRITERIA:** All randomised controlled trials comparing LTRA with a placebo medication in children with non-specific cough. **DATA COLLECTION AND ANALYSIS:** Results of searches were reviewed against pre-determined criteria for inclusion. One eligible trial was identified but no data was available for analysis. It was not possible to separate results from children with non-specific cough from those without. **MAIN RESULTS:** There was no significant difference in all study endpoints between the montelukast and placebo groups (total N=256). **AUTHORS' CONCLUSIONS:** With the lack of evidence, the routine use of LTRA in treating children with non-specific cough cannot be recommended.

Chao S.Y. et al. *Primary school nurses' knowledge/competence pertaining to childhood asthma and its management prior to and following a National Asthma Education Program in Taiwan.* J Asthma. 2003; 40(8) : 927-34.p **Abstract:** The main purpose of the National Asthma Education Program was to provide asthma education to school nurses in Taiwan. It was also designed to enhance the knowledge and competence of school nurses in managing the asthmatic problems that children experience while in school. In addition to providing instruction about current asthma management skills, tools, and other relevant information, the program demonstrated the use of the peak flow meter for asthmatic children. A single, 4-hr session conducted in each county and city in Taiwan, the National Asthma Education Program began on August 1, 1999, and ended December 31, 2000. A total of 829 school nurses joined the program, with an overall attendance rate of 74%. Significant effects of this program on nurses' asthma care knowledge and competence and case management efficacy were noted. The participating school nurses' demographics, however, were found to be irrelevant to these effects. Expecting the training activities to help relieve the anxieties of managing asthmatic cases in the school environment, participants reported that the training was of much benefit to them. Development of a teaching program to elevate school nurses' capabilities in asthmatic student care in the school

environment and the implications of such a program within Taiwanese schools were also discussed.

Chaves T.C. et al. *Correlation between signs of temporomandibular (TMD) and cervical spine (CSD) disorders in asthmatic children.* J Clin Pediatr Dent. 2005; 29(4) : 287-92.p **Abstract:** Neck accessory respiratory muscles and mouth breathing suggest a direct relationship among asthma, Temporomandibular (TMD) and Cervical Spine (CSD) Disorders. This study was performed to evaluate and correlate TMD, CSD in asthmatic and non-asthmatic. Thirty asthmatic children (7.1 +/- 2.6 years old), 30 non-asthmatic predominantly mouth breathing children (Mouth Breathing Group - MBG) (8.80 +/- 1.61 years) and 30 non-asthmatic predominantly nasal breathing children (Nasal Breathing Group - NBG) (9.00 +/- 1.64 years) participated in this study and they were submitted to clinical index to evaluate stomatognathic and cervical systems. Spearman correlation test and Chi-square were used. The level of significance was set at $p < 0.05$. Significant frequency of palpatory tenderness of temporomandibular joint (TMJ), TMJ sounds, pain during cervical extension and rotation, palpatory tenderness of sternocleidomastoids and paravertebrae muscles and a severe reduction in cervical range of motion were observed in AG. Both AG and MBG groups demonstrated palpatory tenderness of posterior TMJ, medial and lateral pterygoid, and trapezius muscles when compared to NBG. Results showed a positive correlation between the severity of TMD and CSD signs in asthmatic children ($r = 0.48$). No child was considered normal to CSD and cervical mobility. The possible shortening of neck accessory muscles of respiration and mouth breathing could explain the relationship observed between TMD, CSD signs in asthmatic children and emphasize the importance of the assessment of temporomandibular and cervical spine regions in asthmatic children.

Chen S.H. et al. *The development and establishment of a care map in children with asthma in Taiwan.* J Asthma. 2004; 41(8) : 855-61.p **Abstract:** BACKGROUND: It is often difficult to predict the timing and frequency of asthma attacks. In addition to interrupting the daily life of both the affected child and his/her family, asthma can also pose sudden danger to a child. Based on clinical observations, many asthma-affected children and their parents must constantly adjust themselves to the uncertainty of the disease, which leads to increased stress on the family. The use of care maps has demonstrated increased efficiency and effectiveness in the care of asthma patients from a variety of settings. OBJECTIVE: We designed this study to construct and evaluate a care map for asthmatic children in Taiwan. Specific attention was placed on comparing the study and control subjects by parental knowledge of asthma, medication used for asthma, hospital readmission, and health care resource usage. SUBJECTS AND METHODS: The care map was constructed by in-depth interviews with eight sets of parents of children with asthma. Forty-four parents of 42 asthma children were randomized into two groups in the Allergic Clinic of the Chang Gung Children's Hospital. The experimental group of 22 parents received individual instruction and training sessions in addition to the regular care provided to the control group of 22 parents. RESULTS: Forty-two children with asthma were surveyed in this study. To examine the reliability and validity of a care map for children with asthma, a quantitative survey was conducted with 42 outpatient parents with asthmatic children. There was less emergency room attending rate in experimental group (6/month; $p < 0.05$) The understanding of the disease was much improved in parents of experimental group (13.85 +/- 1.04 vs. 10.91 +/- 2.14; $p < 0.01$). Furthermore, parents acquired a more positive attitude to asthma, and almost all of the control group had irregular follow-ups by a physician and had irregular use of medication. CONCLUSION: This study emphasizes that a care map in children with asthma (CACM) can be used to educate parents in how to provide the best treatment plan for their children. This study also shows how a CACM can help parents train their children in the best behaviors during asthma attacks. Empathetic assessment and

elimination of cultural barriers, a well-designed educational program, and a mutually developed treatment plan could significantly improve the quality of life for families and specific asthma outcomes.

Chen W.Y. et al. *Synergistic effect of multiple indoor allergen sources on atopic symptoms in primary school children.* Environ Res. 2003; 93(1) : 1-8.p **Abstract:** Accumulating data show that the complex modern indoor environment contributes to increasing prevalence of atopic diseases. However, the dose-response relationship between allergic symptoms and complexity of indoor environmental allergen sources (IEAS) has not been clearly evaluated before. Therefore, we designed this study to investigate the overall effect of multiple IEAS on appearance of asthma (AS), allergic rhinitis (AR), and eczema (EC) symptoms in 1472 primary school children. Among various IEAS analyzed, only stuffed toys, cockroaches, and mold patches fit the model of 'more IEAS, higher odds ratio (OR) of association'. The association of IEAS and AR increased stepwise as more IEAS appeared in the environment (1.71, 2.47, to 2.86). In AS and EC, the association was significant only when all three IEAS were present (1.42, 1.98, to 4.11 in AS; 1.40, 1.76, to 2.95 in EC). These results showed that different IEAS had a synergistic effect on their association with atopic symptoms and also suggest that there is a dose-response relationship between kinds of IEAS and risk of appearance of atopic diseases.

Chen Y. et al. *Gender, environmental tobacco smoke, and pulmonary function in rural children and adolescents: the Humboldt study.* J Agric Saf Health. 2005; 11(2) : 167-73.p **Abstract:** We examined the gender-related association between household exposure to environmental tobacco smoke (ETS) and pulmonary function among 862 children and adolescents aged 6 to 17 years living in the town of Humboldt, Saskatchewan, in 1993. Pulmonary function tests included forced vital capacity (FVC), forced expiratory volume in one second (FEV1), maximum mid-expiratory flow rate (FEF25-75), and flow rates at 75%, 50%, and 25% of vital capacity (Vmax75, Vmax50, and Vmax25). Each pulmonary function test variable was regressed on age, height, weight, and their quadratic and cubic polynomials, with the terms significant at the alpha level of 0.10 being retained. Residuals for the pulmonary function test variables, which are the differences between the observed and predicted values, were calculated. Estimations of ETS exposure were parental smoking status, number of household smokers, total daily cigarette consumption, and number of cigarettes smoked daily at home by household members. Maternal smoking status was significantly related to residual FEF25-75, Vmax75, Vmax50, and Vmax25. Number of household smokers and daily cigarette consumption by household members were significantly associated with FEV1, FEF25-75, Vmax75, Vmax50, and Vmax25, and the association between ETS exposure and pulmonary function was stronger in girls than in boys. Interaction of gender and number of cigarettes smoked daily at home was significantly related to FEF25-75, Vmax75, Vmax50, and Vmax25 among the non-smoking subjects. We concluded that ETS exposure had a larger effect on pulmonary function in girls than in boys.

Chen Y. et al. *Segregation analyses of asthma and respiratory allergy: the Humboldt family study.* Am J Med Genet. 2001; 104(1) : 23-30.p **Abstract:** We performed segregation analyses of asthma and respiratory allergy based on data from 309 nuclear families comprising 1,053 individuals living in the town of Humboldt, Saskatchewan, in 1993, using the REGD program of the S.A.G.E. program package. For adults, information on asthma and history of respiratory allergy was provided by the subjects themselves, and for children by their parents. When asthma was considered as the trait in segregation analysis, models of no major effect, with or without familial effects, were rejected, but they were not rejected after adjusting for history of respiratory allergy. The major gene hypothesis was not rejected before adjusting for history of respiratory

allergy. When respiratory allergy was analyzed as the trait, both major gene and multifactorial models fitted the data well, regardless of whether there was adjustment for asthma or not. Other covariates adjusted for in the segregation analyses were age, sex, number of household smokers, current smoking, number of household members, generation, and house type. The data suggest that a major gene related to respiratory allergy may explain the familial aggregation of asthma.

Chen Y.L. et al. *ABO/secretor genetic complex is associated with the susceptibility of childhood asthma in Taiwan.* Clin Exp Allergy. 2005; 35(7) : 926-32.p **Abstract:** BACKGROUND: Histo-blood groups, ABO, Lewis (Le) and secretor (Se) were found to be associated with lower lung function and wheezing in coal miners as well as in asthmatic children in some studies but not others, possibly reflecting the genetic heterogeneity among different ethnicities and local environmental exposure. OBJECTIVE: The present study was conducted to determine the association between ABO, Lewis and secretor genetic complex with susceptibility of childhood asthma in Taiwan. METHODS: We randomly selected 136 asthmatic children and 161 age-matched controls from a childhood asthma survey conducted in primary schools. ABO and Lewis blood groups were determined by red blood cell agglutination methods. Analysis of Se genotype was performed by PCR with sequence-specific primers. RESULTS: There was a higher prevalence rate in secretor subjects (Se/Se) (odds ratio (OR)=1.7, confidence interval (CI)=1.022-2.938) in asthma as compared with controls. The combined effect of these three blood systems revealed that blood group O/secretor phenotype (Se/Se) (OR=2.7, CI=1.126-6.033), and blood group O/Le(a-b-) (OR=3.6, CI=1.080-11.963, P<0.03) individuals were significantly associated with asthma. The Lewis Le(a-b-) recessive genotype (OR=3.3, CI=1.267-8.482), or the joint blood group O/Le(a-b-) phenotype (OR=5.2, CI=1.259-21.429, P<0.02), was significantly associated with high serum IgE (>500 IU), respectively. There was no association of these three blood systems with the sensitivity of dust mite, Dermatophagoide pteronyssinus, in our study population. CONCLUSIONS: We concluded that blood group O/secretors (Se/Se) and O/Le(a-b-) were associated with childhood asthma, and may act as one of the predominant factors for environmental triggers of allergy for asthmatic children in Taiwan.

Cheong H.S. et al. *Association analysis of interleukin 5 receptor alpha subunit (IL5RA) polymorphisms and asthma.* J Hum Genet. 2005; 50(12) : 628-34.p **Abstract:** The alpha subunit of interleukin 5 receptor (IL5RA) on chromosome 3p26-p24 is known to regulate the development and function of eosinophils. In an effort to discover additional polymorphism(s) in genes whose variant(s) have been implicated in asthma, we investigated the genetic polymorphisms in IL5RA to evaluate the gene as a potential candidate for a host genetic study of asthma. By direct DNA sequencing in 24 individuals, we identified 22 sequence variants within exons and flanking regions including a 1.5-kb promoter region of IL5RA; 10 common polymorphic sites were selected for genotyping in our asthma cohort (n = 587). Two haplotype blocks were identified in a Korean population. Statistical analysis revealed that one promoter SNP, c.-5993A > G, and one ins/del polymorphism in intron 3, c.-480_482insdelGTT, showed significant association with the risk of asthma development. The genetic effects of c.-5993A>G and c.-480_482insdelGTT on asthma were more apparent among atopic subjects. Our findings suggest that polymorphisms in IL5RA might be among the genetic risk factors for asthma development, especially in atopic populations. IL5RA variant/haplotype information identified in this study will provide valuable information for strategies for the control of asthma.

Cheron G. et al. *[Drugs for pediatric emergencies].* Rev Prat. 2001; 51(17) : 1914-8.p **Abstract:** Drugs for pediatric emergencies are useful for respiratory (croup, asthma), cardiologic (hypertensive

crisis, acute congestive heart failure, arrhythmias, hypoxic spells), neurologic (seizures), metabolic (dehydration, hypoglycaemia), infectious (meningococemia) or allergic (anaphylaxis) distresses. Pain management is always important whether to relieve or to prevent the discomfort which would happen during diagnosis or therapeutic procedures.

Chetney R. *Home care "life coaches" help kids win the asthma game.* Caring. 2003; 22(10) : 58-62; quiz 64-5.p **Abstract:** Asthma is a widespread disease that affects more than 20 million Americans and up to 150 million people around the world. The cost of treating asthma is \$14 billion annually. Particularly hard hit are children in inner city areas; researchers have found that 14 percent of inner city adolescent children are diagnosed with asthma. Sentara Home Care Services in Chesapeake, Virginia, has developed an innovative program to improve the management of asthma among children, particularly inner city children, by implementing a system of "Life Coaches" to counsel proper medication use and lifestyle behaviors for these patients and their families.

Chiang C.H. et al. *Evaluation of risk factors for asthma in Taipei City.* J Chin Med Assoc. 2005; 68(5) : 204-9.p **Abstract:** BACKGROUND: Asthma has rarely been studied by evaluating all of its trigger factors in 1 study population. Thus, correlations between the concentration of allergen immunoglobulin (Ig) E antibodies and airway limitation or asthma severity remain unclear. METHODS: Five hundred and seventy-nine asthmatic patients were enrolled, and serum specific IgE antibodies to allergens were analyzed. All suspected trigger factors were assessed by questionnaire, case histories over a 4-year period, and diary card recordings; possible trigger factors were then re-evaluated. RESULTS: Antibodies to the following allergens were found: Dermatophagoide pteronyssinus (59.8% of patients), D. microceras (58.8%), D. farinae (56.8%), cockroach (38.3%), dog dander (26.3%), Candida albicans (13.3%), cat dander (10%), and Cladosporium herbarum (6.6%). A greater prevalence of allergy to dog and cat dander was found than previously. Younger patients were more often positive for mite allergens, and had higher titers of antibodies against such allergens, than older patients. Further, females had a lower concentration of mite allergen antibodies than males. No correlation between the concentration of allergen antibodies and forced expiratory volume in 1 second (FEV1), or the ratio of FEV1:forced vital capacity (FEV1:FVC), was found. In addition, there was no significant change in antibody titers with varying asthma severity. Non-allergenic trigger factors were irritant air inhalants (94.6% of patients), respiratory infection (92.2%), exercise (75.2%), emotional factors (58.8%), drugs and chemical substances (16%). CONCLUSION: There are multiple trigger factors in asthma. Allergenic trigger factors are more common in younger than older patients, whereas non-allergenic trigger factors are more common in older patients. There was no linear correlation between the concentration of specific IgE antibodies and asthma severity or airway limitation; therefore, to prevent asthma attacks in individual asthmatic patients, greater attention should be paid to avoiding all potential trigger factors, and not just house dust mite allergens.

Chiang L.C. *Exploring the health-related quality of life among children with moderate asthma.* J Nurs Res. 2005; 13(1) : 31-40.p **Abstract:** Asthma is one of the most common chronic diseases, impacting more than 10 % of children in Taiwan. The recurrent signs and symptoms and complexity of disease management impact the life quality of children with asthma. The purpose of this study was to describe the content and dimensions of health-related quality of life (HRQOL) among children with moderate asthma by descriptive qualitative research based on in-depth interviews. Eleven children, aged 6-12 years, and their mothers from two medical centers in central Taiwan were interviewed and tape recorded. The transcripts were analyzed using content analysis. Six themes relevant to the children's QOL

with asthma were identified: 1. physical disturbances of signs/symptoms, 2. limitations of activity, 3. emotional distress, 4. discord in parent-child relationships, 5. restrictions in school social life and 6. daily inconvenience of managing the disease. These findings highlight the ways in which the overall quality of life of children is impacted by asthma including the physiological and psychosocial domains. The breadth of these findings may lead to greater insights into the nursing care of children with asthma.

Chiang L.C. et al. *A comparison, by quantitative and qualitative methods, between the self-management behaviors of parents with asthmatic children in two hospitals.* J Nurs Res. 2005; 13(2) : 85-96.p
Abstract: This study compared the self-management behaviors of parents with asthmatic children staying in two hospitals and explored barriers to self-management behaviors by interviewing. 227 parents were recruited for quantitative analysis by completing a self-report structured questionnaire, 94 of these parents were from the Taipei area and 133 were from the Taoyuan area. Sixteen parents were interviewed from this population. The results indicated that the parents in the Taoyuan area had younger age, lower socioeconomic status (SES), and higher exercise limitations for children. Their knowledge, enabling factors, and self-management behaviors were also lower than their counterparts in the Taipei area. The determining factors of self-management behaviors were socioeconomic status, self-efficacy, sources of education, and perceived effectiveness (Adjusted R²= .593) in 227 parents. Six major themes about the influencing factors of self-management were deduced from the interview data: lack of understanding and dislike of the asthma label, less self-perceived severity, lack of understanding about asthma medication, lack of confidence in environmental controls, financial burden of anti-mite products, and doubt about effectiveness. Three major barriers to self-management behaviors of parents in the Taoyuan area were inconsistent use of alternative treatments, overdependence on medical service, and lack of use of peak flow meter. Parents with asthmatic children living in the Taoyuan area had poorer self-management behaviors than those in the Taipei area, and SES was one of the determining factors. The health beliefs of Taoyuan parents included many misconceptions. Conducting the educational needs assessment through quantitative and qualitative methods could provide proficiency information for designing educational content appropriate to specific populations.

Chiang L.C. et al. *Effects of a self-management asthma educational program in Taiwan based on PRECEDE-PROCEED model for parents with asthmatic children.* J Asthma. 2004; 41(2) : 205-15.p
Abstract: This study was conducted to evaluate the comparative effectiveness of two different asthma educational programs. One was self-management asthma education based on the PRECEDE-PROCEED model to change the influential factors based on a previous need assessment study in Taiwan. The other consisted of regular outpatient asthma education. The purposes were: 1) to compare differences in the asthma knowledge, self-efficacy, perceived effectiveness, children's cooperation, doctor-patient communication, and self-management behaviors in the experimental and control groups before education, and 2 weeks, 3 months, and 6 months after education; and 2) to compare differences in drug use, medication utilization, asthma severity, signs/symptoms of asthma, school absenteeism, and exercise ability before education, and 2 weeks, 3 months, and 6 months after education. Parents of asthmatic children were recruited from among outpatients of Chang Gung Children's Hospital, Taoyuan, Taiwan. They were grouped by registration number: those with even numbers were assigned to the experimental group, and those with odd numbers were assigned to the control group. Measurements were collected four times from all parents by means of a questionnaire and chart review. The General Linear Model: Repeat Measurement was used to compare variance differences. The following results were found. 1) Asthma knowledge, self-efficacy, perceived effectiveness, children's cooperation, and self-management behaviors significantly improved after the self-

management asthma educational program based on PRECEDE-PROCEED. Except for perceived effectiveness, all variables still had good effectiveness after 6 months of follow-up. The experimental group was better than the control group in knowledge, children's cooperation, and self-management behaviors at the 3-month follow up, as well as in knowledge and children's cooperation at the 6-month follow-up. 2) In both the experimental and control groups, the educational program had a good impact on the health outcome. The average degree of drug use was reduced from 2.7 to 2.1. The number of visits was reduced from 4.75 to 3.55 per half year in the experimental group, and from 5.8 to 3.48 in the control group. The severity of asthma was reduced from 2.7 to 2.1. The signs/symptoms of asthma decreased, school absenteeism was reduced, and exercise ability improved after education at the 6-month follow-up in both groups. From the results of this study, the theory-based educational program had a good effect on self-management behaviors. From the repeat measurement analysis, we can understand the changing trend of the determinants, behaviors, and outcome indicators. The trend indicated that educational effects were sustained for at least 3 months, with some for 6 months. In order to maintain the educational effects, further specific series of educational programs can be designed based on the patterns of self-management behavior stages every 6 months. The effects of health outcomes may show significant differences using longer follow-up times in future clinical trials.

Chiaromonte L. et al. *Why have a special supplement to the Journal of Asthma for patients?* J Asthma. 2003; 40 Suppl : xv-xix.p

Chiaverini L.C. et al. *Damp housing conditions and asthma in Rhode Island.* Med Health R.I. 2003; 86(5) : 151-3.p

Child F. et al. *Correction of bronchial challenge data for age and size may affect the results of genetic association studies in children.* Pediatr Allergy Immunol. 2003; 14(3) : 193-200.p
Abstract: Meaningful studies of asthma genetics require careful definition of airway hyperresponsiveness (AHR). In children, several studies have emphasized the need for correction of bronchial challenge data for baseline parameters, such as age, gender, lung function and atopic status, when undertaking airway responsiveness measurements. However, few studies have suggested how this should be performed in practice. This study describes a method for the correction of dose-response slopes (DRS) and PC20 values for baseline parameters in children, and illustrates the effect of such corrections on the association of AHR with the glutathione S-transferase GSTP1 Ile105Val polymorphism in children. Skin prick and methacholine challenge testing, measurement of total serum IgE concentration and GSTP1 genotyping were performed in 145 unrelated British children aged 7-18 years. Correction of bronchial challenge results, expressed as both DRS and PC20 values, for age, gender, baseline lung function and atopic status was performed using linear regression and discriminant analysis, respectively. Adjusting bronchial challenge results for the age and size of the child altered AHR status, defined as a PC20 methacholine <8 mg/ml, in 37% of children. Correction for baseline parameters also resulted in a significant reduction in mean DRS (original uncorrected DRS 83.6, corrected DRSc 27.4). This had a marked effect on the results of the association study, unmasking a previously unidentified association between the GSTP1 genotype and AHR in children. Age and size adjustment of bronchial challenge data has a significant effect on AHR status and may influence the results of genetic association studies in children.

Chinn S. et al. *Can the increase in body mass index explain the rising trend in asthma in children?* Thorax. 2001; 56(11) : 845-50.p
Abstract: BACKGROUND: The reported association between asthma and obesity and the documented rise in each over time have led to suggestions that rising obesity might explain the increase in the prevalence of asthma. Trends in both in British children participating in the National Study of Health and Growth were marked from 1982

to 1994. **METHODS:** Odds ratios for trends in asthma and symptoms in 8 and 9 year old children were calculated with and without adjustment for body mass index (BMI). **RESULTS:** In a representative sample of white children the odds ratio per year for asthma was 1.09 (95% CI 1.07 to 1.11) before and after adjustment for BMI for boys and 1.09 (95% CI 1.07 to 1.12) and 1.09 (95% CI 1.05 to 1.12), respectively, for girls. Unadjusted and adjusted odds ratios were also virtually identical for wheeze and "asthma or bronchitis". The lack of effect of adjustment was due to a change in the association between BMI and symptoms with time. **CONCLUSIONS:** Trends in overweight and obesity do not explain the increase in asthma. The evidence points towards the association between asthma and obesity being of recent origin. This may be explained by obesity being a marker of recent lifestyle differences now associated with both asthma and overweight.

Chinn S. et al. *Obesity and asthma in children.* Am J Respir Crit Care Med. 2004; 170(1) : 95; author reply 95-6.p

Chitano P. et al. *Maturation changes in airway smooth muscle shortening and relaxation. Implications for asthma.* Respir Physiol Neurobiol. 2003; 137(2-3) : 347-59.p **Abstract:** Greater airway responsiveness in healthy juveniles is considered a factor in the higher asthma prevalence at a young age compared with adults. Several studies on the contractile response of airway smooth muscle (ASM) from birth to adulthood have addressed the hypothesis that a maturation of ASM plays a role in juvenile airway hyperresponsiveness. Maturation of distinct ASM properties, i.e. force generation, shortening, and relaxation, has been reported, although the majority of the studies have focused on maturation of maximum force and/or sensitivity to contractile agonists. However, in most animal species maturation of the ability to generate force does not correlate with maturation of airway responsiveness. Ontogenesis of ASM shortening has been less extensively studied and the existing reports emphasize an increase during maturation of tissue passive forces opposing shortening. ASM spontaneous relaxation has been very minimally investigated. We have recently demonstrated that the ability of ASM to spontaneously relax during stimulation is sharply reduced in juvenile airway tissue. It remains to be determined the role of these ASM properties in the onset of childhood asthma and whether specific alterations are induced by the occurrence of obstructive airway diseases in young individuals.

Chiu C.Y. et al. *Factors predicting early diagnosis of foreign body aspiration in children.* Pediatr Emerg Care. 2005; 21(3) : 161-4.p **Abstract:** **OBJECTIVES:** To analyze the clinical spectrum of tracheobronchial foreign bodies in children and explore the clinical features which could facilitate early diagnosis. **METHODS:** We retrospectively studied pediatric patients who had aspirated foreign bodies over the past 5 years from July 1998 to July 2003 in a tertiary children hospital in northern Taiwan. Patients were divided into 2 groups according to the elapsed time from aspiration to definite diagnosis as early (< or =24 hours after aspiration) and late diagnosis (>24 hours after aspiration). The 2 groups were compared for clinical features, radiological findings, and the influence of morbidity and mortality of early- and late-diagnosed foreign body aspiration (FBA). **RESULTS:** A total of 53 patients (27 boys, 26 girls) were recruited with a median age of 25.4 +/- 21.3 months. FBA was suspected by the parents in 59% of patients. Sudden onset of cough (72%), dyspnea (64%), and wheeze (60%) were the predominant symptoms and signs. Nuts and peanut (59%) were the most common foreign bodies aspirated. Obstructive emphysema (53%) and normal chest radiograph (34%) were the most frequent radiological findings. Parenchymal consolidation with pneumonia was predominant in the group of late diagnosis (P < 0.05). Bronchial asthma (n = 9), pneumonia (n = 8), and common cold (n = 5) were the most common mistaken diagnoses. Witnessing of choking episode was the most important historical event to pinpoint an early diagnosis of FBA in children (P = 0.002). **CONCLUSIONS:** In children with an

unequivocal choking event while eating even with normal physical and radiographic findings, FBA requires to be excluded by thorough investigations in such instances. Similarly, in toddlers with unexplained persistent cough with refractory parenchymal infiltrates, unrecognized FBA should also be considered. A witnessed choking event is the most important historical information to make an early diagnosis of FBA.

Chiu W.J. et al. *Evaluation of clinical and immunological effects of inactivated influenza vaccine in children with asthma.* Pediatr Allergy Immunol. 2003; 14(6) : 429-36.p **Abstract:** Although annual influenza vaccinations are recommended by many authorities, some doctors may be reluctant to vaccinate asthmatic children because of the risk of inducing bronchial reactivity and exacerbating the asthma. In this study, the effect of split influenza vaccine on clinical symptoms, airway responsiveness and its influence on T lymphocytes was evaluated. Twenty-one asthmatic children with stable asthma were recruited and divided into two groups. Eleven patients who received the influenza vaccine formed the vaccination group and 10 patients who received a placebo formed the placebo group. Forced expiratory volume in 1 s (FEV1), airway response (PC20 methacholine, PC20=provocation concentration causing a 20% fall in FEV1) and the T lymphocyte subset ratio (Th1/Th2) were recorded on day 1 pre-vaccination and day 14 post-vaccination. Patients were also asked to record their peak expiratory flow (PEF) every morning and evening and to complete daily symptom scores over the period of 2 weeks. There were no significant changes in PC20, FEV1, PEF variability, symptom scores and the Th1/Th2 ratio between the vaccination and placebo groups between day 1 pre-vaccination and day 14 post-vaccination. Similar results of PEF variability and asthma symptom score were obtained when the analysis was restricted to the day 1 pre-vaccination and day 3 post-vaccination. Immunization with split influenza vaccine does not exacerbate asthma in children either with a clinical or immunological effect. These results suggest that children with stable asthma can safely be immunized with a split influenza vaccine.

Chmelik E. et al. *Varied presentation of PANDAS: a case series.* Clin Pediatr (Phila). 2004; 43(4) : 379-82.p

Cho S.H. et al. *Possible role of the 4G/5G polymorphism of the plasminogen activator inhibitor 1 gene in the development of asthma.* J Allergy Clin Immunol. 2001; 108(2) : 212-4.p

Cho S.H. et al. *Association between bronchodilating response to short-acting beta-agonist and non-synonymous single-nucleotide polymorphisms of beta-adrenoceptor gene.* Clin Exp Allergy. 2005; 35(9) : 1162-7.p **Abstract:** **BACKGROUND:** With beta-agonists being the most widely used agents in the treatment of asthma, in vitro studies reported that beta(2)-adrenergic receptor (ADRB2) polymorphisms are associated with agonist-promoted down-regulation. **OBJECTIVE:** The present population-based study aimed to evaluate the association between bronchodilating response to inhaled short-acting beta-agonist and two non-synonymous single-nucleotide polymorphisms (SNPs) of ADRB2 (ADRB2-16 and ADRB2-27). **METHODS:** Two hundred and nine children with reduction in forced expiratory volume in 1 s of more than 20% on methacholine bronchial challenge underwent bronchodilating response testing 5 min after the inhalation of 200 mug of albuterol. Of these 209, 195 gave peripheral blood for genotyping of ADRB2 polymorphisms. **RESULTS:** The bronchodilating response was significantly higher in subjects with the homozygous Arg16 than in those with the homozygous Gly16. It was further demonstrated that haplotype pairs of the homozygous Arg16Gln27 and of the heterozygous Arg16Gln27/Gly16Glu27 showed the highest bronchodilating responses, and the haplotype pairs of the homozygous Gly16Gln27 the lowest response. As a whole, the bronchodilating response was more positively associated with the

combined quantity of Arg16 and Glu27 polymorphisms than with that of Arg16 alone. CONCLUSION: Non-synonymous SNPs of ADRB2 at codons 16 and 27 is significantly associated with bronchodilating response to inhaled short acting beta-agonists.

Chong Neto H.J. et al. [Different inhaler devices in acute asthma attacks: a randomized, double-blind, placebo-controlled study]. *J Pediatr (Rio J)*. 2005; 81(4) : 298-304.p **Abstract:** OBJECTIVE: To verify the efficacy, side effects, and cost of treatment of acute asthma attacks, using different inhaler devices. METHODS: This is a randomized, double-blind, placebo-controlled study. Salbutamol was administered via a nebulizer, a metered-dose inhaler (attached to a commercially available spacer device), a homemade non-valved spacer device, or a dry powder inhaler. Assessments were made at zero, 20, 40 and 60 minutes, followed by the application of salbutamol and placebo with another device. Forty children (mean age of 11+/-3.5 years) with acute asthma attacks, were evaluated. Clinical score, forced expiratory volume in one second and side effects were analyzed. The costs for medication and spacer devices were calculated. RESULTS: There is no difference between groups regarding clinical score and variation of forced expiratory volume in one second. There was a major variation in the heart rate response to the nebulizer (35%) compared to the commercially available spacer and dry powder inhaler (15 and 17%) and between the homemade spacer and the commercially available spacer (28 and 15%) (p = 0.004). The nebulizer and homemade spacer caused more tremor (p = 0.02). The cost of treatment was higher for the nebulizer and commercially available spacer (p = 0.0001). CONCLUSIONS: The nebulizer was more expensive and used more medicine, showing the same efficiency. The homemade spacer was cheaper, but presented more side effects. The commercially available spacer was as expensive as the nebulizer, although safer. The dry powder inhaler was cheaper, but, just as the homemade spacer, it also caused tachycardia.

Chong Neto H.J. et al. [Treatment of acute asthma in developing countries]. *J Pediatr (Rio J)*. 2004; 80(1) : 81-2; author reply 82-3.p

Chou H. et al. The prevalence of IgE antibody reactivity against the alkaline serine protease major allergen of *Penicillium chrysogenum* increases with the age of asthmatic patients. *Ann Allergy Asthma Immunol*. 2003; 90(2) : 248-53.p **Abstract:** BACKGROUND: *Penicillium* species are prevalent airborne fungi. However, the prevalence of allergic sensitization to *Penicillium* antigens and the true impact of these ubiquitous fungi on atopic respiratory disorders remain to be determined. OBJECTIVE: The purpose of this study was to analyze the prevalence of immunoglobulin (Ig)E and IgG antibodies against *Penicillium chrysogenum* (Pen ch 13), the alkaline serine protease major allergen of *P. chrysogenum*, in asthmatic patients of different age groups. METHODS: Pen ch 13 was purified from a culture medium of *P. chrysogenum*. The reactivity of IgE and IgG antibodies to Pen ch 13 in the serum samples of 212 asthmatic patients was analyzed by immunoblotting methods. RESULTS: Sixty-nine (33%) of the 212 sera analyzed showed IgE and/or IgG immunoblot reactivity to Pen ch 13. Significant differences in the prevalence of IgE and/or IgG antibody reactivity to Pen ch 13 were found among eight different age groups of 212 asthmatic patients. The frequency of IgE-binding reactivity to Pen ch 13 increased significantly with the age of the patients. It was 7% for the group less than 10 years old and 42% for the group older than 70 years old. In addition, a significant difference between the prevalence of IgE (7%) and IgG (33%) antibodies against Pen ch 13 in the group aged 10 or less was also found. CONCLUSIONS: Our study demonstrates that IgE and IgG antibodies specific for Pen ch 13 were detected in approximately one-third of the 212 asthmatic patients analyzed. Our results suggest that allergic sensitization to Pen ch 13, and possibly to other airborne *Penicillium* species, is more common in older asthmatic patients.

Chou T.Y. et al. The clinical efficacy of in vitro allergen-specific IgE antibody test in the diagnosis of allergic children with asthma. *Acta Paediatr Taiwan*. 2002; 43(1) : 35-9.p **Abstract:** Asthma is a very common respiratory allergic disease in Taiwan. The aims of this study were to investigate the allergen-sensitized profile and its relationship with serum total IgE levels in allergic asthmatic children in Taiwan. Moreover, the number of allergens to be tested for the most efficient and effective diagnosis of allergic diseases was also examined. Total IgE and IgE specific for a panel of common aeroallergens were assayed in 200 serum samples of asthmatic children using Pharmacia CAP system (Pharmacia, Uppsala, Sweden). House dust mites Der p (Dermatophagoides pteronyssinus), Der f (Dermatophagoides farinae), and Bt (Blomia Tropicalis) had the highest sensitized rates at 82.5%, 82.0%, and 72%, respectively. *Candida albican* (14.0%) and Bermuda grass (8.0%) were the most common sensitized fungus and pollen in our subjects, respectively. The accumulated sensitized rate (10%) for pollens was lower than those of fungus (21.5%) and house dust allergens (84%). The average serum total IgE of the allergen-negative asthmatic children (n=30) was significantly lower than that of children with at least one allergen sensitized asthma (n=170) (377.9 +/- 123.6 vs. 1117.8 +/- 235.7 IU/ml, p<0.05). The level of total IgE was significantly correlated with the concentrations of mite-specific IgE antibodies, but not with the numbers of allergen sensitized. In addition, the detection rate was 84% when the 4 most common allergens (Der p, Der f, Dog dander, and cockroach) were tested, similar to the result after testing for all 12.

Chrousos G.P. et al. Effects of mometasone furoate dry powder inhaler and beclomethasone dipropionate hydrofluoroalkane and chlorofluorocarbon on the hypothalamic-pituitary-adrenal axis in asthmatic subjects. *Chest*. 2005; 128(1) : 70-7.p **Abstract:** STUDY OBJECTIVES: Mometasone furoate dry powder inhaler (MF-DPI) [400 mug] is an inhaled corticosteroid (ICS) that is effective in the treatment of asthma. MF-DPI has a low potential for suppression of the hypothalamic-pituitary-adrenal (HPA) axis at its clinical dose. The effect of MF-DPI, 400 microg qd, on the HPA axis was compared to that of beclomethasone dipropionate (BDP) using hydrofluoroalkane (HFA) and chlorofluorocarbon (CFC) propellants via metered-dose inhalers (MDIs) twice daily. DESIGN AND INTERVENTIONS: This randomized, third-party blind, parallel-group study compared the effects of MF-DPI 400 mug one puff qd in the morning (n = 18), HFA-BDP 200 microg two puffs MDI bid (n = 18), and CFC-BDP 400 microg two puffs MDI bid (n = 17) for 14 days on the area under the 24-h serum cortisol concentrations curve (AUC(0-24)) and on total 24-h urinary free cortisol excretion in mild asthmatic subjects. Effects on morning/evening peak expiratory flow (PEF) and on inhaled albuterol use were also assessed. Adverse events that occurred during or > or = 30 days after the study were recorded. RESULTS: The mean decrease from baseline in the serum cortisol concentrations AUC(0-24) in the MF-DPI group was significantly less than in either the HFA-BDP (p = 0.024) or the CFC-BDP (p = 0.011) groups. Decreases in serum cortisol concentrations AUC(0-24) in the two BDP groups did not differ from one another. The MF-DPI group trended toward higher morning and evening PEF than either BDP group. Treatment-associated adverse events were reported by seven subjects in the MF-DPI group, vs one subject in the HFA-BDP and three subjects in the CFC-BDP groups; these were mild, and no subject discontinued treatment due to an adverse event. CONCLUSIONS: Fourteen days of treatment with MF-DPI 400 microg qd was associated with a significantly lesser decrease in the serum cortisol concentrations AUC(0-24) compared with HFA-BDP 200 microg MDI or CFC-BDP 400 microg MDI bid.

Chuchalin A. et al. Formoterol used as needed in patients with intermittent or mild persistent asthma. *Respir Med*. 2005; 99(4) : 461-70.p **Abstract:** OBJECTIVE: To study the effectiveness and safety of as-needed treatment of formoterol compared with the short-acting alternative terbutaline. METHODS: Two double-blind, 12-

month, parallel-group, non-inferiority trials comparing as-needed use of formoterol (Oxis) 4.5 microg and terbutaline (Bricanyl) 0.5 mg via dry-powder inhaler (Turbuhaler), one in 675 patients with intermittent and one in 455 patients with mild persistent asthma, overall 6-87 years of age. Peak expiratory flow (PEF), symptoms, rescue medication use, exacerbations, airway responsiveness (metacholine challenge; subgroup of 127 patients), systemic effects (high single-dose test; subgroup of 87 patients), and safety (adverse events) were assessed. RESULTS: Formoterol 4.5 microg was as effective as terbutaline 0.5 mg with regard to morning PEF (non-inferiority; lower 95% confidence interval limit above -10 L/min). Metacholine sensitivity, exacerbation rates or use of rescue medication did not differ between treatments. Formoterol 4.5 microg was shown to give less systemic effects than terbutaline 6 mg. Both treatments were safe and well tolerated. CONCLUSIONS: Formoterol 4.5 microg used as needed was at least as effective and safe as terbutaline 0.5 mg used as needed in intermittent and mild persistent asthma, and was associated with less systemic effects when administered as high single doses.

Chung H.T. et al. *Association analysis of novel TBX21 variants with asthma phenotypes.* Hum Mutat. 2003; 22(3) : 257.p **Abstract:** Human TBX21 expressed in T Cells (T-BOX21) is a Th1-specific T-box transcription factor that controls the expression of the hallmark Th1 cytokine, IFNG. As a potent candidate gene for asthma genetic study, we have sequenced the full gene of human TBX21, including the -1,500bp promoter region to identify its gene polymorphisms. Twenty-three single nucleotide polymorphisms (SNPs) were identified; one in promoter region (c.-1514T>C), one in 5'UTR (c.-138C>A), two in exon 1 (c.99C>G (p.His33Gln), c.390A>G), sixteen in introns (c.492+806T>C, c.492+1170C>A, c.492+1514G>A, c.492+1907A>C, c.492+2116G>A, c.492+2516A>G, c.492+2953C>T, c.492+4207A>T, c.492+4211A>T, c.492+4985T>A, c.492+4207G>A, c.492+5533C>T, c.492+7889T>A, c.492+8270G>C, c.768+417T>C and c.989+183C>T), one in exon 4 (c.831C>T), one in exon 6 (c.1455G>A), and one in 3'UTR (c.2103A>C). Among twenty-three identified variants, seven were selected for larger scale genotyping (n=721) for asthma association study based on frequencies and location. Haplotypes, their frequencies and linkage disequilibrium coefficients (mid R:D'mid R:) between SNP pairs were estimated. The associations with risk of asthma, skin-test reactivity and total serum IgE levels were analyzed. Using statistical analyses for association of TBX21 polymorphisms with these three asthma phenotypes, no significant signals were detected. In conclusion, we identified twenty-three genetic polymorphisms in the important TBX21 gene, but no significant associations of TBX21 variants with asthma phenotypes were detected. TBX21 variation/haplotype information identified in this study will provide valuable information for future association studies of other immunological diseases.

Chung K.F. et al. *Therapy for cough: active agents.* Pulm Pharmacol Ther. 2002; 15(3) : 335-8.p **Abstract:** Cough is an important defensive reflex of the upper airway and is also a very common symptom of respiratory disease. Cough after an upper respiratory virus infection is transient, and persistent cough is associated with a whole range of conditions such as asthma, rhino-sinusitis, gastro-oesophageal reflux. Treatment directed at these conditions may improve the associated cough. There is often a need, however, to control cough itself, whatever the cause. The most effective drugs in this class are the opioids, such as morphine, codeine or pholcodeine, but at effective doses they have side-effects such as drowsiness, nausea, constipation and physical dependence. Investigations into the cough reflex and into the potential mechanisms of sensitised cough reflex have uncovered several potential targets for novel drugs. New opioids such as k- and d-receptor agonists apart from m-agonists have been developed, in addition to non-opioid, nociceptin. Neurokinin receptor antagonists, bradykinin receptor antagonists, vanilloid receptor VR-1 antagonists may be beneficial by blocking

effects of tachykinins, and sensory nerve activation. Local anaesthetics, blockers of sodium-dependent channels, and maxi-K CA2+-dependent channel activators of afferent nerves are inhibitors of the cough reflex. Some of these novel agents may act centrally or peripherally or at both sites as antitussives. Large scale trials of these novel compounds have not been tried in cough in man, but there is a serious need for more effective antitussives devoid of side-effects.

Cicutto L. et al. *Breaking the access barrier: evaluating an asthma center's efforts to provide education to children with asthma in schools.* Chest. 2005; 128(4) : 1928-35.p **Abstract:** OBJECTIVE: To evaluate an asthma education program for children with asthma that is delivered in their school by certified asthma educators from a local hospital-based asthma center. STUDY DESIGN: Randomized controlled trial. SETTING: Twenty-six elementary schools located in a suburb of Toronto. PARTICIPANTS: A total of 256 children in grades 2 to 5 with asthma and their parents were randomized to control and experimental groups. INTERVENTION: Children in the experimental group received the "Roaring Adventures of Puff" asthma education program over the course of six weekly 1-h sessions. Those in the control group continued receiving usual care. MEASUREMENTS AND RESULTS: Data collection involved measuring asthma quality of life, self-efficacy for managing asthma, school absenteeism, days of interrupted activity, health services use, and parental loss of time from work. Quality of life and self-efficacy data were collected from the children at baseline and 2 months. Telephone parental interviews conducted over 1 year were used to collect data on the remaining variables. Unpaired t test, analysis of variance, and chi2 test were used to determine whether differences existed between the groups. The results are reported as the mean +/- SD. The experimental group demonstrated higher scores than the control group for self-efficacy (3.6 +/- 0.7 vs 3.8 +/- 0.9, respectively; p < 0.05) and quality of life (5.0 +/- 1.4 vs 5.5 +/- 1.4, respectively; p < 0.05). At 1 year, the experimental group demonstrated fewer mean urgent health-care visits (2.5 +/- 2.5 vs 1.7 +/- 1.9 visits per year, respectively; p < 0.01), days of missed school (4.3 +/- 5.7 vs 3.0 +/- 4.4 days per year, respectively; p > 0.05), and days of interrupted activity (9.1 +/- 10.5 vs 6.2 +/- 7.3 days per year; p < 0.01) related to asthma than the control group. There were no differences between the groups for parental work absenteeism or scheduled asthma visits. CONCLUSION: Providing an asthma education program to children in their school can significantly improve quality of life and reduce the burden of childhood asthma.

Ciprandi G. et al. *Long-term cetirizine treatment may reduce new sensitisations in allergic children: a pilot study.* Allerg Immunol (Paris). 2003; 35(6) : 208-11.p **Abstract:** Experimental data demonstrate that mite allergy is characterized by persistent chronic inflammation. This suggests that long-term continuous treatment may be included in the global strategy of allergy management as recently reported. Moreover, most of allergic subjects show polysensitisation. We conducted a study to investigate whether a long-term cetirizine treatment may reduce the occurrence of new sensitisations in children with mite allergy. This study was initially double-blind, randomized, and placebo-controlled, with two parallel groups of 10 children with mite allergy receiving either cetirizine or placebo daily. All children could assume cetirizine as rescue medication (i.e. symptomatic treatment). After six months, parents of continuously-treated children decided to continue the treatment for 3 years. Other subjects continued to assume cetirizine on symptomatic basis. All children were prospectively followed for other 3 years. Outcome measure was skin prick test, yearly performed. Cetirizine-continuously-treated group showed a significant lower incidence of new sensitisations (p = 0.002). In conclusion, cetirizine administered daily for prolonged periods (i.e. 3 years) may decrease the development of new sensitisations in monosensitised children, showing a potential effect of tertiary prevention of allergy.

- Cisse L. et al.** *[Skin tests in allergic children of Ivory Coast]. Arch Pediatr.* 2005; 12(5) : 619.p
- Ciuk J. et al.** *Domestic nitrogen oxide exposure, urinary nitrate, and asthma prevalence in preschool children.* Arch Environ Health. 2001; 56(5) : 433-8.p **Abstract:** A South Australian preschool study carried out in 1993 showed that the prevalence of respiratory symptoms was significantly associated with use of unflued gas appliances for cooking and heating. The authors sought to determine an association between domestic exposure to nitrogen dioxide and the excretion of total urinary nitrate and nitrite, and their association with asthma prevalence. The results indicated that the geometric mean concentrations of nitrogen dioxide were much higher in homes that had natural gas appliance(s) and other types of appliances (i.e., electric and solid fuel). Higher levels of nitrogen dioxide were found in homes of suburban areas with higher prevalence of asthma and respiratory symptoms. Nitrogen dioxide levels were lower in the summer, and there was a higher level in kitchens than in bedrooms. Urinary nitrate excretion was evaluated in 1,335 preschool children from the same sampling areas. No association existed between nitrogen dioxide levels and urinary nitrates, nor was there a relationship between urinary nitrates and asthma prevalence. These findings confirm that there is a positive association between nitrogen dioxide exposure from gas appliances and the prevalence of respiratory symptoms, but urinary nitrate is not a useful biomarker of exposure at these levels.
- Clark J.A. et al.** *Comparison of traditional and plethysmographic methods for measuring pulsus paradoxus.* Arch Pediatr Adolesc Med. 2004; 158(1) : 48-51.p **Abstract:** BACKGROUND: In the evaluation of patients with acute asthma, pulsus paradoxus (PP) is an objective and noninvasive indicator of the severity of airway obstruction. However, in children PP may be difficult or impossible to measure. Indwelling arterial catheters facilitate the measurement of PP, but they are invasive and generally reserved for critically ill patients. OBJECTIVE: To determine the utility of the plethysmographic waveform (PPpleth) of the pulse oximeter in measuring PP. METHODS: Patients from the pediatric intensive care unit, emergency department, and inpatient wards of a tertiary care pediatric hospital were eligible for the study. A total of 36 patients (mean age [SD], 11.2 [4.7] years) were enrolled in the study. Pulsus paradoxus was measured using the traditional auscultatory (PPausc) method with a sphygmomanometer. Pulsus paradoxus was then measured using a blood pressure cuff observing for the disappearance and reappearance of the (PPpleth) on the pulse oximeter. Mean difference and 95% confidence intervals were calculated for each method. The 2 methods were also analyzed for correlation and agreement using the Pearson product moment correlation and a Bland and Altman plot. RESULTS: Patients with status asthmaticus had higher PPausc and PPpleth readings compared with nonasthmatic patients. Pulsus paradoxus measured by plethysmography in patients with and without asthma was similar to PPausc readings (mean difference, 0.6 mm Hg; 95% confidence interval, -0.6 to 2.1 mm Hg). Individual PPpleth readings showed significant correlation and agreement with PPausc readings in patients both with and without asthma. CONCLUSION: Measurement of PP using the pulse oximeter-pulse plethysmographic waveform offers a simple and noninvasive method for evaluating patients with airway obstruction.
- Clark N.M. et al.** *Issues in identifying asthma and estimating prevalence in an urban school population.* J Clin Epidemiol. 2002; 55(9) : 870-81.p **Abstract:** This article first presents salient issues related to identifying children in urban schools who might benefit from asthma services. It discusses a brief questionnaire for identifying cases and problems in estimating asthma prevalence. Subsequently, results of case detection in 14 urban schools are presented and discussed in light of these issues. The questionnaire was employed with parents of 4,653 African-American children in Detroit. Results suggest that determining number, type, and frequency of symptoms may be necessary to ascertain prevalence of asthma. Using only number and type produced a rate of asthma of 25%. Adding frequency provided a more conservative estimate of 19%. About 9% of children exhibiting symptoms of asthma had no physician diagnosis. Only 25% with symptoms reflecting mild persistent, 35% with moderate persistent, and 26% with severe persistent disease had prescriptions for anti-inflammatory medicine. Further, 23% of children with asthma-like symptoms had no prescription for asthma medicine of any type. CONCLUSIONS: (1) low-cost procedures can be used in schools to identify children with suspected undiagnosed and undertreated asthma; (2) prevalence estimates for asthma in the group of urban school children studied are among the highest in the United States; and (3) asthma is undertreated in this sample.
- Clark N.M. et al.** *Effects of a comprehensive school-based asthma program on symptoms, parent management, grades, and absenteeism.* Chest. 2004; 125(5) : 1674-9.p **Abstract:** STUDY OBJECTIVE: This study assessed the impact of a comprehensive school-based asthma program on symptoms, grades, and school absences in children, and parents' asthma management practices. DESIGN: Randomized controlled trial. SETTING: Fourteen elementary schools in low-income neighborhoods in Detroit, MI. PARTICIPANTS: Eight hundred thirty-five children with asthma in grades 2 through 5 and their parents. INTERVENTION: The intervention entailed six components for children, their parents, classmates, and school personnel to encourage and enable disease management. MEASUREMENTS AND RESULTS: Parents completed telephone interviews and the schools provided data at baseline and 24 months after intervention. At follow-up, treatment children with persistent disease had significant declines in both daytime (14% fewer, $p < 0.0001$) and nighttime (14% fewer, $p < 0.0001$) symptoms. Among children with both mild intermittent and persistent disease, those in the treatment group had 17% fewer daytime symptoms ($p < 0.0001$) but 40% more nighttime symptoms. Treatment children had higher grades for science ($p < 0.02$) but not reading, mathematics, or physical education. No differences in school absences for all causes between groups were noted in school records. However, parents of treatment group children reported fewer absences attributable to asthma in the previous 3 months (34% fewer, $p < 0.0001$) and 12 months (8% fewer, $p < 0.05$). Parents of treatment children had higher scores (2.19 greater, $p = 0.02$) on an asthma management index. The program may have stimulated attention to symptoms at night by parents of children with mild intermittent disease. Overall, the intervention provided significant benefits, particularly for children with persistent asthma.
- Clark N.M. et al.** *Case 1: assessment. A new educational program for the parents of children with asthma.* Paediatr Respir Rev. 2003; 4(4) : 347, 349.p
- Clark N.M. et al.** *The role of behavioural theories in educational interventions for paediatric asthma.* Paediatr Respir Rev. 2003; 4(4) : 325-33.p **Abstract:** Controlling paediatric respiratory disease requires a significant change in the behaviour of all stakeholders: patient, family, clinician, community and health system. The good management of asthma by patients requires that they learn what works and does not work for them given their particular circumstances. Asthma interventions can help patients to improve their self-regulation and achieve better health status, quality of life and personal goals. Many asthma interventions do not, however, achieve change because they are not based on sound theories of behaviour. They fail to teach patients how to observe, judge and react appropriately to their change efforts. Successful interventions have been based on theoretical principles and have generally combined strategies for preventing and managing an asthma episode and managing the social and behavioural factors associated with the disease.

- Clavenna A. et al.** *Inappropriate use of anti-asthmatic drugs in the Italian paediatric population.* Eur J Clin Pharmacol. 2003; 59(7) : 565-9.p
Abstract: OBJECTIVE: To evaluate anti-asthmatic drug prescriptions in a large Italian paediatric population. METHODS: Prescriptions involving 417,559 children younger than 14 years old dispensed during 2000 by the retail pharmacies of 17 Italian local health units participating in the ARNO project were analysed. RESULTS: In the study, 92,890 children (22.2%) received at least one anti-asthmatic drug prescription. The prevalence of prescriptions was higher in children less than 1 year old, significantly decreased with increasing age, and was higher in boys than in girls. Of children treated with anti-asthmatic drugs, 71.5% received prescriptions of less than three boxes. Beclomethasone, salbutamol, flunisolide and fluticasone were the most prescribed drugs. Beclomethasone and flunisolide were prescribed mostly as nebulised suspension. CONCLUSIONS: The data suggest that anti-asthmatic drugs are often prescribed for diseases different from asthma and that many children are exposed to treatments for which there is no evidence of efficacy.
- Clifton V.L. et al.** *Increased anti-oxidant enzyme activity and biological oxidation in placenta of pregnancies complicated by maternal asthma.* Placenta. 2005; 26(10) : 773-9.p **Abstract:** Our previous work has demonstrated that alterations in placental function are associated with changes in fetal development in pregnancies complicated by asthma. The pathophysiology of asthma in adults and children and intrauterine growth restriction during pregnancy are associated with oxidative stress. Based on this information, we examined whether placental anti-oxidant pathways and markers of biological oxidation were altered in pregnancies complicated by asthma. Anti-oxidant enzyme activities of superoxide dismutase, glutathione peroxidase and thioredoxin reductase, thioredoxin concentrations, lipid and protein oxidation levels were measured in placenta of pregnancies complicated by asthma and compared to uncomplicated, non-asthmatic pregnancies. Placental tissue homogenates of pregnancies complicated by asthma demonstrated significantly increased levels of lipid peroxidation (25.7±1.8 micromol/mg protein versus 12.1±1.6 micromol/mg protein, P=0.008) and protein carbonyl concentrations (414.6±51.4 units/mg protein versus 222.3±32.6 units/mg protein, P=0.0032) when compared to non-asthmatic controls. The activities of the anti-oxidant proteins superoxide dismutase (2.17±0.09 units/mg protein versus 1.67±0.09 units/mg protein, P=0.014) and thioredoxin reductase (54.0±6.9 units/mg protein versus 28.7±6.0 units/mg protein, P=0.009) were significantly increased in the presence of maternal asthma. Placental thioredoxin levels (102.9±5.3 ng/mg protein versus 92.9±8.6 ng/mg protein, P=0.37) and glutathione peroxidase activity (27.3±2.2 mmol/min/mg protein versus 28.3±2.2 mmol/min/mg, P=0.83) were not significantly different in pregnancies complicated by asthma and non-asthmatic pregnancies. There was no effect of fetal sex, asthma severity or treatment for asthma on these pathways. Maternal asthma during pregnancy is associated with increased placental enzymatic anti-oxidant capacity and also increased protein oxidation suggesting there is a compensatory increase in anti-oxidant activity in response to increased oxidative stress.
- Coates A.L.** *Asthma--clinical and physiological assessment.* Paediatr Respir Rev. 2004; 5 Suppl A : S89-92.p
- Cobos N. et al.** *[Pilot study on knowledge about asthma and its treatment among Spanish teachers].* Med Clin (Barc). 2001; 117(12) : 452-3.p
Abstract: This was a study aimed to know the knowledge about asthma. SUBJECTS AND METHOD: 933 teachers of 27 schools from 7 cities (children aged between 4 and 15 years) using a self-administered questionnaire Half of them knew asthma prevalence and its hereditary nature. Nearly all related asthma with allergy, 38% with exercise, 25% had students who suffered from asthma attacks in the school, and 91% admitted to have limited information and wish to improve it. CONCLUSION: Our survey reveals that Spanish teachers have a limited information about asthma.
- Cockcroft D.W. et al.** *Methacholine challenge: test-shortening procedures.* Chest. 2001; 120(6) : 1857-60.p **Abstract:** STUDY OBJECTIVES: Validation of test-shortening procedures for the 2-min tidal breathing methacholine challenge method. DESIGN: Retrospective chart review. SETTING: Tertiary-care university clinical pulmonary function laboratory. PATIENTS: One thousand subjects aged 10 to 85 years (mean ± SD, 44.5 ± 16.0 years), 44.5% male, referred for methacholine challenge. INTERVENTION: Two-minute tidal breathing methacholine challenge was performed, with both physician and technician access to published test-shortening procedures. MEASUREMENTS AND RESULTS: There were 315 positive test results (provocative concentration of methacholine causing a 20% fall in FEV(1) [PC(20)] < or = 8 mg/mL) and 685 negative test results. The subjects with positive test results were less likely to be male (39.1 vs 47.5%; p < 0.02) and had lower FEV(1) (91.8 ± 14.9% predicted vs 97.2 ± 13.9% predicted; p < 0.001). The average starting PC(20) was between 0.5 mg/mL and 1.0 mg/mL; the most common PC(20) was 1 mg/mL (67%). There were 431 skipped concentrations in 380 subjects. The mean number of methacholine inhalations was 3.7 ± 1.1 (3.9 ± 0.1 for negative test results vs 3.3 ± 1.2 for positive test results; p < 0.001). Eighteen subjects had a > or = 20% FEV(1) fall on the first inhalation, and 11 subjects had a > or = 20% FEV(1) fall after a skipped concentration. In only one case (0.1%) an FEV(1) fall > or = 40% on the first concentration was reported, compared with no cases after a skipped concentration and seven cases with a > or = 40% FEV(1) fall after a routine doubling dose step-up. CONCLUSIONS: The 2-min tidal breathing methacholine test in clinical practice can be safely shortened to an average of less than four inhalations using starting concentrations based on FEV(1), asthma medication, and clinical features, and by occasionally omitting concentrations.
- Codina R. et al.** *Sensitization to soybean hull allergens in subjects exposed to different levels of soybean dust inhalation in Argentina.* J Allergy Clin Immunol. 2000; 105(3) : 570-6.p **Abstract:** BACKGROUND: Soybean hulls (SHs) have been identified as the source of aeroallergens responsible for soybean asthma outbreaks. However, the prevalence of sensitization to SH allergens in subjects from Argentina, a country where soybeans are produced, is unknown. OBJECTIVE: The purpose of this study was to determine the prevalence of sensitization to SH by in vivo and in vitro tests in subjects with asthma or allergic rhinitis and in control subjects from Argentina who have been exposed to different levels of soybean dust inhalation (SDI). METHODS: Exposure to SDI is defined as follows: (1) direct = occupational, (2) indirect = proximity to soybean fields or grain elevators, and (3) urban = urbanized areas without a known source of SDI. Two groups were studied. Group 1 consisted of 365 subjects with asthma or allergic rhinitis and group 2 (control group) of 50 healthy individuals. Subjects from both groups were classified according to their exposure to SDI. All subjects completed standard questionnaires. Prick skin tests (STs) with an SH extract and with common allergens were performed on all subjects. Specific IgE and IgG4 to SH were measured in sera of 51 of 56 subjects from group 1 who had a positive ST to SH and in all sera from group 2. RESULTS: Fifty-six (15.3%) subjects from group 1 and no subjects from group 2 had a positive ST to SH (wheat SH/wheat histamine >=0.5). In group 1, positive STs to SH were 38.7%, 20.3%, and 8.2% in subjects with direct, indirect, and urban exposures, respectively (P <.001). Monosensitization to SH is absent in all subjects from group 1. The percent of subjects with positive STs to mites, pollen, and molds was highest in those with a positive ST to SH versus those with a negative ST to SH (P <.01). Asthmatic patients with a positive ST to SH, compared with those exclusively sensitized to mites, had a higher frequency of daily or weekly symptoms (59.4% vs 25.7%, respectively, P <.001) and a higher percent of glucocorticoid dependence (52.8% vs 34%, respectively, P

<.01). Percent positive IgE in group 1 and group 2 were 39.2% and 10% (P <.001) and percents positive IgG4 are 27.4% and 12%, respectively (not significant). In subjects from group 1 and group 2 with direct exposure percents positive IgE are 58.3% and 13.3% (P <.001) and percents positive IgG4 were 75% and 20%, respectively (P <.02). IgG4 in group 1 was significantly higher in subjects with direct exposure compared with subjects with indirect or urban exposure. CONCLUSION: This study demonstrated that there was (1) a high prevalence of sensitivity to SH in subjects with asthma or allergic rhinitis from Argentina and (2) an association between sensitivity to SH and severity of asthma and level of exposure to SDI.

- Coffey M.J. et al.** *Ethical assessment of clinical asthma trials including children subjects.* Pediatrics. 2004; 113(1 Pt 1) : 87-94.p Abstract: BACKGROUND: The inclusion of children with asthma in clinical asthma trials is increasing, including their participation in placebo-controlled trials (PCTs). The objectives of this study are to assess whether children with asthma have been harmed by their participation in PCTs. METHODS: Seventy clinical asthma trials involving children published between January 1998 and December 2001 that involved distinct US research populations were identified. Studies were reviewed to determine whether all subjects with more than mild asthma received daily antiinflammatory medication as recommended by national guidelines. Sixty-two clinical asthma trials included data about subject withdrawal and were analyzed for the frequency of asthma exacerbations. RESULTS: Forty-five studies were designed as PCTs and did not require that all subjects with more than mild asthma receive antiinflammatory medications. Of 24,953 subjects, 4653 (19%) for whom data are available withdrew from research, and 1247 subjects (9.4%) withdrew from PCTs due to asthma exacerbations compared with 358 subjects (3.1%) in other trials. In PCTs, subjects withdrew more frequently from the placebo arms than the active-treatment arms and did so more frequently because of an asthma exacerbation (667 or 15% vs 580 or 6.5%). Fifty-two studies enrolled both children and adults, although only 1 performed subset analysis of the children. CONCLUSIONS: Subjects enrolled in PCTs of asthma have been exposed to unnecessary risks and harms. Clinical asthma trials involving children and adults do not benefit children as a class because they rarely provide subset analysis of children subjects.
- Cohen H.A. et al.** *Bacterial contamination of spacer devices used by asthmatic children.* J Asthma. 2005; 42(3) : 169-72.p Abstract: OBJECTIVES: To investigate bacterial contamination in spacer devices used by asthmatic children and the device maintenance procedures practiced by parents. METHODS: Spacer devices used by 62 asthmatic children were examined. Swabs taken from the inner surface of the reservoirs and face masks were cultured. Parents were interviewed regarding their spacer cleaning and disinfection routines. RESULTS: Bacterial contamination was noted in 22 reservoirs (35.5%) and 16 masks (25.8%). Pseudomonas aeruginosa was isolated from 21.0% of the reservoirs and 14.5% of the face masks, Klebsiella pneumoniae from 6.5% and 4.8%, and Staphylococcus aureus from 9.7% and 8.1%, respectively. Only 34 parents (54.8%) reported that they received cleaning and maintenance instructions from the medical staff at initiation of spacer use by their child, and only 38 (61.8%) cleaned the device after each use. CONCLUSION: Bacterial contamination is common in spacer devices. This study demonstrates that contamination rates are significantly lower when parents clean and actually dry (preferably with an air blower) spacer devices after each use. Spacer device maintenance should be emphasized in education programs for managing asthma.
- Cohet C. et al.** *Infections, medication use, and the prevalence of symptoms of asthma, rhinitis, and eczema in childhood.* J Epidemiol Community Health. 2004; 58(10) : 852-7.p Abstract: BACKGROUND: The "hygiene hypothesis" postulates that

infections during infancy may protect against asthma and atopy. There is also some evidence that antibiotic and/or paracetamol use may increase the risk of asthma. METHODS: The study measured the association between infections, and medication use early in life and the risk of asthma at age 6-7 years. It involved 1584 children who had been notified to public health services with serious infections at age 0-4 years, and 2539 children sampled from the general population. For both groups, postal questionnaires were completed by parents. RESULTS: There was little difference in the prevalence of current wheezing between the childhood infections group (prevalence = 23.5%) and the general population group (prevalence = 24.3%). There was also little difference whether the major site of infection was gastrointestinal (prevalence = 24.1%), invasive (prevalence = 24.6%) or respiratory (prevalence = 21.1%). However, in both groups, there were associations with antibiotic (OR = 1.78, 95% CI 1.49 to 2.14) or paracetamol (OR = 1.38, 95% CI 1.04 to 1.83) use in the first year of life or recent paracetamol use (OR = 2.10, 95% CI 1.78 to 2.49) and current wheezing. There was a weak protective effect of childhood infections in children who had not used antibiotics in the first year of life (OR = 0.78, 95% CI 0.55 to 1.10). CONCLUSIONS: These findings are consistent with other evidence that antibiotic use early in life may increase the risk of asthma. They are also consistent with some preliminary evidence associating paracetamol use with an increased risk of asthma. Any protective effect of notifiable childhood infections was weak.

- Collie D.D.** *Comparative, complementary and relevant: the immunological basis of ovine lung allergic responses.* Clin Exp Allergy. 2003; 33(3) : 282-6.p
- Combescore C. et al.** *Assessment of variations in control of asthma over time.* Eur Respir J. 2003; 22(2) : 298-304.p Abstract: Control and severity of asthma are two different but complementary concepts. The severity of asthma could influence the control over time. The aim of this study was to demonstrate this relationship. A total 365 patients with persistent asthma (severity) were enrolled and followed-up prospectively. Data were analysed using a continuous time homogeneous Markov model of the natural history of asthma. Control of asthma was defined according to three health states which were qualified: optimal, suboptimal and unacceptable control (states 1, 2 and 3). Transition forces (denoted $\lambda(i,j)$ from state i to state j) and transition probabilities between control states were assessed and the results stratified by asthma severity were compared. Models were validated by comparing expected and observed numbers of patients in the different states. Transition probabilities stabilised between 100-250 days and more rapidly in patients with mild-to-moderate asthma. Patients with mild-to-moderate asthma in suboptimal or unacceptable control had a high probability of transition directly to optimal control. Patients with severe asthma had a tendency to remain in unacceptable control. A Markov model is a useful tool to model the control of asthma over time. Severity modified clearly the health states. It could be used to compare the performance of different approaches to asthma management.
- Comino E. et al.** *Management of children after presenting to hospital with acute asthma but not requiring admission.* Aust Fam Physician. 2002; 31(5) : 494-6.p Abstract: OBJECTIVE: To examine the treatment of asthma in children aged 4-15 years in the 12 months following presentation to hospital with acute asthma but not requiring admission. METHOD: Questionnaire based survey addressing the child's use of health services, contact with general practitioners before presentation, use of asthma management plans, symptom frequency, and management of asthma. RESULTS: Sixty-six parents (response rate 50%) completed questionnaires. Children usually experienced infrequent episodic symptoms of asthma, and had good or excellent health (68%). Twenty-two children reported no medical follow up post-emergency department (ED). Of the 39 children who had been reviewed by their GP post-ED, 51% (n = 20) recalled discussing the reasons for presentation to ED with the GP,

41% (n = 16) had a lung function measurement and 64% (n = 25) had discussed ways to better manage the child's asthma to avoid the need for future ED attendance. Most parents of children with asthma (n = 57, 86%) recalled the GP explaining how to manage their child's asthma, but only 35 (61.4%) recalled the GP ever writing down these instructions. **CONCLUSION:** Children with acute asthma who do not require admission may be better managed in the community if there is greater recourse to GP care, use of written management guidelines and opportunities for additional community care are taken up. Further work is needed to identify strategies that will enable GPs to do this.

Comino E.J. *What explains falling asthma mortality?* Med J Aust. 2004; 180(11) : 595.p

Contreras J.P. et al. *Allergen-induced cytokine production, atopic disease, IgE, and wheeze in children.* J Allergy Clin Immunol. 2003; 112(6) : 1072-7.p **Abstract:** **BACKGROUND:** The early childhood allergen-induced immune responses associated with atopic disease and IgE production in early life are not well understood. **OBJECTIVE:** We assessed the relationship of allergen-induced cytokine production by PBMCs to both atopic disease and to IgE increase in a cohort of children with a parental history of allergy or asthma (n = 112) at a median of 2 years of age. We examined cockroach (Bla g 1)-induced, house dust mite (Der f 1)-induced, and cat (Fel d 1)-induced cytokine secretion, including secretion of IFN-gamma, IL-13, IL-10, and TNF-alpha. We investigated whether distinct cytokine patterns associated with atopic disease can be detected in immune responses of children. **METHODS:** PBMCs were isolated, and allergen-induced cytokine secretion was analyzed by means of ELISA. Atopic disease was defined as physician- or nurse-diagnosed eczema or hay fever. Increased IgE was defined as an IgE level of greater than 35 U/mL to dust mite, cockroach, cat, and egg white or a total IgE level of 60 U/mL or greater. **RESULTS:** Compared with children without atopic disease, children with atopic disease had lower Der f 1 (P =.005) and Bla g 2 (P =.03) allergen-induced IFN-gamma levels. Compared with children without increased IgE (n = 95), those with increased IgE (n = 16) had higher Der f 1-induced (P =.006) and Fel d 1-induced (P =.005) IL-13 levels and lower Bla g 2-induced (P =.03) IFN-gamma levels. Compared with children with neither atopic disease nor repeated wheeze, children with both atopic disease and repeated wheeze had lower levels of allergen-induced IFN-gamma (P =.01 for Der f 1 and P =.02 for Bla g 2) cytokine secretion. **CONCLUSION:** In young children at risk for asthma or allergy, decreased allergen-induced IFN-gamma secretion is associated with atopic disease and, in some cases, with increased IgE levels. Increased allergen-induced IL-13 secretion is most strongly associated with early life increase of IgE.

Cooper C. et al. *Psychological morbidity and caregiver burden in parents of children with Tourette's disorder and psychiatric comorbidity.* J Am Acad Child Adolesc Psychiatry. 2003; 42(11) : 1370-5.p **Abstract:** **OBJECTIVE:** To investigate the mental health and caregiver burden in parents of children with Tourette's disorder (TD) compared with parents of children with asthma. **METHOD:** A cross-sectional cohort survey was conducted at TD and pediatric asthma hospital outpatient clinics over a 6-month period. Main outcome measures were parent mental health (General Health Questionnaire [GHQ]-28) and caregiver burden (Child and Adolescent Impact Assessment) scores. **RESULTS:** The response rate achieved was 89.7%. Of the parents of children with TD, 76.9% achieved caseness on the GHQ-28 compared with 34.6% of the parents of children with asthma; this effect remained significant after controlling for demographic variables. Parents of children with TD also experienced greater caregiver burden, and this burden was significantly correlated with GHQ caseness. **CONCLUSIONS:** Parents of children with TD are at risk of psychiatric morbidity; an intervention targeting caregiver burden might be helpful in reducing this.

Cooper W.O. et al. *Corticosteroid prescription filling for children covered by Medicaid following an emergency department visit or a hospitalization for asthma.* Arch Pediatr Adolesc Med. 2001; 155(10) : 1111-5.p **Abstract:** **OBJECTIVE:** To identify predictors of corticosteroid prescription filling following an emergency department (ED) visit or a hospitalization for asthma. **DESIGN:** A retrospective cohort study. **PATIENTS:** Tennessee children (defined as those aged 2-17 years in this study) covered by Medicaid were included in the cohort if they had an ED visit or a hospitalization for asthma between July 1, 1995, and December 31, 1997. **MAIN OUTCOME MEASURES:** Prescriptions filled in the child's name for an oral corticosteroid within 7 days of the latest ED visit or hospitalization for asthma. **RESULTS:** Of 6035 Tennessee children covered by Medicaid with an ED visit for asthma and of 2102 covered by Medicaid with a hospitalization for asthma during the study period, less than half (44.8% following an ED visit and 55.5% following a hospitalization) had prescriptions filled for oral corticosteroids within 7 days. Factors independently predicting a child's not having an oral corticosteroid prescription filled included older age, black race, and residence in rural regions of the state. Conversely, children with oral corticosteroid prescriptions in the previous 6 months were more likely to have oral corticosteroid prescriptions filled following an ED visit for asthma, and children with more than 3 beta-agonist prescriptions in the previous 6 months were more likely to have oral corticosteroid prescriptions filled following a hospitalization for asthma. **CONCLUSIONS:** Overall, fewer than half of Tennessee children covered by Medicaid had an oral corticosteroid prescription filled following an ED visit or a hospitalization for asthma. Age, race, and county of residence predicted failure to have a prescription filled. Further study is needed to determine whether variations in corticosteroid prescription filling relate to physician practice, family behavior, or both.

Cooper W.O. et al. *Oral corticosteroid use among children in TennCare.* Ambul Pediatr. 2002; 2(5) : 375-81.p **Abstract:** **BACKGROUND:** Lack of information about medication effects and use in children is a long-standing and troublesome policy issue. Documenting patterns of use for medications with potential for suboptimal use and adverse effects, such as oral corticosteroids, would be useful. **OBJECTIVE:** To describe the use of oral corticosteroids among children enrolled in TennCare, Tennessee's managed care program for Medicaid enrollees and uninsured individuals. **DESIGN:** A retrospective cohort study. **DRUG EXPOSURE:** Children enrolled in TennCare who had prescriptions filled in their name for oral corticosteroids during 1998 were identified. Descriptive information included age, race, sex, and county of residence. We identified possible indications for corticosteroid use for new users by searching encounter files for encounters temporally related to the index prescription. Subsequent use of corticosteroids was measured in the 365 days after the index prescription. **RESULTS:** Of 400 724 children continuously enrolled in TennCare during the study period, 29 362 (7327 per 100 000) children had a prescription filled for an oral corticosteroid. Steroid prescription filling was more common among young children and male children and less common among black children. Children in rural counties had oral corticosteroid prescriptions filled at a higher rate than children residing in urban counties. Nearly 75% of corticosteroid users filled only 1 prescription during the study period; 1319 children filled 4 or more prescriptions. Asthma was the most common indication for oral corticosteroid use (16%), whereas 1 in 5 users (22%) had an unknown indication for oral corticosteroid use. **CONCLUSIONS:** A large number of children enrolled in TennCare had a prescription for oral corticosteroids filled in 1998. Further population-based studies describing the development of adverse effects in users of corticosteroids would be important.

Corburn J. et al. *Urban asthma and the neighbourhood environment in New York City.* Health Place. 2006; 12(2) : 167-79.p **Abstract:** Asthma is now the leading cause of emergency room visits, hospitalizations, and missed school days in New York City's poorest

neighbourhoods. While most research focuses on the influence of the indoor environment on asthma, this study examines the neighbourhood effects on childhood asthma, such as housing and ambient environmental hazards. Using Geographic Information Science (GI Science) we identify neighbourhoods with elevated concentrations of childhood asthma hospitalizations between 1997 and 2000 in US census tracts, analyze the sociodemographic, housing characteristics, and air pollution burdens from stationary, land use and mobile sources in these areas. The paper reveals the importance of distinguishing the specific and often different combinations of poor housing conditions, outdoor air pollution and noxious land uses that contribute to the high incidence of asthma in impoverished urban neighbourhoods.

Corren J. et al. *Omalizumab, a recombinant humanized anti-IgE antibody, reduces asthma-related emergency room visits and hospitalizations in patients with allergic asthma.* J Allergy Clin Immunol. 2003; 111(1) : 87-90.p **Abstract:** BACKGROUND: Prevention of serious asthma exacerbations is an important therapeutic goal in patients with asthma. OBJECTIVE: The purpose of this study was to investigate the effect of omalizumab (Xolair), a recombinant humanized monoclonal anti-IgE antibody, on the rate of serious exacerbations during long-term therapy. METHODS: A pooled analysis was completed of 3 multicenter, randomized, double-blind, placebo-controlled phase III studies with omalizumab in adults/adolescents aged > or =12 years (n = 1071) and in children aged 6 to 12 years (n = 334) who required treatment with inhaled corticosteroids for allergic asthma. Rates of serious asthma exacerbations were computed and compared between omalizumab- and placebo-treated patients. Serious exacerbations were those leading to unscheduled outpatient visits, emergency room treatment, or hospitalization during 1 year of treatment. RESULTS: In all, 767 patients were treated with omalizumab (at least 0.016 mg/kg/IgE [IU/mL], administered subcutaneously every 4 weeks). Another 638 patients were treated with placebo. The rate of unscheduled, asthma-related outpatient visits was lower for the omalizumab-treated patients than for the placebo-treated patients (rate ratio [95% CI], 0.60 [0.44, 0.81]; P <.01), as were asthma-related emergency room visits (rate ratio [95% CI], 0.47 [0.24, 1.01]; P =.05). Importantly, hospitalizations for asthma were markedly reduced in patients receiving omalizumab (rate ratio [95% CI], 0.08 [0.00, 0.25]; P <.01). CONCLUSION: Omalizumab reduces the rate of serious asthma exacerbations and the need for unscheduled outpatient visits, emergency room treatment, and hospitalization in patients with moderate-to-severe allergic asthma.

Coskun S. et al. *Standard dose of inhaled albuterol significantly increases QT dispersion compared to low dose of albuterol plus ipratropium bromide therapy in moderate to severe acute asthma attacks in children.* Pediatr Int. 2001; 43(6) : 631-6.p **Abstract:** BACKGROUND: Beta-2 agonist therapy has previously shown to increase the QT dispersion (QTd) in asthmatic patients and increased QTd has been well documented in association with cardiac arrhythmias and sudden death. However, the data concerning the effect of low doses of beta-2 agonist therapy in combination with the anticholinergic agents to potentiate bronchodilatation on QTd in asthmatic children are limited. The objectives of this study was to investigate the changes on QTd during both the standard dose of nebulized albuterol therapy and low dose nebulized albuterol plus inhaled ipratropium therapy to assess the potential arrhythmogenic risk of these two treatment strategies in children with acute asthmatic attacks. METHODS: Forty-three children with the diagnosis of moderate to severe acute asthma were enrolled in the study. Standard dose of nebulized albuterol therapy (0.15 mg/kg) were administered to 20 patients (group 1) and low dose of nebulized albuterol (0.075 mg/kg) plus nebulized ipratropium bromide therapy (250 microg/dose) were given to the remaining 23 patients (group 2). Respiratory distress score, peak expiratory flow rate, arterial blood pressure, O₂ saturation, serum potassium and urea nitrogen levels

were studied and QT interval parameters were measured from the standard 12-lead electrocardiograms at baseline and after treatment. RESULTS: Significant improvement was achieved in respiratory distress score and peak expiratory flow rate after three dose inhalation. No significant difference was observed between the pre and post-treatment values of serum potassium, blood urea nitrogen, O₂ saturation and arterial blood pressure values. The evaluation of the corrected QTd (QTcd) showed that while there was no statistical difference in the pre and post-treatment values in group 2 (30.4+/-3.1 msn vs 32.1+/-3.9 msn), QTcd was found to be significantly increased in group 1 after treatment (29.0+/-3 msn vs 40.6+/-5.1 msn, P<0.0001). CONCLUSION: The data of the present study suggest that the increase of the QTd is more prominent with the use of a standard dose of albuterol compared to low dose albuterol plus ipratropium therapy. Therefore, it may be concluded that a low dose of albuterol plus ipratropium bromide therapy may be preferred to avoid rhythm disturbances in asthmatic children.

Cosmes Martin P.M. et al. *[Sensitization to Castanea sativa pollen and pollinosis in northern Extremadura (Spain)].* Allergol Immunopathol (Madr). 2005; 33(3) : 145-50.p **Abstract:** BACKGROUND: Castanea sativa pollen allergy has generally been considered to be uncommon and clinically insignificant. In our geographical area (Plasencia, Caceres, Spain) Castanea sativa pollen is a major pollen. OBJECTIVE: To determine the atmospheric fluctuations and prevalence of patients sensitized to Castanea pollen in our region and to compare this sensitization with sensitizations to other pollens. METHODS: Patients with respiratory symptoms attending our outpatient clinic for the first time in 2003 were studied. The patients underwent skin prick tests with commercial extracts of a battery of inhalants including Castanea sativa pollen. Serologic specific IgE to Castanea sativa pollen was determined using the CAP system (Pharmacia and Upjohn, Uppsala, Sweden). Airborne pollen counts in our city were obtained using Cour collection apparatus over a 4-year period (2000 to 2003). RESULTS: The most predominant pollens detected were (mean of the maximal weekly concentrations over 4 years in pollen grains/m³): Quercus 968, Poacea 660, Olea 325, Platanus 229, Pinus 126, Cupresaceae 117, Plantago 109, Alnus 41, Populus 40, Castanea 32. We studied 346 patients (mean age: 24.1 years). In 210 patients with a diagnosis of pollinosis, the percentages of sensitization were: Dactylis glomerata 80.4%, Olea europea 71.9%, Fraxinus excelsior 68%, Plantago lanceolata 62.8%, Chenopodium album 60.9%, Robinia pseudoacacia 49%, Artemisia vulgaris 43.8%, Platanus acerifolia 36.6%, Parietaria judaica 36.1%, Populus nigra 32.3%, Betula alba 27.6%, Quercus ilex 21.4%, Alnus glutinosa 20.9%, Cupressus arizonica 7.6% and Castanea sativa 7.1%. Fifteen patients were sensitized to Castanea sativa and 14 had seasonal rhinoconjunctivitis and asthma. Ten patients had serum specific IgE to Castanea pollen (maximum value: 17.4 Ku/l). Castanea pollen is present in our area in large amounts from the 23rd to the 28th weeks of the year, with a peak pollen count in the 25th week. CONCLUSIONS: The most important allergenic pollens in northern Extremadura were Poaceae, Olea europaea and Plantago sp. The prevalence of sensitization to Castanea sativa pollen was very low (7.1%). Most sensitized patients had asthma and polysensitization. Castanea sativa pollen is not a major cause of pollinosis in our area.

Cotterell E.M. et al. *Child and parent satisfaction with the use of spacer devices in acute asthma.* J Paediatr Child Health. 2002; 38(6) : 604-7.p **Abstract:** OBJECTIVE: To evaluate child and parent satisfaction with the use of spacers in acute asthma. METHODS: All parents of children presenting to the emergency department of Sydney Children's Hospital over a 3-month period with mild to moderately severe acute asthma who were treated with bronchodilators by spacer device were asked to complete an anonymous questionnaire. Children aged 8 years and older completed a separate questionnaire independently. RESULTS: One hundred and eleven of 158 parents (70%) responded. The majority

(84%) found it 'easy' or 'very easy' to use the spacer and 85% reported that they intended to use the spacer at home. Of those parents who had previously used a nebulizer (n = 73), 84% said that the spacer was easier to use, 77% said that the spacer was better tolerated by their child and 84% said that overall they preferred the spacer. Seventeen of 31 children aged 8-14 years treated with a spacer (55%) responded to the satisfaction survey. All respondents found it 'easy' or 'OK' to use the spacer and the majority (82%) 'liked it' or thought 'it was OK'. The majority of children (82%) said that they preferred using spacers because it was quicker (29%) or easier to use (53%). CONCLUSION: The use of spacer devices in mild to moderately severe acute asthma is highly acceptable for children and parents; the majority prefer this mode of drug delivery to nebulization.

Counil F.P. et al. *Training of aerobic and anaerobic fitness in children with asthma.* J Pediatr. 2003; 142(2) : 179-84.p Abstract: OBJECTIVE: To assess the effect of a training protocol on aerobic and anaerobic fitness in children with asthma. STUDY DESIGN: Sixteen boys (mean age: 13 years; range: 10-16 years) with mild-to-moderate asthma participated in a rehabilitation program that included 6 weeks of individualized training on a cycle ergometer. Two groups were randomly formed: the control group (CG, n = 7) and the training group (TG, n = 9), which exercised at an intensity set at the heart rate corresponding to the ventilatory threshold, with 1-minute sprints against the maximal aerobic power (MAP) every 4 minutes. Session duration was 45 minutes, 3 sessions per week. Changes in maximal oxygen uptake (VO(2)max), MAP, short-term peak power (PP), and pulmonary function were assessed. RESULTS: Two patients of the training group did not complete the study. Pulmonary function remained unchanged in both groups. Improvement in both aerobic and anaerobic fitness was significant only in the training group (TG vs CG): VO(2)max +18% +/- 2.1% versus +9% +/- 4.5% (P <.05), MAP +32% +/- 5% versus 12% +/- 7% (P <.05), PP +21% +/- 5.7% versus +8.8% +/- 10% (P <.01). CONCLUSION: Exercise training with high-intensity bouts is well tolerated in children with mild-to-moderate asthma. When included in a global rehabilitation program, this type of training improves both aerobic and anaerobic fitness. Anaerobic activities should be considered in sports rehabilitation programs for children with asthma.

Covar R.A. et al. *Progression of asthma measured by lung function in the childhood asthma management program.* Am J Respir Crit Care Med. 2004; 170(3) : 234-41.p Abstract: From the Childhood Asthma Management Program cohort, which was randomly assigned to receive budesonide, nedocromil, or placebo for 4-6 years, we determined the prevalence of and factors associated with at least 1% per year loss in postbronchodilator FEV(1)% predicted. Participants who had a significant reduction in postbronchodilator FEV(1)% predicted (SRP), comprised 25.7% of the cohort (n = 990). Using logistic regression, predictors of SRP at baseline were younger age (p = 0.0005), male sex (p < 0.0001), clinic (p = 0.02), and higher postbronchodilator FEV(1)% predicted (p = 0.02). Examination of the SRPs indicated that the effect of baseline lung function was such that the higher the lung function, the less steep the reduction in postbronchodilator FEV(1)% predicted (p < 0.0001). A similar proportion of SRPs was found in each treatment group. Among the SRPs, the rate of reduction in postbronchodilator FEV(1)% predicted was similar in all treatment groups. At a single site where biomarker assessment was performed, SRPs also had more prominent eosinophilic inflammation during the washout period. The course and mechanisms of lung function reduction or slow lung growth velocity in children with asthma must be defined.

Covar R.A. et al. *Relations between exhaled nitric oxide and measures of disease activity among children with mild-to-moderate asthma.* J Pediatr. 2003; 142(5) : 469-75.p Abstract: OBJECTIVE: Exhaled

nitric oxide (FE(NO)) was evaluated in children with asthma after 4 to 6 years of treatment with budesonide, nedocromil, or albuterol as needed. STUDY DESIGN: FE(NO), spirometry, total eosinophil count, and serum eosinophil cationic protein levels were obtained from 118 children at the Denver site of the Childhood Asthma Management Program upon completion of treatment and after a 2- to 4-month washout. RESULTS: Budesonide-treated patients had significantly lower median (1st, 3rd quartile) FE(NO) (21.5 [13.2, 84.4] vs 62.5 [26.2, 115.0] ppb, P <.01) and eosinophil cationic protein levels (17.4 [10.1, 24.3] vs 24.0 [15.4, 33.9] mg/dL, P =.05) compared with placebo, whereas no differences were noted between nedocromil and placebo groups. After washout, FE(NO) levels were similar between the three treatments. FE(NO) levels significantly correlated with degree of bronchial hyperresponsiveness, bronchodilator reversibility, allergen skin prick tests, serum IgE, and total eosinophil count. FE(NO) levels were also higher in patients with nocturnal symptoms and in patients requiring beta-agonist use at least once weekly. CONCLUSIONS: Budesonide therapy was more effective than nedocromil in reducing FE(NO). Unfortunately, the effects of long-term budesonide were not sustained after its discontinuation. FE(NO) may be a complementary tool to current practice guidelines in assessing asthma control and medication response.

Covarrubias A.E. et al. *Frequency of exercise-induced asthma in a group of children and adolescents with mild asthma attending a summer camp.* Rev Alerg Mex. 2005; 52(2) : 72-6.p Abstract: BACKGROUND: Exercise-induced asthma is a transitory bronchospasm, which occurs after 6 to 8 minutes of continuous exercise. Diagnosis is done by a suggestive clinical history and by 15 to 20% post-challenge fall in FEV1. It happens in about 6 to 13% of general population, 90% of asthmatic individuals and 40% of individuals with allergic rhinitis. OBJECTIVE: To know the frequency of asthma induced by exercise in a group of asthmatic children and teenagers who went to a summer camp. MATERIAL AND METHODS: A cross-sectional, descriptive and observational study, which included 33 patients suffering from intermittent mild asthma, was based on espirometric measurements made before and after 8 minutes of continuous exercise (running). None of them had previous diagnosis of exercise-induced asthma. FEV1 greater than or equal to 15% was considered exercise-induced asthma. The test was performed at a room temperature of 73F and humidity of 40%. All patients were asymptomatic before the study and were given short-acting inhaled beta2-agonists as rescue medication, which was not administered during the 12 previous hours to the test. Data analysis was made by means of descriptive statistic. RESULTS: Thirty-three children aged 8-16 years with diagnosis of asthma were studied, with an average age of 12.5 years; 42.4% were female and 57.5% male. Of the 33 patients, 6 had (18.2%) a 15% fall in FEV1 after exercise; 50% of these patients showed exercise-induced mild asthma, 33% moderate and 17% severe. At the end of the test, in six patients (100%) FEV1 increased by 15%, five minutes after the administration of a beta2-agonist. CONCLUSIONS: Exercise-induced asthma is frequent among asthmatic pediatric patients, occurring in 18.8% of this study. Likelihood of having exercise-induced asthma must be deliberately investigated in all asthmatic patients, in order to establish an opportune diagnosis of this condition and provide recommendations of preventing therapy.

Cowie R.L. et al. *Asthma education and management programs in Canada.* Can Respir J. 2001; 8(6) : 416-20.p Abstract: OBJECTIVE: To establish the number and type of asthma patient education programs throughout Canada. DESIGN: National survey. SETTING: Canada. METHODS: Over a three-year period, contact was made with individuals and groups offering educational services for patients with asthma. Education given as part of a physician's consultation or a pharmacist's dispensing of medications for asthma was not considered a patient education program for the purposes of the survey. Contact was initially established by asking staff from

well known asthma programs to provide lists of other such programs in their provinces or regions. Asthma programs were also identified from notices presented at Canada's Third and Fourth National Conferences on Asthma and Education. Lung associations, lay organizations and industry representatives affiliated with the Canadian Network for Asthma Care helped to supplement the list. Once identified, each patient education program was contacted by telephone and by mail to complete a 26-item questionnaire about their program. The province of Quebec was not included in the survey because it already had a province-wide, structured asthma education program and register. RESULTS: Seventy-four asthma education and management programs were identified outside Quebec. Staff in these programs were registered nurses (n=46), respiratory therapists (n=48) and other health professionals (n=21). Forty-one programs stated that at least one member of their staff had been trained as an asthma educator. In 71 programs, the initial patient encounter was of at least one hour's duration. Physician referral was required by 41 programs. The province of Quebec has a joint asthma education program provided by 114 asthma education centres throughout the province under the umbrella of the Quebec Asthma Education Network (QAEN). This comprehensive program is provided in hospitals and community centres by specialized educators - nurses, pharmacists or respiratory therapists - to patients referred by their physicians. CONCLUSIONS: A three-year search for asthma education programs in Canada identified 74 patient education programs (outside Quebec) for an asthma population estimated to exceed 1.2 million. For the province of Quebec, an integrated asthma education program is provided through a network of 114 education centres - the QAEN. The present survey shows that there has been progress in establishing asthma education programs in Canada, although there are significant regional differences in the availability of such programs.

Cowie R.L. et al. *Inhaled corticosteroid therapy does not control asthma.* Can Respir J. 2004; 11(8) : 555-8.p Abstract: BACKGROUND: Randomized clinical trials demonstrate efficacy and show that inhaled corticosteroid therapy can control asthma, but details concerning their effectiveness in achieving this goal in the community are lacking. OBJECTIVES: To determine whether inhaled corticosteroid therapy is effective in controlling asthma and to examine the rates of asthma control in relation to inhaled corticosteroid use outside the realm of randomized controlled trials. METHODS: Different populations were examined cross-sectionally to determine whether self-reported use of inhaled corticosteroids was associated with control of asthma. Subjects with asthma in the community and those attending a university-based asthma program were studied. The definition of asthma control was based on the recommendations of the Canadian Consensus Report. The elements of asthma control were examined in the context of the subject's stated use and dose of the inhaled corticosteroid. RESULTS: Asthma was controlled in 20% (95% CI 18.7% to 21.3%) of the 3427 subjects included in the present study. Only 15% (95% CI 13.5% to 16.5%) of the 2437 subjects using inhaled corticosteroids exhibited asthma control compared with 33% (95% CI 31.1% to 35.9%) of the 990 subjects not using inhaled corticosteroids (P<0.000001). CONCLUSIONS: Although it is known that inhaled corticosteroid therapy can result in asthma control in most individuals with asthma, the present study has shown that this result may not be attained outside the realm of randomized clinical trials. Inhaled corticosteroid use for asthma in a 'real world' setting appears to reflect disease severity.

Crabbe H. et al. *The use of a European telemedicine system to examine the effects of pollutants and allergens on asthmatic respiratory health.* Sci Total Environ. 2004; 334-335 : 417-26.p Abstract: The experience of using a telemedicine feasibility study to integrate respiratory health response and environmental stimuli information is presented. The effects of ambient air quality, pollen and local environment conditions on asthmatic patients' lung function were

investigated through the use of a novel European health telematic system. The Medical Diagnosis, Communication and Analysis Throughout Europe (MEDICATE) project developed and tested the feasibility of using a telemedicine system for chronic asthmatics in London, UK, and Barcelona, Spain. The key to this was the determination of the real time health (lung function) response to the ambient environment and allergens. Air quality, pollen and environmental lifestyle information were related to respiratory measurements for recruited asthmatic patients in the study through the design of a dedicated environmental management system (EMS) database. In total, 28 patients completed the study trial, subject to ambulatory monitoring of spirometric lung function (PEF, FEV(1) and FVC) up to four times a day over a 2-week period recorded during the year 2000. Alongside this, ambient air quality and pollen counts were used to represent local exposure to potential environmental stimuli. Personal questionnaire interviewing collected additional data about patient lifestyles, social-economic conditions and quality of life perceptions. The methods and indicative results of integrating environmental and health data in this respect are examined. Assessment tools such as GIS and object-orientated databases were designed to locate and compile environmental information about the patients' locations and lifestyles in the study areas (London and Barcelona). Socioeconomic and lifestyle factors, such as exposure to smoking, pets, personal journey lengths and modes, income, household occupancy and domestic fuel use, were found to have limited detectable effects on the patients' basic lung function levels. Patients' gender, age and predicted PEF were significantly associated with the 2-week mean and minimum respiratory measurements. Lung function data were compared with air quality and pollen indicators to examine relationships on a daily or lagged-day basis controlling for confounding factors. The paper discusses the new methodology and the practicalities of using the telemedical system as a tool for assessing the impacts of environmental stimuli on respiratory health.

Craig-McFeely P.M. et al. *Prospective observational cohort safety study to monitor the introduction of a non-CFC formulation of salbutamol with HFA134a in England.* Int J Clin Pharmacol Ther. 2003; 41(2) : 67-76.p Abstract: OBJECTIVE: To monitor the safety of a salbutamol MDI with a hydrofluoroalkane propellant (Ventolin Evohaler) during its introduction into primary care use in England. METHODS: Prospective observational cohort study. 1,365 GPs in England submitted data on 10,472 regular users of Ventolin MDI, over five 3-month periods of observation between October 1, 1998 and December 31, 1999. The primary aim was to compare event rates occurring before and after the introduction of Ventolin Evohaler. The secondary aim was a comparison of event rates between users of Ventolin Evohaler and Ventolin MDI. The main outcome measures were: indication for use of Ventolin MDI, assessment of disease severity, event rates during each period of observation; deaths, pregnancies, reported adverse drug reactions and reasons for discontinuation of MDI. Event rates were adjusted using a ratio for under-reporting derived from a validation study on 4.6% of the study population and stratified by severity of indication. RESULTS: The primary indication was asthma in 94%, distributed by severity as 47% mild, 44% moderate and 9% severe; 13% were children. By October 1999, 52.7% of the 8,973 remaining patients had transitioned to Ventolin Evohaler. There was no increase in major or minor events observed following the introduction of Ventolin Evohaler. No serious adverse events, abnormal pregnancy outcomes or deaths have been related to Ventolin MDI or Ventolin Evohaler. The validation study showed a degree of under-reporting. CONCLUSION: These results on a large cohort of community patients in England indicate that Ventolin Evohaler is well tolerated among asthmatics.

Crampton P. et al. *Comparison of private for-profit with private community-governed not-for-profit primary care services in New Zealand.* J Health Serv Res Policy. 2004; 9 Suppl 2 : 17-22.p

Abstract: OBJECTIVE: To compare the characteristics of patients, their disease patterns, and the investigation and referral patterns in private community-governed not-for-profit and private for-profit primary care practices in New Zealand. METHODS: Observational study using a representative survey of visits to general practitioners in New Zealand. Practices were categorised according to their ownership: private for-profit or private community-governed not-for-profit. Patient socio-demographic characteristics, treated prevalence and other characteristics of presenting problems, morbidity burden, numbers of investigations and referral patterns were compared. RESULTS: Compared with for-profit practices, community-governed not-for-profit practices served a younger, largely non-European population, nearly three-quarters of whom had a means-tested benefit card (community services card), 10.5% of whom were not fluent in English, and the majority of whom lived in the 20% of areas ranked as the most deprived (by the NZDep2001 index of socio-economic deprivation). Patients visiting not-for-profit practices were diagnosed with more problems, including higher rates of asthma, diabetes and skin infections, but lower rates of chest infections. The duration of visits was also significantly longer. No differences were observed in the average number of laboratory tests ordered. The odds of specialist referral were higher in for-profit patients when confounding variables were controlled for. CONCLUSIONS: Community-governed not-for-profit practices in New Zealand serve a poor, largely non-European population who present with somewhat different rates of various problems compared with patients at for-profit practices. The study highlights for communities, policy-makers and purchasers the importance of community-governed not-for-profit practices in meeting the needs of low-income and minority population groups.

Crater D.D. et al. *Asthma hospitalization trends in Charleston, South Carolina, 1956 to 1997: twenty-fold increase among black children during a 30-year period.* Pediatrics. 2001; 108(6) : E97.p **Abstract:** OBJECTIVE: The increase in asthma prevalence has been documented worldwide, affecting many races living in many different climates. Multiple studies have demonstrated that the most striking prevalence and morbidity of asthma in the United States has been in black children, but little research has determined the scale of the increase, or specifically when the disease became severe in this group. This study sought to determine exactly when the rise in asthma hospitalizations among black patients began and what the pattern of asthma hospitalizations has been in different races and age groups over a 40-year period in 1 urban area. METHODS: A retrospective chart review of discharges from the Medical University of South Carolina was conducted from 1956 to 1997. Charts with the primary discharge diagnosis of asthma were examined for discharge date, race, and age group (0- to 4-year-olds, 5- to 18-year-olds, 19- to 50-year-olds, > or =51-year-olds). The diagnostic codes used were based on the International Classification of Diseases (ICD)-6, 1956-1957; ICD-7, 1958-1967; ICD-8, 1968-1978; and ICD-9, 1979-1997. Over the period studied, this hospital was the primary inpatient provider for children in this area, and the only provider for uninsured children. Between 1960 and 1990, the racial makeup of the area remained stable, as did the percentage of blacks living at the poverty level. The raw number of asthma discharges, rate per 10 000 discharges of the same race, and rate per 100 000 population in Charleston County were tabulated for each age group and racial category. RESULTS: Over the time period examined, there has been a progressive increase in asthma hospitalizations in black individuals of all age groups and in whites under 18 years. The most striking increase has been in black children 0 to 18 years old (figure). The increase either as raw values or as a rate per 100 000 began around 1970, and was linear. This increase in black children discharged with asthma as a rate per 100 000 population was 20-fold: the rate increased from 18 in 1970 to 370 in 1997. Asthma discharges as a rate per 10 000 black children discharged increased by 24-fold from 1960 to 1997. Total discharges from the hospital increased from 49 000 to 128 000 per year over this period. Blacks made up only 28% of discharges in 1957, but that proportion increased to 56% in 1960

and remained relatively stable over the following 35 years. The increase seen in white children 0 to 18 years of age as a rate per 100 000 population was 5-fold and began around 1980. Both increases seem to be consistent over the time period studied, and continued to 1997. [figure: see text]. CONCLUSIONS: Among a predominantly poor black population living in a southern US city, there has been a steady increase in childhood asthma hospitalizations over the past 30 years. A significant although less dramatic rise has occurred in white children. Over this time period, although there have been many changes in lifestyle that could have contributed to this rise, there have been no major changes in housing conditions for poor patients. In addition, Medicaid coverage for children in South Carolina did not change significantly until 1999. The time course of these increases parallels increases reported in other Western populations, suggesting that there must be 1 or more common factors contributing to the rise. Many explanations have been offered for the changes in incidence and severity of asthma. The scale of the change, time course, and linearity of the increase in this study represent a challenge to many of the hypotheses proposed to explain this epidemic.

Crestani E. et al. *Parental asthma as a risk factor for the development of early skin test sensitization in children.* J Allergy Clin Immunol. 2004; 113(2) : 284-90.p **Abstract:** BACKGROUND: Recent epidemiologic evidence has challenged the paradigm suggesting a direct causal relationship between allergic sensitization and asthma. OBJECTIVE: We sought to investigate the role of a familial predisposition for asthma in the development of atopy in children. METHODS: Subjects were participants in the Tucson Children's Respiratory Study. Skin tests to aeroallergens were performed in parents and in children at ages 6, 11, and 16 years. Parents were considered asthmatic if they reported physician-confirmed asthma. Parents were divided into 4 phenotypes on the basis of skin sensitization (Skt+ or Skt-) and asthma status (As+ or As-): Skt-/As-, Skt-/As+, Skt+/As-, and Skt+/As+. RESULTS: Children's allergic sensitization differed among parental phenotypes at all ages (P <.0001). Children in the Skt+/As- and Skt+/As+ groups were significantly more likely to be allergic than children in the Skt-/As-group at all ages. Among children with allergic parents, those with at least one parent with asthma were significantly more likely to have positive skin test responses than those with nonasthmatic parents at age 6 years (52.4% vs 37.4%, P <.005) and 11 years (70.1% vs 55.6%, P <.005) but not at age 16 years (82.3% vs 75.1%, P =.180). Results were independent of wheezing in the child and of the characteristics of atopy in parents. The Skt-/As+ group had too few subjects for meaningful comparisons. CONCLUSION: Among children of atopic parents, parental asthma is a risk factor for allergic sensitization in early childhood. The strong association between allergic sensitization and asthma is at least in part explained by an increased susceptibility to allergen sensitization in subjects predisposed to asthma.

Crighton E.J. et al. *A population based time series analysis of asthma hospitalisations in Ontario, Canada: 1988 to 2000.* BMC Health Serv Res. 2001; 1(1) : 7.p **Abstract:** BACKGROUND: Asthma is a common yet incompletely understood health problem associated with a high morbidity burden. A wide variety of seasonally variable environmental stimuli such as viruses and air pollution are believed to influence asthma morbidity. This study set out to examine the seasonal patterns of asthma hospitalisations in relation to age and gender for the province of Ontario over a period of 12 years. METHODS: A retrospective, population-based study design was used to assess temporal patterns in hospitalisations for asthma from April 1, 1988 to March 31, 2000. Approximately 14 million residents of Ontario eligible for universal healthcare coverage during this time were included for analysis. Time series analyses were conducted on monthly aggregations of hospitalisations. RESULTS: There is strong evidence of an autumn peak and summer trough seasonal pattern occurring every year over the 12-year period (Fisher-Kappa (FK) = 23.93, p > 0.01; Bartlett Kolmogorov Smirnov (BKS) = 0.459, p <

0.01). This pattern was observed in both sexes. However, young males (0-4 years) were hospitalised at two to three times the rate of females of the same age. Rates were much lower in the older age groups. A downward trend in asthma hospitalisations was observed in the total population over the twelve-year period ($\beta = -0.980$, $p < 0.01$). CONCLUSIONS: A clear and consistent seasonal pattern was observed in this study for asthma hospitalisations. These findings have important implications for the development of effective management and prevention strategies.

Crimi N. et al. *Bradykinin and tachykinin-induced leukotriene release in airway virus infections.* Am J Respir Crit Care Med. 2005; 172(4) : 511; author reply 511-2.p

Crimmins E.M. et al. *Life with and without disease: women experience more of both.* J Women Aging. 2002; 14(1-2) : 47-59.p Abstract: This paper examines gender differences in life with and without six major diseases, including both mortal and morbid conditions. Disease prevalence and health behavior data are from the 1993-1995 National Health Interview Surveys for the United States. Vital registration data are the source of mortality rates used in computing life expectancy. The Sullivan method is used to estimate life lived with and without disease and risky behavior for men and women at various ages. Women live more years with each of the diseases examined, and, for arthritis, the extended years with disease are greatest. Women also live more years than men free of each of these diseases with the exception of arthritis. Gender differences in life without two health-risk behaviors are also discussed. Men spend more years of their lives overweight and have fewer years during which they see a doctor.

Croen L.A. et al. *Maternal autoimmune diseases, asthma and allergies, and childhood autism spectrum disorders: a case-control study.* Arch Pediatr Adolesc Med. 2005; 159(2) : 151-7.p Abstract: OBJECTIVE: To investigate the association between physician-documented diagnoses of maternal autoimmune diseases, allergies, and asthma around the time of pregnancy and subsequent diagnoses of autism in children. DESIGN: A case-control study nested within a cohort of infants born between January 1995 and June 1999. SETTING: Northern California Kaiser Permanente Medical Care Program. PARTICIPANTS: Cases ($n = 420$) were children with at least 1 diagnosis of an autism spectrum disorder (ASD) recorded in Kaiser Permanente outpatient clinical databases. Controls ($n = 2100$) were children without an ASD diagnosis who were frequency matched to cases on sex, birth year, and hospital of birth. MAIN OUTCOME MEASURES: Frequencies of maternal immunologic disorders were compared between cases and controls with a χ^2 statistic, and relative risks were estimated by crude and adjusted odds ratios and 95% confidence intervals using logistic regression. RESULTS: The final study population included 407 cases and 2095 controls. A similar proportion of case and control mothers had a diagnosis of any autoimmune disease in the 4-year period surrounding pregnancy (10.3% vs 8.2%, $P = .15$). After adjustment for maternal factors, only 1 autoimmune condition, psoriasis, was significantly associated with ASDs (adjusted odds ratio, 2.7; 95% confidence interval, 1.3-5.8). A greater than 2-fold elevated risk of ASD was observed for maternal asthma and allergy diagnoses recorded during the second trimester of pregnancy. CONCLUSIONS: These findings suggest that maternal autoimmune disorders present in women around the time of pregnancy are unlikely to contribute significantly to autism risk. Further etiologic investigations are needed to confirm these results and should include objective documentation of diagnoses and consider a larger set of maternal immune-related conditions, including asthma and allergies.

Cross C.E. *The antioxidant milieu at asthmatic respiratory tract surfaces.* Pediatr Res. 2003; 53(3) : 365-8.p

Cui T. et al. *The association analysis of FcepsilonRIbeta with allergic asthma in a Chinese population.* Chin Med J (Engl). 2003; 116(12) : 1875-8.p Abstract : OBJECTIVE: To investigate the link between the polymorphism of -109 and Glu237 in the high-affinity IgE receptor beta (FcepsilonRIbeta) gene and susceptibility to allergic asthma in a Chinese population. METHOD: Blood samples from 216 allergic asthma patients and 198 age- and sex-matched controls were studied. A -109C/T and a coding variant Glu237Gly in FcepsilonRIbeta were detected with polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). RESULTS: The genotype frequencies were 0.403 for -109T/T, 0.491 for -109T/C and 0.106 for -109C/C in allergic asthma in a Chinese population. No significant difference in the distribution of -109C/T polymorphism was found between allergic asthma subjects and healthy controls, however, homozygosity for the -109T allele was associated with increased total plasma IgE levels in subjects with allergic asthma ($F = 4.020$, $P < 0.05$). The allele frequency of Gly237 in the patients and control was 0.236 and 0.136 respectively. There was a significant association between the Gly/Gly genotype and allergic asthma. Among allergic asthma patients Gly237 was significantly associated with high IgE levels. CONCLUSIONS: These results suggest that the Gly237 variant of the FcepsilonRIbeta gene is involved in the development of allergic asthma. The -109C/T and Glu237Gly polymorphisms are two of the genetic factor identified thus far, which affect total plasma IgE levels of allergic asthma patients in a Chinese population.

Currie J. *Health disparities and gaps in school readiness.* Future Child. 2005; 15(1) : 117-38.p Abstract: The author documents pervasive racial disparities in the health of American children and analyzes how and how much those disparities contribute to racial gaps in school readiness. She explores a broad sample of health problems common to U.S. children, such as attention deficit hyperactivity disorder, asthma, and lead poisoning, as well as maternal health problems and health-related behaviors that affect children's behavioral and cognitive readiness for school. If a health problem is to affect the readiness gap, it must affect many children, it must be linked to academic performance or behavior problems, and it must show a racial disparity either in its prevalence or in its effects. The author focuses not only on the black-white gap in health status but also on the poor-nonpoor gap because black children tend to be poorer than white children. The health conditions Currie considers seriously impair cognitive skills and behavior in individual children. But most explain little of the overall racial gap in school readiness. Still, the cumulative effect of health differentials summed over all conditions is significant. Currie's rough calculation is that racial differences in health conditions and in maternal health and behaviors together may account for as much as a quarter of the racial gap in school readiness. Currie scrutinizes several policy steps to lessen racial and socioeconomic disparities in children's health and to begin to close the readiness gap. Increasing poor children's eligibility for Medicaid and state child health insurance is unlikely to be effective because most poor children are already eligible for public insurance. The problem is that many are not enrolled. Even increasing enrollment may not work: socioeconomic disparities in health persist in Canada and the United Kingdom despite universal public health insurance. The author finds more promise in strengthening early childhood programs with a built-in health component, like Head Start; family-based services and home visiting programs; and WIC, the federal nutrition program for women, infants, and small children. In all three, trained staff can help parents get ongoing care for their children.

Custovic A. et al. *Manchester cohort.* Pediatr Pulmonol Suppl. 2004; 26 : 12-3.p

da Cunha A.J. [Asthma and ascariasis: ongoing controversy]. *J Pediatr* (Rio J). 2003; 79(3) : 199-200.p

da Cunha S.S. et al. Lower prevalence of reported asthma in adolescents with symptoms of rhinitis that received neonatal BCG. *Allergy*. 2004; 59(8) : 857-62.p Abstract: BACKGROUND: BCG is a vaccine used against tuberculosis and leprosy and is an immunostimulant that primes T(H)1 lymphocytes to produce cytokines that antagonize atopy both in animal models and in man. Considering that atopy is the main risk factor for asthma, one can hypothesize that vaccination inducing T(H)1 responses, such as BCG, can be protective against asthma. METHODS: OBJECTIVE: To estimate the association between neonatal BCG vaccination and prevalence of asthma among adolescents. STUDY DESIGN: Cross-sectional study with schoolchildren aged 12-16 years. The presence of a scar compatible with BCG was used as a surrogate of neonatal vaccination. A self administered structured questionnaire was prepared based on that used by the International Study of Asthma and Allergies in Childhood. The prevalence of asthma was categorized according to the report of lifetime wheeze, lifetime asthma, lifetime asthma among those referring allergy and among those referring allergy and sneezing. RESULTS: Neonatal BCG vaccination was not associated with the overall prevalence of reported wheezing or asthma. However, in the subgroup reporting current allergy and sneezing, neonatal BCG was associated with a 37% reduction of prevalence of lifetime asthma. CONCLUSIONS: In the population we surveyed, neonatal BCG scar was associated with a reduction in the risk of asthma only in individuals with a past history suggestive of allergic rhinitis.

da Silva Ezequiel O. et al. Evaluation of the acarofauna of the domiciliary ecosystem in Juiz de Fora, State of Minas Gerais, Brazil. *Mem Inst Oswaldo Cruz*. 2001; 96(7) : 911-6.p Abstract: From August 1999 to January 2000, samples of house dust were collected from 160 domiciles in the city of Juiz de Fora, State of Minas Gerais, Brazil. In 36 of these domiciles kitchen samples were obtained. Prevalence rate was 77.5%, varying according to the geographical sector. There were found 2,278 specimens of mites, with 1,530 (67.2%) in the adult stage and 748 (32.8%) in immature forms. The main species found were *Dermatophagoides pteronyssinus*, *D. farinae*, *Euroglyphus maynei*, *Blomia tropicalis* and *Tyrophagus putrescentiae*. In a minor incidence we found *Lepidoglyphus destructor*, *Suidasia pontificiae*, *Chortoglyphus arcuatus*, *Cheyletus malaccensis*, *C. fortis*, *Ker bakeri*, *Cheletonella vespertilionis*, *C. caucasica* and others. *C. vespertilionis* and *C. caucasica* were identified for the first time in the domiciliary ecosystem and in Brazil. The abundance rate and the infestation intensity were analyzed. There was a varied correlation between climatic conditions and positive domiciles and number of mites. The difference between the number of positive domiciles in the urban area and in the expanding urban area was significant and so was the difference between samples from the domiciles compared to those from the kitchens.

Daengsuwan T. et al. Allergen sensitization to aeroallergens including *Blomia tropicalis* among adult and childhood asthmatics in Thailand. *Asian Pac J Allergy Immunol*. 2003; 21(4) : 199-204.p Abstract: To study prevalence of allergen sensitization among asthmatics in Thailand, skin prick tests (SPT) were performed in 84 pediatric, 71 adult asthmatics and 71 adult volunteers. Allergen extracts used for testing included common allergens in Thailand and in Singapore. The incidence of positive SPT to any allergen among the three groups (childhood, adult patients and adult controls) were 64.3%, 43.7% and 35.2%, respectively. *Dermatophagoides* were the most common allergens sensitized by both pediatric (58.3%) and

adult asthmatics (40.8%). Twenty-four children (28.6%) and 8 adult patients (11.3%) were sensitized to storage mites (*Blomia tropicalis* and/or *Austroglyphus malaysiensis*). All patients sensitized to *Blomia tropicalis* were sensitized to *Dermatophagoides*. Twenty-seven percent and 15.5% of childhood and adult asthmatics were sensitized to cockroach allergens. The rates of sensitization to oil palm pollen in childhood and adult asthmatics were 8.3% and 5.6%, respectively. Sensitization to other pollens and spores were less than 5%. This study confirms the importance of *Dermatophagoides* among Thai asthmatics.

Dagoye D. et al. Domestic risk factors for wheeze in urban and rural Ethiopian children. *QJM*. 2004; 97(8) : 489-98.p Abstract: BACKGROUND: To identify which environmental exposures underpin the emergence of asthma epidemics, we need to study epidemics as they appear, as is now happening in the Jimma region of Ethiopia. We have previously studied risk factors for asthma in adults in Jimma and have now completed a survey of young children. AIM: To establish the prevalence of asthma in urban and rural children in Jimma, and to identify locally important risk factors. DESIGN: Cross-sectional survey. METHODS: All children aged 1-5 years living in Jimma town and three surrounding rural regions were identified. Data were collected using an interviewer-led questionnaire, and consenting children had skin prick tests to house dust mite and cockroach. RESULTS: We surveyed 7155 children, of whom 3623 (51%) were female and 4285 (60%) lived in the urban area. The prevalence of wheeze in the last year was 3.4%, and was lower in the rural area (OR 0.47; 95%CI 0.34-0.66). In the urban area, the main risk factors for wheeze were a longer duration of breastfeeding, use of kerosene, and environmental tobacco smoke, while living with animals was protective. In rural children, the main risk factors were a positive skin prick test and living with animals. DISCUSSION: The prevalence of wheeze in children in the Jimma region is low, particularly in rural children. In addition to having an impact on disease prevalence, place of residence also appears to modify the impact of environmental risk factors for wheeze.

Dahlgren J. et al. Health effects on nearby residents of a wood treatment plant. *Environ Res*. 2003; 92(2) : 92-8.p Abstract: OBJECTIVES: The aim of the study was to evaluate the health status of nearby residents of a wood treatment plant who had sustained prolonged low-level environmental exposure to wood processing waste chemicals. METHODS: A population of 1269 exposed residents who were plaintiffs or potential plaintiffs in a lawsuit against the wood treatment plant were evaluated by questionnaire for a health history and symptoms. A representative sample of 214 exposed subjects was included in the analysis. One hundred thirty-nine controls were selected from 479 unexposed volunteers and matched to the exposed subjects as closely as possible by gender and age. Subjects and controls completed additional questionnaires and were evaluated by a physician for medical history and physical examination, blood and urine testing, neurophysiological and neuropsychological studies, and respiratory testing. Environmental sampling for wood processing waste chemicals was carried out on soil and drainage ditch sediment in the exposed neighborhood. RESULTS: The exposed subjects had significantly more cancer, respiratory, skin, and neurological health problems than the controls. The subjective responses on questionnaires and by physician histories revealed that the residents had a significantly greater prevalence of mucous membrane irritation, and skin and neurological symptoms, as well as cancer. (Exposed versus unexposed, cancer 10.0% versus 2.08%, bronchitis 17.8% versus 5.8%, and asthma by history 40.5% versus 11.0%) There were significantly more neurophysiologic abnormalities in adults of reaction time, trails A and B, and visual field defects. CONCLUSIONS: Adverse health effects were significantly more prevalent in long-term residents near a wood treatment plant than in controls. The results of this study suggest that plant emissions from wood treatment facilities should be reduced.

Dai Z.K. et al. *Correlation of pulmonary ^{99m}Tc -DTPA ventilation and ^{99m}Tc -MAA perfusion scans with pulmonary function tests in asymptomatic asthmatic children.* Nucl Med Commun. 2003; 24(7) : 819-24.p **Abstract:** Our objective was to examine and correlate ^{99m}Tc -diethylenetriaminopentaacetic acid (^{99m}Tc -DTPA) ventilation and ^{99m}Tc -macroaggregated albumin (^{99m}Tc -MAA) perfusion (V/Q) lung scans with spirometry in asymptomatic asthmatic children. We evaluated 89 subjects (age range, 6-15 years; mean age, 9.4 years), all with at least 70% predicted forced expiratory volume in 1 s (FEV₁). There were four V/Q scan patterns: normal in 38 (42.7%), inhomogeneous ventilation in 11 (12.4%), matched defects in 25 (28.3%) and mismatched perfusion defects in 13 (14.6%). The maximal mid-expiratory flow rate (MMEF) of the normal scan group was significantly different from that in the other groups. The MMEF of the inhomogeneous group was significantly different from that in the matched defect group and the mismatched perfusion defect group. No other significant differences in spirometric indices were found. In two children with perfusion defects, pulmonary arteriograms demonstrated no obstructive lesions. In conclusion, lung scans provide diagnostic information in asymptomatic asthmatic children, even when they are uncooperative. Abnormal scans are common in these children and are significantly correlated with reduced MMEF (% predicted), reflecting small airway flow obstruction. The pathophysiology of V/Q defects in asymptomatic asthmatic children warrants further investigation.

Dalby R. et al. *A review of the development of Respimat Soft Mist Inhaler.* Int J Pharm. 2004; 283(1-2) : 1-9.p **Abstract:** Respimat Soft Mist Inhaler (SMI) is a new generation inhaler from Boehringer Ingelheim developed for use with respiratory drugs. The device functions by forcing a metered dose of drug solution through a unique and precisely engineered nozzle (the uniblock), producing two fine jets of liquid that converge at a pre-set angle. The collision of these two jets generates the soft mist. The soft mist contains a high fine particle fraction of approximately 65 to 80%. This is higher than aerosol clouds from conventional portable inhaler devices, such as pressurized metered dose inhalers (pMDIs) and dry powder inhalers (DPIs). In addition, the relatively long generation time of the aerosol cloud (approximately 1.5s) facilitates co-ordination of inhalation and actuation—a major problem with pMDIs. These features, together with the slow velocity of the soft mist, result in larger amounts of the drug reaching the lungs and less being deposited in the oropharynx compared with either pMDIs or DPIs. Generation of the soft mist from Respimat SMI is purely mechanical, so propellants are not necessary. The innovative design of Respimat SMI, using water-based drug formulations, ensures patients receive consistent and reliable doses of the drug with each actuation. The device was initially tested in scintigraphic lung deposition studies and produced encouraging results when compared with the chlorofluorocarbon-based pMDI (CFC-MDI). Subsequent clinical studies have confirmed that Respimat SMI is effective and safe in delivering bronchodilators to patients with asthma or chronic obstructive pulmonary disease.

Dales R.E. et al. *Influence of outdoor aeroallergens on hospitalization for asthma in Canada.* J Allergy Clin Immunol. 2004; 113(2) : 303-6.p **Abstract:** **BACKGROUND:** The risk of hospitalization for asthma caused by outdoor aeroallergens is largely unknown. **OBJECTIVE:** The objective of this study was to determine the association between changes in outdoor aeroallergens and hospitalizations for asthma from the Pacific coast to the Atlantic coast of Canada. **METHODS:** A daily time series analysis was done to test the association between daily changes in aeroallergens and daily changes in hospitalizations for asthma during a 7-year period between 1993 and 2000 in 10 of the largest cities in Canada. Results were adjusted for long-term trends, day of the week, climate, and air pollution. **RESULTS:** A daily increase, equivalent to the mean value of each allergen, was associated with the following percentage increase in asthma hospitalizations: 3.3% (95% CI, 2.3 to 4.1) for basidiomycetes, 3.1%

(95% CI, 2.8 to 5.7) for ascomycetes, 3.2% (95% CI, 1.6 to 4.8) for deuteromycetes, 3.0% (95% CI, 1.1 to 4.9) for weeds, 2.9% (95% CI, 0.9 to 5.0) for trees, and 2.0% (95% CI, 1.1 to 2.8) for grasses. After accounting for the independent effects of trees and ozone, the combination of the 2 was associated with an additional 0.22% increase in admissions averaged across cities (P <.05). **CONCLUSION:** These findings provide evidence for the hypothesis that aeroallergens are an important cause of severe asthma morbidity across Canada, and in some situations there might be a modest synergistic adverse effect of ozone and aeroallergens combined.

Dales R.E. et al. *Influence of family income on hospital visits for asthma among Canadian school children.* Thorax. 2002; 57(6) : 513-7.p **Abstract:** **BACKGROUND:** A study was undertaken to investigate the mechanisms by which socioeconomic status may influence asthma morbidity in Canada. **METHODS:** A total of 2968 schoolchildren aged 5-19 years with reported asthma were divided into three family income ranges. Hospital visits and risk factors for asthma, ascertained by questionnaire, were compared between the three groups. **RESULTS:** The mean (SE) annual period prevalence of a hospital visit was 25.0 (3.1)% among schoolchildren with household incomes of less than \$20 000 Canadian compared with 16.0 (1.3)% among those with incomes of more than \$60 000 (p<0.05). Students with asthma from lower income households were more likely to be younger and exposed to environmental tobacco smoke and cats, and their parents were more likely to have a lower educational attainment and be unmarried (p<0.05). Across all income groups, younger age, lower parental education, having unmarried parents, and regular exposure to environmental tobacco smoke were each associated with an increase in risk of a hospital visit (p<0.05). No increased risk was detected due to sex, having pets, and not taking dust control measures. Although not statistically significant at p<0.05, there may have been an interactive effect between income and susceptibility to environmental tobacco smoke. In the lower income group those children who were regularly exposed to second hand smoke had a 79% higher risk of a hospital visit compared with a 45% higher risk in the higher income group. In a logistic regression model the association between income and hospital visit was no longer significant after adjusting for differences in reported exposure to passive smoking. **CONCLUSION:** Socially disadvantaged Canadian schoolchildren have increased asthma morbidity. Exposure to cigarette smoke appears to be one important explanation for this observation.

Daley-Yates P.T. et al. *Relationship between systemic corticosteroid exposure and growth velocity: development and validation of a pharmacokinetic/pharmacodynamic model.* Clin Ther. 2004; 26(11) : 1905-19.p **Abstract:** **BACKGROUND:** Use of high-dose oral corticosteroids (CSs) can reduce growth velocity (GV) in children, whereas use of low-dose topical CSs has either no effect or transient effects on short-term growth and no effect on final adult height. Despite the large body of literature on this topic, some fundamental questions remain concerning the relationship between CS exposure and growth effects. **OBJECTIVES:** The aims of this study were to determine the relationship between CS exposure and GV in children receiving CS therapy for asthma or rhinitis, and to examine whether there is likely to be a link between GV and cortisol suppression. **METHODS:** Data from 32 published studies of the effect on growth of inhaled, intranasal, and oral CSs, including delivery by dry powder inhaler, metered-dose inhaler, and aqueous nasal spray, were consolidated by expressing CS exposure in cortisol equivalents using a physiologically based pharmacokinetic/pharmacodynamic approach. The relationship between change in GV and CS exposure in cortisol equivalents was described using a nonlinear sigmoid maximum-effect (E(max)) model with the following parameters: E(max) = -5.9 cm/y; steady-state unbound AUC for 50% reduction in GV, in cortisol equivalents = 20,000 ng.h/L; Hill constant = 1.2; and change in GV at zero systemic exposure = 0.06 cm/y. Validation was achieved by comparing the model's predictions with data from 5

studies that were not included in the model development. The model was also used to predict the potential of various CS regimens to reduce GV. RESULTS: Exploratory data analysis established that change in GV was highly correlated with exposure in cortisol equivalents ($P < 0.001$). CSs with high systemic bioavailability by the intranasal route were predicted to have short-term growth effects exceeding the clinical equivalence limit for change in GV (± 0.8 cm/y), whereas those with lower bioavailability were predicted to produce systemic exposures below the threshold for significant effects on GV. The findings were similar for inhaled CSs and for regimens combining delivery by the intranasal and inhaled routes. In descending order, the model predicted the following ranking of the potential of the various intranasal, inhaled, and oral regimens to reduce GV, expressed as fractions or multiples of the pediatric dose (in microg/d): oral prednisolone 5000 microg/d, 0.14; inhaled beclomethasone dipropionate metered-dose inhaler 400 microg/d, 0.54; inhaled budesonide dry powder inhaler 400 microg/d, 0.66; intranasal triamcinolone acetonide aqueous nasal spray 220 microg/d, 0.74; inhaled triamcinolone acetonide metered-dose inhaler 400 microg/d, 0.75; intranasal beclomethasone dipropionate aqueous nasal spray 336 pg/d, 0.89; inhaled mometasone furoate dry powder inhaler 200 microg/d, 2.4; intranasal budesonide aqueous nasal spray 128 microg/d, 2.5; inhaled fluticasone propionate dry powder inhaler 200 microg/d, 2.6; intranasal mometasone furoate aqueous nasal spray 100 microg/d, 120; and intranasal fluticasone propionate aqueous nasal spray 100 pg/d, 150. Values >1 are predictive of no significant effect on GV. The model predicted that a 10% to 15% reduction in plasma cortisol concentration should be detectable at the lower equivalence limit for growth reduction (-0.8 cm/y). The validation procedure showed that the model was capable of predicting the results of the 5 comparative growth studies not included in model development with a correlation coefficient of 0.98. CONCLUSIONS: Growth effects appear to be nonlinearly related to CS exposure; therefore, no-effect exposure should be possible for CSs with low systemic exposure. Growth inhibition appears unlikely to occur in the absence of detectable reductions in cortisol concentrations.

Damps-Konstanska I. et al. [Serum eosinophil cationic protein (ECP) in patients with perennial rhinitis and atopic dermatitis, allergic to house dust mites]. *Pol Merkuriusz Lek.* 2005; 19(114) : 765-8.p
Abstract: Eosinophil Cationic Protein (ECP) is released from activated eosinophils during the inflammation process. THE AIM: of the study was to evaluate levels of ECP in serum of patients with perennial rhinitis (with and without asthma) and atopic dermatitis allergic to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. Further it was designed to compare ECP levels in patients treated with allergen-specific immunotherapy (IT) and in patients treated symptomatically. MATERIAL AND METHODS: The study group included 94 patients allergic to house dust mite: 42 patients with perennial rhinitis not treated with IT, 24 patients with perennial rhinitis and/or asthma treated with IT and 28 patients with atopic dermatitis. In the control group were 21 healthy volunteers. In the group treated with IT questionnaire of efficacy and safety was performed. RESULTS: The serum level of ECP was measured using immunofluorometric assay. In the group with perennial rhinitis treated with IT mean level of ECP was 6,5 ug/l, whereas in the group not treated with IT--15,78 microg/l ($p < 0.05$). In patients with atopic dermatitis ECP level was the highest--23,04 microg/l \pm 4,98 and was significantly different than in the group of healthy volunteers--7,2 microg/l \pm 1,1 ($p = 0,0048$). CONCLUSIONS: Serum ECP concentration may be prognostic factor in specific immunotherapy.

Daniel P.F. et al. Measurement of exhaled nitric oxide in young children during tidal breathing through a facemask. *Pediatr Allergy Immunol.* 2005; 16(3) : 248-53.p
Abstract: Measurement of exhaled nitric oxide (eNO) offers a non-invasive means for assessment of airway inflammation. The currently available methods are difficult to apply in preschool children. We evaluated four methods potentially

applicable for eNO measurement during tidal breathing in young children. eNO was assessed during tidal breathing in 24 children, 2-7 yr old, using a facemask which separated nasal and oral airflow. Facemasks with and without a one-way valve allowing exhalation through the nose were used. Expiratory flow control was not attempted. Measurements of eNO were performed both on-line and off-line. In 11 children, 8-12 yr old, measurements were compared with the standard single breath on-line method. eNO was significantly lower applying the one-way valve in on-line and off-line measurements in comparison with measurements without the valve [4.6 and 3.9 parts per billion (ppb) vs. 6.9 ppb and 6.5 ppb]. The mean within subject coefficient of variation (CV) was significantly lower in on-line measurements with the one-way valve (9.6%) compared with the other three methods (18.8, 27.7 and 29.3% respectively). Measurements with a facemask fitted with a one-way valve yielded similar eNO levels as the standard single breath method (7.0 ppb vs. 6.9 ppb) and reproducibility (9.8% vs. 7.1%). In conclusion, reproducible measurements of eNO can be obtained without control of expiration flow using a facemask fitted with a one-way valve on the nasal compartment. The likely explanation to this is that the one-way valve reduces the admixture of nasal NO, thereby improving the reliability of eNO measurements.

Das U.N. Breast-feeding, atopy, and asthma. *J Allergy Clin Immunol.* 2004; 113(5) : 1002; author reply 1002-3.p

Dashash N.A. et al. Prescribing for asthmatic children in primary care. *Are we following guidelines?* *Saudi Med J.* 2003; 24(5) : 507-11.p
Abstract: OBJECTIVE: Guidelines for asthma management have been developed both locally and internationally. The aim of this study was to evaluate the adherence of primary care physicians in the National Guard Iskan Primary Care Center to these guidelines. METHODS: The records of 206 asthmatic children who visited the National Guard Iskan Primary Care Center, Jeddah, Kingdom of Saudi Arabia, during the months of February 1998 through June 1998, were reviewed. The following data was extracted from them; presenting symptoms, number of visits, names of asthma medications, whether doses were documented or not and number of times antitussives were prescribed. RESULTS: The most common presenting complaint was cough followed by wheeze and shortness of breath (mean SD, 14 13.8, 8.8 10.3 and 4.4 5.8). Oral salbutamol was the most frequently prescribed medication. The doses of asthma medications were not documented in 37.3% of cases. Preventive therapy was prescribed to 35.4% of children and emergency steroids were prescribed to 30.6% of children. The mean age of asthmatic children receiving inhaled medications was significantly higher than those other forms of therapy ($p < 0.00001$). Antitussives were prescribed 2,536 times (mean 12.3). CONCLUSION: Prescribing for asthmatic children did not conform to national guidelines for treatment of asthma. These findings suggest that ways need to be found: (i) to increase the use of current asthma management guidelines by practitioners; (ii) to improve documentation of prescribed medications and their dosage and; (iii) to improve education of parents in home management measures.

Dauer E.H. et al. Clinical characteristics of eosinophilic esophagitis in children. *Ann Otol Rhinol Laryngol.* 2005; 114(11) : 827-33.p
Abstract: OBJECTIVES: The role of eosinophilic esophagitis (EE) in aerodigestive tract disorders in children is underestimated and overlooked, primarily because of a lack of understanding of this disorder by otolaryngologists. We sought to better characterize the clinical presentation of EE in order to increase awareness among otolaryngologists. METHODS: We retrospectively reviewed 71 children with biopsy-proven EE to determine the most common symptoms and laboratory findings that should increase the clinical suspicion of EE. RESULTS: Dysphagia, food impaction, and emesis were the most common symptoms in children with EE. Asthma was the most common airway diagnosis. Rhinosinusitis was the most common otolaryngological diagnosis. Food allergy was present in

60% of the children tested. Eighty-three percent of the children with elevated immunoglobulin E levels had thick linear streaking or patchy white exudate of the esophagus seen on esophagoscopy. Other major medical comorbidities existed in more than half of the children with EE, of which psychiatric disorders and other disorders of the aerodigestive tract were the most common. CONCLUSIONS: Eosinophilic esophagitis may contribute to treatment failure in patients with common and complicated aerodigestive tract disorders. To encourage clinicians to avoid overlooking the diagnosis, we present an evaluative algorithm to increase the suspicion of this entity.

Davey G. et al. *Use of acetaminophen and the risk of self-reported allergic symptoms and skin sensitization in Butajira, Ethiopia.* J Allergy Clin Immunol. 2005; 116(4) : 863-8.p **Abstract:** BACKGROUND: Studies in developed countries suggest that acetaminophen use is associated with increased risk of asthma, but it is unclear whether this association is causal. OBJECTIVE: To determine the relation among acetaminophen use, asthma, and allergy, and to explore potential biases in acetaminophen use, in a developing country population. METHODS: We surveyed 7649 adults and children from Butajira, Ethiopia, collecting data on self-reported symptoms of allergic disease, skin sensitization to Dermatophagoides pteronyssinus and cockroach, acetaminophen use, and potential confounders. We then collected detailed data on indications for acetaminophen use and reasons for aspirin avoidance in a nested follow-up study. RESULTS: Allergic symptoms increased significantly with frequency of acetaminophen use, with odds ratios in those using >3 tablets in the past month relative to none 1.89 (95% CI, 1.51-2.36) for wheeze, 2.14 (1.72-2.67) for nocturnal shortness of breath, 2.52 (1.99-3.20) for rhinitis, and 1.90 (1.39-2.61) for eczema. Cockroach sensitization was also more common in the highest acetaminophen category (odds ratio, 1.40; 95% CI, 1.10-1.79), but D pteronyssinus sensitization was not. Less than 1% of participants with asthma or wheeze in our nested study reported avoidance of aspirin because of asthma symptoms. None volunteered using acetaminophen to treat allergic symptoms. CONCLUSION: There is a dose-related association between acetaminophen use and self-reported allergic symptoms in this population that is not a result of aspirin avoidance, reverse causation, or other bias. Acetaminophen may therefore be involved in the etiology of asthma and allergic disease.

Davey G. et al. *Wheeze, allergic sensitization and geohelminth infection in Butajira, Ethiopia.* Clin Exp Allergy. 2005; 35(3) : 301-7.p **Abstract:** BACKGROUND: The effect of geohelminth infection on wheeze and allergen sensitization is inconsistent across different epidemiological studies. OBJECTIVE: To investigate the association between self-reported wheeze, self-reported asthma, allergic sensitization and geohelminth infection in urban and rural areas of Butajira, southern Ethiopia. METHODS: Questionnaire data on wheeze, asthma and a range of confounding variables was gathered in a cross-sectional study of 7649 people aged 5 years or more from the Butajira Rural Health Project database. Allergic skin sensitization to Dermatophagoides pteronyssinus and cockroach was measured, and a stool sample collected for qualitative and quantitative geohelminth analysis. RESULTS: Wheeze was weakly associated with allergic sensitization to D. pteronyssinus and cockroach (odds ratios (OR) 1.21, 95% confidence interval (CI) 0.98-1.51, and 1.27, 95% CI 1.00-1.62, respectively). Self-reported asthma was related to sensitization to D. pteronyssinus only (OR 4.09, 95% CI 2.86-5.84). Geohelminths were present in 33.8% of participants, and the median egg load in infested individuals was 6 eggs/g. Overall, presence of any geohelminths was associated with a diminished risk of cockroach sensitization (adjusted OR 0.82, 95% CI 0.68-0.99) but there were no significant protective effects of any geohelminth infection against wheeze or asthma. CONCLUSION: In a developing country community with relatively low geohelminth prevalence and intensity, we found weak association between allergic sensitization and

wheeze, but no evidence of a protective effect of geohelminths against wheeze or asthma.

David G.L. et al. *Nicotinamide adenine dinucleotide (phosphate) reduced:quinone oxidoreductase and glutathione S-transferase M1 polymorphisms and childhood asthma.* Am J Respir Crit Care Med. 2003; 168(10) : 1199-204.p **Abstract:** Nicotinamide adenine dinucleotide (phosphate) reduced:quinone oxidoreductase (NQO1) and glutathione S-transferase (GST) M1 are phase II enzymes important in response to oxidative stress, such as occurs during exposure to ozone. We examined the relationship between functionally significant polymorphisms in NQO1 (Pro187Ser) and GSTM1 (homozygous deletion) and asthma risk in children with high lifetime exposure to ozone. We enrolled children with asthma from the allergy referral clinic at a public pediatric hospital in Mexico City, together with their parents. We assayed for the Pro187Ser polymorphism in NQO1 using a polymerase chain reaction-restriction fragment length polymorphism assay and for the presence of GSTM1 by polymerase chain reaction among 218 case-parent triads. We did not find strong evidence of an association between NQO1 genotype alone and asthma risk. However, among subjects with homozygous deletion of GSTM1, carriers of a serine allele were at significantly reduced risk of asthma compared with Pro/Pro homozygotes (relative risk = 0.4; 95% confidence interval, 0.2-0.8). The p value for difference in relative risk for NQO1 by GSTM1 genotype = 0.013. These data are consistent with a protective effect of the NQO1 Ser allele in this population of GSTM1-null children with high ozone exposure.

Davies G.M. et al. *The effect of montelukast versus usual care on health care resource utilization in children aged 2 to 5 years with asthma.* Clin Ther. 2004; 26(11) : 1895-904.p **Abstract:** BACKGROUND: Limited clinical data are available on the long-term effects of asthma controller therapy on the utilization of health care resources in pediatric patients with asthma. OBJECTIVE: The objective of this study was to compare the effects of long-term treatment with montelukast and usual care on health care resource use in children with asthma. METHODS: Pediatric patients aged 2 to 5 years with asthma who had completed a 3-month, double-blind, double-dummy clinical trial comparing montelukast 4 mg and placebo were asked to participate in an open-label, controlled extension study comparing montelukast 4 mg and usual care. Usual care was defined as cromolyn or inhaled corticosteroid therapy. Health care resource utilization was measured in terms of oral corticosteroid use and numbers of physician visits, emergency department visits, and hospitalizations. RESULTS: Of 618 patients who completed the primary phase of the study, 516 (83.5%) participated in the extension study. Data from 506 patients (302 without previous asthma maintenance therapy, 204 with) were included in the analysis. During the extension phase, patients who received montelukast and had not used previous asthma maintenance therapy were followed for a mean of 329.5 days; those who received usual care and CONCLUSION: In this open-label study, pediatric patients aged 2 to 5 years with mild to moderate persistent asthma receiving long-term therapy with montelukast had similar rates of asthma-related health care resource utilization compared with those receiving usual care with cromolyn or inhaled corticosteroids.

Davis L.E. et al. *Asthma in New York City.* J Asthma. 2003; 40 Suppl : 55-61.p

Davis R.L. et al. *Pneumococcal conjugate vaccine in children.* N Engl J Med. 2004; 350(1) : 84-5; author reply 84-5.p

Davoli C.T. *"Home-Sick": the effect of a child's environment on health.* Arch Pediatr Adolesc Med. 2002; 156(9) : 853-4.p

- De Baets F. et al.** *Exercise-induced respiratory symptoms are poor predictors of bronchoconstriction.* *Pediatr Pulmonol.* 2005; 39(4) : 301-5.p **Abstract:** Exercise-induced asthma (EIA) is a possible cause of poor physical performance in children. No data are available on the value of respiratory symptoms to discriminate children with bad physical fitness from children with EIA. We evaluated respiratory symptoms in school-age children during and after exercise in relation to EIA. The population of 149 primary schools (849 classes with 15,241 children) was enrolled in the study. EIB was assessed using the 6-min free-running-test (6MFRT) in 15,241 children. At the end or at premature arrest of the 6MFRT, signs reported by the children and clinical symptoms observed by supervising physicians were recorded. Peak flow measurements were obtained before and 5 and 10 min after the 6MFRT, a decrease of 15% or more being defined as significant. The 6MFRT was positive in 7.4% of primary schoolchildren. Girls were more likely to have a positive test than boys (8.5% vs. 6.4%, $P < 0.001$), and children living in urban areas more than those living in rural areas (8.9% vs. 7.0%, $P < 0.01$). Premature arrest was seen in 3.5% (i.e., $n = 353$) of the children. The main reasons for premature arrest were dyspnea and chest pain. Among them, only 21% had a positive 6MFRT, while 89% with a positive 6MFRT could terminate the test. Premature arrest, breathlessness, chest tightness, wheezing, and cough had a positive predictive value to detect a EIA of 21.9%, 20.8%, 36.4%, 41.2%, and 28.3%, respectively, and a sensitivity of 10.8%, 29.5%, 14.9%, 4.8%, and 13.0%, respectively. In conclusion, EIA was detected in 7.4% of schoolchildren. A slightly higher incidence was observed in girls and children from an urban area. Neither premature arrest nor clinical signs and symptoms were good predictors of EIA in primary schoolchildren.
- de Benedictis F.M. et al.** *Effects of 2 inhaled corticosteroids on growth: results of a randomized controlled trial.* *Arch Pediatr Adolesc Med.* 2001; 155(11) : 1248-54.p **Abstract:** OBJECTIVE: To compare the long-term effect of treatment with fluticasone propionate or beclomethasone dipropionate on growth in asthmatic children. DESIGN: Prospective, multicenter, randomized, double-blind, parallel-group study. SETTING: Children requiring regular treatment with inhaled corticosteroids and with a sexual maturity rating of Tanner stage 1 (prepubertal). PATIENTS: Three hundred forty-three children aged 4 to 11 years with asthma. The growth population (excluding patients with protocol violations likely to affect growth measurements) included 277 patients. INTERVENTIONS: Fluticasone propionate or beclomethasone dipropionate, both at a dosage of 200 microg administered twice daily via a dry powder inhaler (Diskhaler) for 12 months. MAIN OUTCOME MEASURES: Growth velocity, lung function, and serum and urinary cortisol levels. RESULTS: The adjusted mean growth velocity in the fluticasone group was significantly greater than that in the beclomethasone group (5.01 [SE, 0.14] vs 4.10 [SE, 0.15] cm/y; difference, 0.91 cm; 95% confidence interval, 0.63-1.20 cm; $P < .001$). Both treatments improved lung function, with significant differences in favor of fluticasone. Adverse events were similar in both groups, and there were no significant differences in effect on serum and urinary cortisol levels. CONCLUSIONS: The more favorable risk-benefit ratio of fluticasone indicates that this agent is preferable to beclomethasone for the long-term treatment of children with asthma, especially if moderate doses are required.
- de Boer R.** *Allergens, Der p 1, Der f 1, Fel d 1 and Can f 1, in newly bought mattresses for infants.* *Clin Exp Allergy.* 2002; 32(11) : 1602-5.p **Abstract:** BACKGROUND: To avoid allergen exposure of newborn babies, the use of a new mattress for the baby bed may be recommended. However, it is not certain that new mattresses are always free of allergens. OBJECTIVE: In the present study the allergen content of new infant mattresses was investigated. METHODS: Dust samples were vacuumed from 90 new mattresses for infant beds bought in 50 different Dutch shops, and the concentrations of Der p 1, Der f 1, Fel d 1 and Can f 1 were determined by radioimmunoassays. RESULTS: Most mattresses contained some allergen and often the allergen concentrations were surprisingly high. Only 15 of the 90 mattresses contained no detectable amounts of any of the four allergens. The highest concentration found for each allergen was 3.1, 46.5, 20.2 and 95.7 microg/g of dust, respectively. However, the total amount of allergen in a mattress was still rather low because the new mattresses contained only modest amounts of dust. Baby mattresses more often contained an increased allergen load than the larger, standard-sized, infant mattresses. This may be caused by differences in manufacturing procedure. Also, mattresses that were sold without a plastic encasement more often contained an increased allergen load. CONCLUSIONS: It is advisable to buy a mattress that is wrapped in plastic, but it may still contain a substantial amount of allergen. Thorough vacuuming of a newly bought mattress before it is installed on a child's bed, is also advisable. After instalment, regular vacuuming of the mattress and washing of the bed linen as well as measures to eliminate allergen reservoirs in other parts of the house are important, because our observations indicate that mattresses easily pick up allergens from the environment.
- de Diego Damia A.** *[Asthma: from child to adult].* *Arch Bronconeumol.* 2003; 39(2) : 51-3.p
- de Frutos Martinez C. et al.** *[Agreement between tracheal auscultation and pulmonary function in methacholine bronchial inhalation challenge in asthmatic children].* *An Esp Pediatr.* 2002; 56(4) : 304-9.p **Abstract:** BACKGROUND: PC wheezing (PCw) is defined as the concentration of methacholine at which wheeze is detected on auscultation of the trachea. PCw has been suggested as a measure of bronchial hyperresponsiveness in methacholine challenge testing (MCT). OBJECTIVE: The aim of this study was to determine the agreement between the concentration of methacholine that produces a 20 % decrease in forced expiratory volume in 1 second (FEV1) (PC20) and PCw in MCT in asthmatic children. PATIENTS AND METHODS: Eighteen asthmatic children with a mean age of 11.5 years (range: 6-16 years) were studied. Fifteen of the children were under treatment with inhaled glucocorticoids. MCT was performed according to the guidelines of the American Thoracic Society (1999) using a Hudson nebulizer calibrated to obtain a mean output of 0.14 ml/min. After each nebulization, two independent observers registered FEV1 and tracheal auscultation. FEV1 was determined by forced spirometry 30 and 90 seconds after the end of nebulization and PC20 was registered (exponential model). Respiratory rate and transcutaneous oxygen saturation were continuously monitored. Tracheal auscultation was performed at 0, 60 and 120 seconds after the end of nebulization. The end point was defined as the appearance of wheezing over the trachea. The values of PC20 and PCw, as well as the concentration of methacholine corresponding to a decrease in FEV1 equal to or higher than 20 %, were compared using Student's matched pairs-test and Wilcoxon's test. The degree of agreement between variables was compared by using Bland-Altman's test. RESULTS: MCT was positive in 17 of 18 patients. No differences were found between PC20 and PCw ($p 0.15$). Both variables showed agreement in 12 of 17. A clear association was found between both measures (log PCw, log PC20): $R: 0.92$; $p < 0.001$. The mean decrease in FEV1 on reaching PCw was 24.8 % (range: 10-41). No adverse effects were observed. CONCLUSION: The agreement between PC20 and PCw in MCT in asthmatic children is excellent. PCw could be helpful in determining bronchial hyperresponsiveness in young asthmatic children in whom spirometry is not feasible.
- de Jong N.W. et al.** *Immunoblot and radioallergosorbent test inhibition studies of allergenic cross-reactivity of the predatory mite *Amblyseius cucumeris* with the house dust mite *Dermatophagoides pteronyssinus*.* *Ann Allergy Asthma Immunol.* 2004; 93(3) : 281-7.p **Abstract:** BACKGROUND: In 1999, an extensive study among bell pepper growers showed that a predatory mite, *Amblyseius cucumeris*, is a potentially relevant source of occupational allergens

because 23% of the population had positive skin prick test reactions. **OBJECTIVE:** To investigate whether cross-reactivity between *A. cucumeris* and *Dermatophagoides pteronyssinus* is responsible for the cosensitization to both mite species found in 58.7% of *A. cucumeris*-sensitized greenhouse workers. **METHODS:** Fifteen serum samples from greenhouse workers with work-related inhalant allergy and a positive radioallergosorbent test (RAST) reaction to *A. cucumeris* or *D. pteronyssinus* were selected for immunoblot analysis using extracts of both mites. A subselection ($n = 5$) was used for RAST and immunoblot inhibition to investigate potential cross-reactivity. **RESULTS:** On immunoblot, 2 distinct patterns were observed: one pattern showed common protein bands in *A. cucumeris* and *D. pteronyssinus* blots suggestive of cross-reactivity between *A. cucumeris* and *D. pteronyssinus* and the other pattern showed no shared protein bands. *Dermatophagoides pteronyssinus* RAST inhibition with *A. cucumeris* extract was low in 4 serum samples (<25% inhibition) and nearly absent in 1 serum sample; *A. cucumeris* RAST inhibition with *D. pteronyssinus* extract was high in 1 serum sample (75% inhibition), low in 2 serum samples (35% and <15% inhibition), and absent in 2 serum samples. These results were confirmed by immunoblot inhibition experiments. **CONCLUSIONS:** *Amblyseius cucumeris*, a new occupational allergen, has species-specific antigens and common antigens that are cross-reactive with the house dust mite *D. pteronyssinus*.

de la Rosa Lopez J.H. et al. [Errors in the technique of using measured-dose inhalers in asthmatic children and adolescents]. *Rev Alerg Mex.* 2002; 49(1) : 8-10.p **Abstract:** **BACKGROUND:** The MDI's are widely used in the treatment of asthma and are relatively easy to use. The response to this medicament is influenced by several facts that include the physical characteristics of the container and the technique used by the patient. **OBJECTIVE:** To identify the mistakes made by asthmatic children and teenagers in the use of the MDI's. **MATERIAL AND METHODS:** This paper was a descriptive and observational study in 57 asthmatic patients who were between 5 to 17 years. For the evaluation of the inhalation technique we used a placebo without a spacer. There are 5 steps for the correct use of the inhaled medications: 1) opening, 2) agitation, 3) coordination between inhalation and the shoot of the MDI's, 4) a deep breath and holding it for at least 6 seconds. **RESULTS:** 20 of the 57 patients (35%) followed all the steps correctly. The most frequent mistake was to take the deep breath, which was performed only by 20 (35%) out of the children. The second mistake we found in this study was the up holding inspiration at least for 6 seconds, which was done properly only by 31 patients (54%). **CONCLUSIONS:** The implantation of inhaled therapy programs directed and performed by specialists is recommended.

de Meer G. et al. *Early childhood environment related to microbial exposure and the occurrence of atopic disease at school age.* *Allergy.* 2005; 60(5) : 619-25.p **Abstract:** **BACKGROUND:** There is a growing body of evidence that the early childhood environment with respect to day care attendance, older siblings, pet ownership, and early life airway infections may protect from developing atopic disease. Few studies have distinguished between atopic sensitization and symptoms, and none have evaluated independent contributions for all of these different environmental conditions. **OBJECTIVE:** Examine independent effects on atopic sensitization and symptoms of day care attendance, older siblings, pet ownership, and early infancy's airway disease. **METHODS:** A cross-sectional survey among 8-13-year-old school children with complete data for 1555 children. **RESULTS:** After adjustment for confounders, atopic sensitization occurred less frequently in children that had attended a day care centre (OR: 0.73, 95% CI: 0.55-0.98) or had a cat or dog before 2 years of age (OR: 0.78, 95% CI: 0.61-0.99). Having older siblings yielded a nonsignificant trend towards protection (OR: 0.88, 95% CI: 0.70-1.11). For symptoms, there was no relation with having older sibs, day care attendance and pet ownership, although there was a trend towards protection for the

combination of atopy and symptoms. In contrast, children with doctors' treated airway disease before age 2, more frequently reported recent symptoms of wheeze, asthma, rhinitis, or dermatitis (all $P < 0.05$). **CONCLUSION:** Early life environmental exposure to day care, or pets may protect against atopic sensitization. Protection against symptoms only occurred if atopic sensitization was present as well.

de Meer G. et al. *Bronchial hyper-responsiveness to hypertonic saline and blood eosinophilic markers in 8-13-year-old schoolchildren.* *Clin Exp Allergy.* 2004; 34(8) : 1226-31.p **Abstract:** **BACKGROUND:** In adult asthma, bronchial hyper-responsiveness (BHR) to indirect stimuli reflects eosinophilic activation more closely than BHR to stimuli that directly cause smooth muscle contraction. **AIM:** To assess the relationship between BHR to the indirect stimulus hypertonic saline (HS), blood eosinophil numbers, and serum eosinophilic cationic protein (ECP) in children with and without current wheeze. **METHODS:** A cross-sectional survey among 8-13-year-old schoolchildren, using the International Study of Asthma and Allergic disease in Childhood questionnaire, bronchial challenge with HS, skin prick tests, serum IgE, blood eosinophil counts and ECP (in a subset). Based upon the presence of current wheeze (WHE) and BHR, we defined three case groups (WHE+BHR+, WHE-BHR+, WHE+BHR-) and the reference group (WHE-BHR-). By regression analyses, each case group was compared with the reference group for differences in atopic sensitization, blood eosinophil counts and serum ECP. **RESULTS:** Complete data were obtained for 470 children. BHR was present in 103 children (22%), 66 being asymptomatic and 37 symptomatic. Children of all three case groups were more often atopic. Sensitization to indoor allergens particularly occurred in children with BHR, irrespective of symptoms ($P < 0.05$). Children with WHE+BHR+ had highest values for blood eosinophils and serum ECP ($P < 0.05$). Children with WHE-BHR+ had less severe responsiveness. In atopic children with WHE+BHR+, serum ECP was higher than in children with WHE-BHR- ($P < 0.05$). **CONCLUSIONS:** BHR to HS is associated with blood markers of eosinophilic activation, particularly in atopic children.

Dean T. *The Cochrane Collaboration and its contribution towards the management of allergic diseases.* *Clin Exp Allergy.* 2002; 32(9) : 1269-73.p

Debley J.S. et al. *The prevalence of ibuprofen-sensitive asthma in children: a randomized controlled bronchoprovocation challenge study.* *J Pediatr.* 2005; 147(2) : 233-8.p **Abstract:** **OBJECTIVE:** To determine the prevalence of ibuprofen-sensitive asthma in school-aged children with mild or moderate persistent asthma. **STUDY DESIGN:** A randomized, double-blind, placebo-controlled, crossover bronchoprovocation challenge study in children 6 to 18 years of age with mild or moderate persistent asthma. Patients received a single dose of ibuprofen or placebo, per randomization, and then returned 2 to 7 days later to repeat the procedures after taking that study drug not received at the first visit. At each visit, patients performed spirometry before and (1/2), 1, 2, and 4 hours after administration of study drug. We defined bronchospasm as a $> \text{or} = 20\%$ decrease from baseline in the forced expired volume in the first second (FEV1) and ibuprofen sensitivity as bronchospasm following administration of ibuprofen but not placebo. **RESULTS:** Of the 127 patients screened, 100 (mean age, 11 years) completed the study. Two patients met criteria for ibuprofen-sensitive asthma, resulting in a prevalence of 2% (95% CI: 0.2%-7%). Neither patient was known to have had any exposure to ibuprofen before the study. **CONCLUSION:** The prevalence of ibuprofen-sensitive asthma was low but non-zero in this group of children with mild or moderate asthma. The possibility of ibuprofen-induced bronchospasm should be considered before administering ibuprofen to children with asthma.

- Debley J.S. et al.** *Childhood asthma hospitalization risk after cesarean delivery in former term and premature infants.* Ann Allergy Asthma Immunol. 2005; 94(2) : 228-33.p Abstract: BACKGROUND: Cesarean delivery modifies infant gut bacterial flora composition, which may result in hindered tolerance to allergenic substances, thereby increasing the risk of asthma in accordance with the hygiene hypothesis. Results of previous studies regarding an association between birth route and asthma are conflicting, and these studies have not evaluated some potential confounding effects, including prematurity and maternal asthma. OBJECTIVE: To determine whether cesarean delivery in full-term and premature infants increases the risk of subsequent childhood asthma hospitalization. METHODS: We conducted a case-control study using the Washington State Birth Events Record Database linked to statewide hospitalization data. The study included 2,028 children hospitalized for asthma (cases) and 8,292 age-matched controls. RESULTS: Cesarean delivery was modestly associated with an increased risk of asthma hospitalization (odds ratio [OR], 1.20; 95% confidence interval [CI], 1.04-1.39). However, when analyzed separately, there was an association between cesarean delivery and asthma hospitalization in premature infants (OR, 1.90; 95% CI, 1.09-3.02) but not in full-term infants (OR, 1.15; 95% CI, 0.97-1.34). CONCLUSIONS: Cesarean delivery was associated with subsequent asthma hospitalization only in premature infants. Because mothers with asthma are reported to have increased rates of cesarean delivery and premature delivery, other factors in addition to the hygiene hypothesis, including genetic and in utero influences associated with maternal asthma, may contribute to the increased risk of asthma in premature infants.
- Dechene L.** *TH1/TH2 immune response.* J Allergy Clin Immunol. 2002; 110(3) : 539-40; author reply 540.p
- Decoufle P. et al.** *Increased mortality in children and adolescents with developmental disabilities.* Paediatr Perinat Epidemiol. 2002; 16(4) : 375-82.p Abstract: A population-based cohort of 10-year-old children with mental retardation, cerebral palsy, epilepsy, hearing impairment or vision impairment, who were ascertained at 10 years of age in a previous study conducted in metro Atlanta during 1985-87, was followed up for mortality and cause of death information. We used the National Death Index to identify all deaths among cohort members during the follow-up period (1985-95). We estimated expected numbers of deaths on the basis of actual age-, race- and sex-specific death rates for the entire Georgia population for 1989-91. The objective was to quantify the magnitude of increased mortality and evaluate the contribution of specific disabilities to mortality among children and adolescents with one or more of five developmental disabilities. A total of 30 deaths were observed; 10.1 deaths were expected, yielding an observed-to-expected mortality ratio of almost three to one. The numbers of observed deaths exceeded those of expected deaths, regardless of the number of disabilities present, but the ratios were statistically significant (at the 95% confidence level) only in children with three or more co-existing disabilities. In general, the magnitude of the mortality ratios was directly related to various measures of the severity of the person's disability. An exception to this pattern was the elevated mortality from cardiovascular disease among cohort members with isolated mental retardation (three observed deaths vs. 0.2 expected). The specific underlying causes of death among other deceased cohort members included some that were the putative cause of the developmental disability (e.g. a genetic syndrome) and others that could be considered intercurrent diseases or secondary health conditions (e.g. asthma). Prevention efforts to decrease mortality in adolescents and young adults with developmental disabilities may need to address serious conditions that are secondary to the underlying disability (i.e. infections, asthma, seizures) rather than towards injuries, accidents and poisonings, the primary causes of death for persons in this age group in the general population.
- Dehlink E. et al.** *Absence of systemic immunologic changes during dose build-up phase and early maintenance period in effective specific sublingual immunotherapy in children.* Clin Exp Allergy. 2006; 36(1) : 32-9.p Abstract: BACKGROUND: Sublingual immunotherapy (SLIT) has been reported to be a safe treatment for inhalant allergies in children. Yet the immunologic mechanisms resulting in clinical improvement are poorly understood. OBJECTIVE: To identify early systemic immunologic changes during the first 8 weeks of clinically effective SLIT to grass pollen, tree pollen or house dust mite in paediatric patients with allergic rhinoconjunctivitis and/or asthma. METHODS: Peripheral blood mononuclear cells and plasma samples of 13 children with reduced symptoms after 1 year of SLIT were obtained before therapy and at 2 and 8 weeks after the initiation of SLIT. Allergen-specific lymphocyte proliferation assays were performed, and allergen-induced cytokine production (IL-2, IL-4, IL-10, IFN-gamma, and TGF-beta(1)) was measured by ELISA and flow cytometry. Allergen-specific IgE, IgG1, IgG4, and IgA levels in plasma samples were determined in ELISA. RESULTS: During the first 8 weeks of successful SLIT, allergen-specific lymphoproliferation (n=13) as well as levels of allergen-specific intracellular (n=8) and secreted cytokines (n=9) did not change significantly. In addition, no alterations in levels of allergen-specific Igs (n=7) were observed. CONCLUSION: We could not find any early systemic immunologic changes during the first 8 weeks of clinically effective SLIT to inhalant allergens in paediatric patients with allergic rhinoconjunctivitis and/or asthma.
- Del Rio-Navarro B.E. et al.** *A comparative study of bronchodilator reversibility with albuterol, between asthma symptomatic and asymptomatic children according to ISAAC questionnaire in Mexico City.* Allergol Immunopathol (Madr). 2004; 32(6) : 334-9.p Abstract: BACKGROUND: Asthma is an important childhood disease. Recent surveys of the International Study of Asthma and Allergies in Childhood (ISAAC) suggest that the prevalence of asthma is increasing but these surveys do not include any pulmonary tests to confirm the possible diagnosis of asthma. OBJECTIVE: To compare bronchodilator reversibility with the albuterol test in symptomatic and asymptomatic 6-7-year-old children with asthma participating in the ISAAC survey and living in Mexico City. PATIENTS AND METHODS: We performed an observational, descriptive, comparative, cross sectional study in children participating in phase 3b of the ISAAC study. According to the ISAAC questionnaire children were classified as asthma symptomatic or asymptomatic. Both groups had bronchodilator reversibility with the albuterol test, using the guidelines of the American Thoracic Society to confirm or rule out the diagnosis of asthma. RESULTS: The asymptomatic group had a baseline FEV1 of 1.70 +/- 0.34 l/sec (mean +/- SD) and an endpoint FEV1 of 1.76 +/- 0.42 l/sec; in the symptomatic group the respective values were 1.51 +/- 0.41 l/sec and 1.57 +/- 0.44 l/sec (p < 0.05). A positive reversibility test was found in 13/136 (9.6 %) children in the asymptomatic group and in 22/112 (19.6 %) children in the symptomatic group (p < 0.05). CONCLUSION: Because of its low sensitivity, bronchodilator reversibility cannot be considered a diagnostic tool to confirm diagnosis of asthma.
- Delacourt C.** *[Asthma in children].* Rev Prat. 2001; 51(19) : 2157-64.p
- Delacourt C.** *[Physiopathology of the cough].* Arch Pediatr. 2001; 8 Suppl 3 : 600-602.p Abstract: Cough is initiated from organs innervated by the vagus nerve. The larynx and the lower airways are the main sites involved in cough initiation. Cough is mainly triggered by mechanical stimuli, especially at the laryngeal level, and also by inflammatory stimuli and chemical irritants. Two receptor types are involved in the cough reflex: the irritant receptors (IR) and the C fibers. IR are directly involved in cough initiation whereas stimulated C fibers act essentially through tachykinin release, which in turn activates IR. Cough in asthma was initially thought to be related to

the bronchospasm reflex, but seems in fact mainly due to airway inflammation.

Delacourt C. et al. *Relationship between bronchial responsiveness and clinical evolution in infants who wheeze: a four-year prospective study.* Am J Respir Crit Care Med. 2001; 164(8 Pt 1) : 1382-6.p **Abstract:** Recurrent illness involving wheezing during the first years of life is transient in most children. The role of bronchial hyperresponsiveness as a factor influencing the persistence of wheezing from infancy to school age remains unknown. In a prospective study we investigated whether infants who wheezed and subsequently developed persistent asthma differed from infants who wheezed and later became asymptomatic either in the initial degree of bronchial hyperresponsiveness or in the persistence of bronchial hyperresponsiveness with age. One hundred and twenty-nine infants with three or more wheezing episodes before 2 yr of age were followed during 4 yr with a clinical evaluation and a methacholine challenge performed every 6 mo until the child was 4 yr old and once per year thereafter. The clinical score significantly improved with time in most children. The proportion of children with persistent wheezing after 2 and 4 yr of follow-up was only 31% and 20%, respectively. Persistent wheezers had significantly lower VmaxFRC values at initial evaluation and higher SRaw values at the end of follow-up than infants who became asymptomatic. We used transcutaneous oxygen tension (PtcO₂) to measure the response to methacholine. No significant difference in PD(15) PtcO₂ between groups with subsequently different clinical progression was observed at initial evaluation. Bronchial hyperresponsiveness persisted 4 yr later in all children but children with persistent wheezing showed significantly lower PD(15) PtcO₂ values than children who became asymptomatic, as early as 30 mo of age. However, an acceptable early PD(15) PtcO₂ cut-off point predictive for subsequent clinical progression could not be identified. The level of bronchial hyperresponsiveness in infants who wheezed was not predictive of the persistence of asthma 4 yr later.

Delacourt C. et al. *Comparison of the forced oscillation technique and the interrupter technique for assessing airway obstruction and its reversibility in children.* Am J Respir Crit Care Med. 2001; 164(6) : 965-72.p **Abstract:** The forced oscillation technique (FOT) and interrupter technique are particularly attractive for pediatric use as they require only passive cooperation from the patient. We compared the sensitivity and specificity of these methods for detecting airway obstruction and its reversibility in 118 children (3-16 yr) with asthma or chronic nocturnal cough. FOT (R(0) and R(16)) and interruption (Rint) parameters were measured at baseline and after bronchodilator inhalation (n = 94). Rint was significantly lower than R(0), especially in children with high baseline values. Baseline parameters were normalized for height and weight [R(SD)]. In children able to perform forced expiratory maneuvers (n = 93), the best discrimination between those with baseline FEV₁ < 80% or > or = 80% of predicted values was obtained with R(0)(SD). At a specificity of 80%, R(0)(SD) yielded 66% sensitivity, whereas Rint(SD) yielded only 33% sensitivity. Similarly, postbronchodilator changes in R(0)(SD) [DeltaR(0)(SD)] yielded the best discrimination between children with and without significant reversibility in FEV₁. At a specificity of 80%, DeltaR(0)(SD) yielded 67% sensitivity and DeltaRint(SD) yielded 58% sensitivity. In children unable to perform forced expiratory maneuvers (n = 25), FOT, contrary to the interrupter technique, clearly identified a subgroup of young children with high resistance values at baseline, which returned to normal after bronchodilation. We conclude that, in asthmatic children over 3 yr old, FOT measurements provide a more reliable evaluation of bronchial obstruction and its reversibility compared with the interrupter technique, especially in young children with high baseline values.

Delfino R.J. et al. *Respiratory symptoms and peak expiratory flow in children with asthma in relation to volatile organic compounds in exhaled breath and ambient air.* J Expo Anal Environ Epidemiol. 2003; 13(5) : 348-63.p **Abstract:** Indoor volatile organic compounds (VOCs) have been associated with asthma, but there is little epidemiologic work on ambient exposures, and no data on relationships between respiratory health and exhaled breath VOCs, which is a biomarker of VOC exposure. We recruited 26 Hispanic children with mild asthma in a Los Angeles community with high VOC levels near major freeways and trucking routes. Two dropped out, three had invalid peak expiratory flow (PEF) or breath VOC data, leaving 21. Children filled out symptom diaries and performed PEF maneuvers daily, November 1999-January 2000. We aimed to collect breath VOC samples on asthma episode and baseline symptom-free days, but six subjects only gave samples on symptom-free days. We analyzed 106 breath samples by GC-MS. Eight VOCs were quantifiable in >75% of breath samples (benzene, methylene chloride, styrene, tetrachloroethylene, toluene, m,p-xylene, o-xylene, and p-dichlorobenzene). Generalized estimating equation and mixed linear regression models for VOC exposure-response relationships controlled for temperature and respiratory infections. We found marginally positive associations between bothersome or more severe asthma symptoms and same day breath concentrations of benzene [odds ratio (OR) 2.03, 95% confidence interval (CI) 0.80, 5.11] but not other breath VOCs. Ambient petroleum-related VOCs measured on the same person-days as breath VOCs showed notably stronger associations with symptoms, including toluene, m,p-xylene, o-xylene, and benzene (OR 5.93, 95% CI 1.64, 21.4). On breath sample days, symptoms were also associated with 1-h ambient NO₂, OR 8.13 (1.52, 43.4), and SO₂, OR 2.36 (1.16, 4.81). Consistent inverse relationships were found between evening PEF and the same ambient VOCs, NO₂, and SO₂. There were no associations with O₃. Given the high traffic density of the region, stronger associations for ambient than for breath VOCs suggest that ambient VOC measurements were better markers for daily exposure to combustion-related compounds thought to be causally related to acute asthma. Alternatively, the low sample size of symptom responses (15-21 responses per 108 breath samples) may have led to the nonsignificant results for breath VOCs.

Delgado A. et al. *Nebulizers vs metered-dose inhalers with spacers for bronchodilator therapy to treat wheezing in children aged 2 to 24 months in a pediatric emergency department.* Arch Pediatr Adolesc Med. 2003; 157(1) : 76-80.p **Abstract:** OBJECTIVE: To determine if administration of albuterol by a metered-dose inhaler with a spacer device is as efficacious as administration of albuterol by nebulizer to treat wheezing in children aged 2 years and younger. DESIGN: Double-blind, randomized, placebo-controlled clinical trial. SETTING: Pediatric emergency department. PATIENTS: From a convenience sample of wheezing children aged 2 to 24 months, 85 patients were enrolled in the nebulizer group and 83 in the spacer group. INTERVENTIONS: The nebulizer group received a placebo metered-dose inhaler with a spacer followed by nebulized albuterol. The spacer group received albuterol by a metered-dose inhaler with a spacer followed by nebulized isotonic sodium chloride solution. Treatments were given every 20 minutes by a single investigator blinded to group assignment. MAIN OUTCOME MEASURES: The primary outcome was admission rate. Pulmonary Index score and oxygen saturation were measured initially and 10 minutes after each treatment. RESULTS: The nebulizer group had a significantly higher mean (SD) initial Pulmonary Index score compared with the spacer group (7.6 [2.5] vs 6.6 [2.0]; P = .002). With the initial Pulmonary Index score controlled, children in the spacer group were admitted less (5% vs 20%; P = .05). Analyses also revealed an interaction between group and initial Pulmonary Index score; lower admission rates in the spacer group were found primarily in children having a more severe asthma exacerbation. CONCLUSION: Our data suggest that metered-dose inhalers with spacers may be as efficacious as nebulizers for the emergency department treatment of wheezing in children aged 2 years or younger.

- Dell S. et al.** *Breastfeeding and asthma in young children: findings from a population-based study.* Arch Pediatr Adolesc Med. 2001; 155(11) : 1261-5.p Abstract : OBJECTIVE: To evaluate the association between breastfeeding and asthma in young Canadian children. METHODS: Baseline data from the National Longitudinal Survey of Children and Youth (a population-based study of child health and well-being) were used. A weighted sample of 331 100 (unweighted n = 2184) children between the ages of 12 and 24 months, whose biological mother reported data on breastfeeding and asthma, were included. Outcomes included parental report of physician-diagnosed asthma and wheeze in the previous year. Breastfeeding was categorized by duration as follows: less than 2 months, 2 to 6 months, 7 to 9 months, and longer than 9 months. Logistic regression analyses were conducted with breastfeeding duration dichotomized at various cutoffs. Important potential confounders were considered in the adjusted analyses. Published statistical methods appropriate for the sampling strategy were used. RESULTS: The prevalence of asthma was 6.3%; and wheeze, 23.9%. Almost half of the children (44.0%) were breastfed for less than 2 months. After adjustment for smoking, low birth weight, low maternal education, and sex, a duration of breastfeeding for 9 months or less was found to be a risk factor for asthma (odds ratio, 2.39; 99% confidence interval, 0.95-6.03) and wheeze (odds ratio, 1.54; 99% confidence interval, 1.04-2.29). A dose-response effect was observed with breastfeeding duration. CONCLUSIONS: A longer duration of breastfeeding appears to be protective against the development of asthma and wheeze in young children. More public health efforts should be directed toward increasing the initiation and duration of breastfeeding.
- Dell S.D. et al.** *Childhood asthma admissions: determinants of short stay.* Pediatr Allergy Immunol. 2001; 12(6) : 327-30.p Abstract: The objective of this study was to identify the determinants of short hospital stay (< 24 h) among children admitted because of an acute asthma exacerbation. Computerized health records were used to identify children with a discharge diagnosis of asthma (ICD code 493.0) at the Hospital for Sick Children, Toronto, during the period October 1994 to October 1995. Cases were children with a length of hospital stay of < 24 h (short-stay group) and controls were children with a length of stay of > 24 h (long-stay group). Clinical and demographic data were extracted from the medical record. Over the 12-month period, 485 children were hospitalized because of asthma. Of these, 121 (25%) had short-stay admissions (< 24 h), whereas 364 (75%) had long-stay admissions (> 24 h). Simple random sampling was used to select 85 children from each of the two groups. There were no differences between the two groups regarding language, primary care physician, asthma history, management prior to emergency department (ED) presentation, respiratory rate on presentation, use of the observation unit, and time in the ED. Logistic regression analyses identified three variables associated with short hospital stay: milder asthma (adjusted odds ratio [OR] 4.9), male gender (adjusted OR 2.4), and availability of a delivery device at home (adjusted OR 2.0). In conclusion, many children admitted to hospital because of an asthma exacerbation have short, yet expensive, hospital stays. The results of this study highlight the importance of developing alternative models of health care delivery for asthmatic children requiring short hospital contact.
- Devadason S.G. et al.** *Age-associated factors influencing the efficacy of various forms of aerosol therapy.* J Aerosol Med. 2002; 15(3) : 343-5.p
- Devereux G.** *The increase in allergic disease: environment and susceptibility. Proceedings of a symposium held at the Royal Society of Edinburgh, 4th June 2002.* Clin Exp Allergy. 2003; 33(3) : 394-406.p
- Devoy M.** *Use of inhaled corticosteroids in children.* Arch Dis Child. 2003; 88(5) : 461.p
- Dey A.N. et al.** *Summary health statistics for U.S. children: National Health Interview Survey, 2003.* Vital Health Stat 10. 2005; (223) : 1-78.p Abstract: OBJECTIVES: This report presents both age-adjusted and unadjusted statistics from the 2003 National Health Interview Survey (NHIS) on selected health measures for children under 18 years of age, classified by sex, age, race, Hispanic origin, family structure, parent's education, family income, poverty status, health insurance coverage, place of residence, region, and current health status. The topics covered are asthma, allergies, learning disability, Attention Deficit Hyperactivity Disorder (ADHD), use of prescription medication, respondent-assessed health status, school-loss days, usual place of health care, time since last contact with a health care professional, unmet dental needs, time since last dental contact, and selected measures of health care access. SOURCE OF DATA: The NHIS is a multistage probability sample survey conducted annually by interviewers of the U.S. Census Bureau for the Centers for Disease Control and Prevention's National Center for Health Statistics and is representative of the civilian noninstitutionalized population of the United States. Data are collected for all family members during face-to-face interviews with adults present at the time of interview. Additional information about children is collected for one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. SELECTED HIGHLIGHTS: In 2003, most U.S. children under 18 years of age had excellent or very good health (83%). However, 10% of children had no health insurance coverage, and 5% of children had no usual place of health care. Thirteen percent of children had ever been diagnosed with asthma. An estimated 8% of children 3-17 years of age had a learning disability, and an estimated 6% of children had ADHD.
- Dey A.N. et al.** *Summary health statistics for U.S. children: National Health Interview Survey, 2002.* Vital Health Stat 10. 2004; (221) : 1-78.p Abstract: OBJECTIVES: This report presents both age-adjusted and unadjusted statistics from the 2002 National Health Interview Survey on selected health measures for children under 18 years of age, classified by sex, age, race, Hispanic origin, family structure, parent's education, family income, poverty status, health insurance coverage, place of residence, region, and current health status. The topics covered are asthma, allergies, learning disability, Attention Deficit Hyperactivity Disorder (ADHD), use of prescription medication, respondent-assessed health status, school-loss days, usual place of health care, time since last contact with a health care professional, unmet dental needs, time since last dental contact, and selected measures of health care access. SOURCE OF DATA: The NHIS is a multistage probability sample survey conducted annually by interviewers of the U.S. Census Bureau for the Centers for Disease Control and Prevention's National Center for Health Statistics and is representative of the civilian noninstitutionalized population of the United States. Data are collected during face-to-face interviews with adults present at the time of interview. Information about children is collected for one randomly selected child per family in face-to-face interviews with an adult proxy respondent familiar with the child's health. SELECTED HIGHLIGHTS: In 2002, most U.S. children under 18 years of age had excellent or very good health (84%). However, 10% of children had no health insurance coverage, and 5% of children had no usual place of health care. Twelve percent of children had ever been diagnosed with asthma. An estimated 8% of children 3-17 years of age had a learning disability, and an estimated 7% of children had ADHD.
- Dhar S. et al.** *Correlation of the severity of atopic dermatitis with absolute eosinophil counts in peripheral blood and serum IgE levels.* Indian J Dermatol Venereol Leprol. 2005; 71(4) : 246-9.p Abstract: BACKGROUND: Although a number of epidemiological studies,

showing incidence and prevalence of atopic dermatitis, were available, scant attention has been paid to the correlation between the parameters of the disease like severity, absolute eosinophil count and IgE level, which has been known to be associated inconsistently. Hence this study was undertaken. **METHODS:** A total of 102 patients of atopic dermatitis, both children and adults, and 107 age matched controls were studied at the Pediatric Dermatology clinic, Institute of Child Health and department of Dermatology, AMRI-Apollo hospitals, Kolkata. **RESULTS:** The average age of onset of atopic dermatitis was observed to be 4.55 years. Both the average absolute eosinophil count and IgE levels in patients of atopic dermatitis were significantly higher than that of the controls. Each of these parameters showed significant correlation with severity of the disease and showed a nonhomogeneous distribution reflected by significant association with personal history of bronchial asthma and family history of atopy, when both parents were atopic. **CONCLUSIONS:** Our study shows that clinical activity of the disease as recorded by the "SCORAD" index can be used as an indicator of the hematological abnormalities as well as to some extent as a prognostic indicator. Family history of atopy correlates with the hematological abnormalities only if both parents are involved and bronchial asthma is the only associated atopic condition which correlates with the parameters of the disease .

Di Rienzo V. et al. *Long-lasting effect of sublingual immunotherapy in children with asthma due to house dust mite: a 10-year prospective study.* Clin Exp Allergy. 2003; 33(2) : 206-10.p **Abstract:** **BACKGROUND:** Subcutaneous immunotherapy for respiratory allergy has shown a long-lasting efficacy after its discontinuation, whereas this evidence is still lacking for sublingual immunotherapy, despite the fact that it is widely used. **OBJECTIVE:** We aimed to evaluate whether a long-lasting effect of SLIT occurs, in a prospective parallel group controlled study. **METHODS:** Sixty children (mean age 8.5 years) suffering from allergic asthma/rhinitis due to mites were subdivided into two matched groups: 35 underwent a 4- to 5-year course of SLIT with standardized extract and 25 received only drug therapy. The patients were evaluated at three time points (baseline, end of SLIT and 4 to 5 years after SLIT discontinuation) regarding presence of asthma, use of anti-asthma drugs, skin prick tests and specific IgE. **RESULTS:** We found that in the SLIT group there was a significant difference vs. baseline for the presence of asthma ($P \leq 0.001$) and the use of asthma medications ($P \leq 0.01$), whereas no difference was observed in the control group. The mean peak expiratory flow result was significantly higher in the active group than in the control group after 10 years. No change was seen as far as new sensitizations were concerned. Specific IgE showed a near-significant increase (baseline vs. 10 years, $P = 0.06$) only in the control group. **CONCLUSION:** Our study demonstrates that sublingual immunotherapy is effective in children and that it maintains the clinical efficacy for 4 to 5 years after discontinuation.

Dickinson A.R. et al. *Managing it: a mother's perspective of managing a pre-school child's acute asthma episode.* J Child Health Care. 2002; 6(1) : 7-18.p **Abstract:** Over the last decade asthma management strategies have required families to take increased responsibility for the assessment and treatment of their child's asthma. This exploratory descriptive study informed by grounded theory examines the experience of mothers in managing their pre-school child's acute asthma attack at home. The study reveals that mothers perceive that they are responsible for the management of their pre-school child during an acute asthma episode, a process they described as 'managing it'. This process involves mother in 'working on treatment', 'making the call', 'watching' and 'calming', while the husband/partner, family, friends and health professionals are 'supporting treatment'. This study suggests that nurses and doctors need to move away from the current paternalistic view of health care delivery in acute settings and embrace the concepts of support and partnership in the care of the pre-school child with asthma and their family.

Diez U. et al. *Redecoration of apartments promotes obstructive bronchitis in atopy risk infants--results of the LARS Study.* Int J Hyg Environ Health. 2003; 206(3) : 173-9.p **Abstract:** Findings by other authors indicate that exposure to chemical emissions from indoor paint is related to asthma symptoms in adults. In their first years of life children are receptive to obstructive airway diseases. The aim of this study was to investigate the influence of redecoration of the apartment on airway symptoms in infants during the first two years of life. The Leipzig Allergy Risk Children Study (LARS) is a birth cohort study with the following inclusion criteria: double positive family atopy anamnesis, cord blood IgE > 0.9 kU/l, or low birth weight between 1500-2500 g. Within the context of LARS, 186 parents of risk children completed a questionnaire on the respiratory symptoms of their children and the redecoration of their apartment at the end of the first and second year of life. A total 22% of the children suffered from obstructive bronchitis once or more during their first year, and 11% experienced this condition during their second year of life. Redecoration of the apartment had a significant influence on the appearance of obstructive bronchitis in the first (OR 4.1 95% CI 1.4-11.9) and in the second year of life (OR 4.2 95% CI 1.4-12.9). (The OR are adjusted for cord blood-IgE > 0.9 kU/l, birth weight < or = 2500 g, male sex and double positive parental atopy anamnesis, dampness, smoking or pet in the apartment). Simultaneous contamination from redecoration activities and additional exposures such as smoking, a pet or dampness in the apartment increased the risk for obstructive bronchitis in the first year (OR 9.1; 95% CI 2.3-34.8) as well as in the second year (OR 5.1; 95% CI 1.6-15.6). Our data suggest that redecoration of the apartment is associated with the development of acute inflammations, but not with a chronic influence on the airways in atopy risk infants. At an exposure to more than one environmental factor, pronounced effects were seen.

Dik N. et al. *Physician-diagnosed asthma and allergic rhinitis in Manitoba: 1985-1998.* Ann Allergy Asthma Immunol. 2006; 96(1) : 69-75.p **Abstract:** **BACKGROUND:** A worldwide increase has been noted in the prevalence of asthma, but the data for other allergic disorders are less consistent. **OBJECTIVE:** To study 14-year trends in utilization of physician resources for asthma and compare them to trends for allergic rhinitis. **METHODS:** We studied visits to physicians by Manitoba residents for asthma (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 493) and allergic rhinitis (ICD-9 code 477) between 1985 and 1998. Prevalence and incidence of physician resources utilization were calculated annually for the total population and by age groups. Aggregate statistics and frequency of physician resources utilization were also analyzed. **RESULTS:** The prevalence and incidence of physician resources utilization for asthma increased more than for allergic rhinitis; differences were most striking in the youngest age groups. In adults, the differences were smaller and changed little with time. Most of the increase in asthma care occurred in children and in people without allergic rhinitis. Overall, 17% of Manitobans were diagnosed as having asthma, and the average asthmatic patient made 6 visits. Approximately 14% had an allergic rhinitis diagnosis, each person being seen twice on average. Coexistence of asthma and allergic rhinitis led to increased physician resources utilization for each of the conditions. **CONCLUSIONS:** Trends in utilization of physician resources for allergic rhinitis differed strikingly from trends for asthma, particularly in the youngest age group. Asthma and allergic rhinitis affected comparable proportions of the population, but a diagnosis of asthma resulted in much higher utilization of physician resources. The relationship of physician-diagnosed asthma and atopy, as indicated by the diagnosis of allergic rhinitis, appears to have weakened with time in children but not in adults.

Dik N. et al. *Risk of physician-diagnosed asthma in the first 6 years of life.* Chest. 2004; 126(4) : 1147-53.p **Abstract:** OBJECTIVE: The objective of this cohort study was to determine if complications of pregnancy and labor, characteristics at birth, and exposure to infections influence the incidence of asthma in the first 6 years of life. DESIGN: We identified all children born between 1980 and 1990 in the Province of Manitoba, Canada. We used records of physician contacts (inpatient and outpatient) and services of the universal provincial health insurance plan to follow up 170,960 children from birth to the age of 6 years to identify the first diagnosis of asthma. Information on mothers and siblings was also obtained to determine family history of disease and exposure to infections. RESULTS: During the study period, a diagnosis of asthma was made in 14.1% of children by the age of 6 years. The incidence was higher in boys than in girls, in those with family history of allergic diseases. It was higher in urban than in rural areas, and lowest in those born in winter. Asthma was more likely in those with low birth weight and premature birth. Certain congenital abnormalities and complications of pregnancy and labor also increased the risk of asthma. The risk of asthma increased with maternal age. Both upper and lower respiratory infections increased the risk of subsequent asthma, and this effect was more important than exposure to familial respiratory infections, which also tended to increase asthma risk. The risk of asthma decreased with the number of siblings when siblings had a history of allergic disorders. CONCLUSIONS: In addition to genetic influences, intrauterine and labor conditions are determinants of asthma. Exposure to both upper and lower respiratory tract infections increases the risk; these infections do not explain the protective effect associated with the increasing number of siblings.

Dinakar C. et al. *Infants and toddlers without asthma with eczema have elevated exhaled nitric oxide levels.* J Allergy Clin Immunol. 2006; 117(1) : 212-3.p

Dinakar C. et al. *Real-life environmental tobacco exposure does not affect exhaled nitric oxide levels in asthmatic children.* J Asthma. 2005; 42(2) : 113-8.p **Abstract:** Serial measurement of exhaled nitric oxide (eNO) has been shown to be a good noninvasive marker of asthma control. Active smoking decreases eNO levels. The effect of real-life environmental exposure to tobacco smoke (ETS) on eNO levels is not known. Our objective was to study the impact of environmental tobacco exposure on eNO levels in asthmatic and non-asthmatic children. Single breath off-line collection of eNO was performed in asthmatic and non-asthmatic children with and without ETS. Urine was collected for cotinine/nicotine analysis. Fifty-seven children were enrolled, of which 25 were asthmatic and 32 had smoke exposure. One active smoker was excluded from the data analysis. The mean eNO was 11.1 ppb (n = 31; SD = 18.5) in those passively exposed vs. 11.1 ppb (n = 25; SD = 19.9) among the unexposed (not statistically significant). The mean eNO was 6.1 (n = 32; SD = 4.4) among the non-asthmatics and 17.8 (n = 24; SD = 27.4) among the asthmatics (p = 0.02; CI: 1.9-21.6). Real-life environmental tobacco exposure does not appear to decrease eNO levels in asthmatic children. Off-line collection of exhaled nitric oxide with a Mylar collection device helps differentiate asthmatics from non-asthmatics.

Dinelli D.L. et al. *Case management of asthma for family practice patients: a pilot study.* Mil Med. 2002; 167(3) : 231-4.p **Abstract:** OBJECTIVE: Asthma is a chronic inflammatory disease of the airways that affects between 14 and 15 million persons in the United States. It is responsible for more than 470,000 hospitalizations annually and an estimated \$6 billion in total medical cost. The Asthma Case Management Program instituted at our hospital is based on the concept of patient self-management. It involves patient education, a home treatment plan (HTP), and physician/nurse follow-up. This study was performed to determine whether an organized case management program improves outcomes and cost in family practice asthma patients. STUDY DESIGN: A prospective cohort

study of 48 asthmatic patients was conducted with a retrospective review. Data were obtained from health, pharmacy, and computer records. PATIENTS AND METHODS: Forty-eight asthma patients, ages 1 year to adult, assigned to the Family Practice Department were enrolled in the Asthma Case Management Program. This cohort was offered asthma education from a provider trained in national asthma guidelines. Most of these patients received a coordinated HTP completed by their primary care provider. The asthma case manager initiated regularly scheduled nursing follow-up. Hospital admissions, emergency department and clinic visits, number of chest radiographs, and use of beta 2 agonists and anti-inflammatory drugs were recorded for a mean of 6 months before and 6 months after the intervention. Twenty-eight patients who had received the HTP as part of their intervention were compared with 12 patients who did not. A cost analysis was completed. RESULTS: All measured parameters showed favorable changes after intervention. Statistically significant decreases in clinic visits, chest radiographs ordered, beta 2 agonists, and oral anti-inflammatory drugs were obtained with the 28 patients who received the HTP. Six-month resource savings after intervention were estimated at \$19,677.42 (\$491.90 per patient). Ninety-three percent of these savings are attributed to those patients with the HTP. There were no statistically significant improvements and considerably fewer savings for those patients not on the HTP. CONCLUSION: A combined intervention consisting of patient education, a coordinated self-monitoring plan, and patient follow-up was associated with improved care and economic outcomes in this group. The greatest clinical improvement and resource savings are clearly seen in those patients who have received the HTP as part of their asthma case management. Every effort should be made to include the HTP as the central part of asthma case management.

Dogru H. et al. *Asymptomatic IgE mediated food hypersensitivity in patients with nasal polyps.* Asian Pac J Allergy Immunol. 2003; 21(2) : 79-82.p **Abstract:** The aim of this prospective study is to compare the prevalence of atopy in patients afflicted by nasal polyps with the atopy prevalence in healthy volunteers without nasal polyps, since systemic allergy and allergy in the nasal mucosa are still being debated as underlying causes for nasal polyps. Thirty-four cases with nasal polyposis without asthma and history of allergy or atopic disease were enrolled in the study and compared with 20 healthy volunteer controls in respect to asymptomatic food hypersensitivity. Hypersensitivity for 48 kinds of commonly consumed food in Turkey was investigated by an epicutaneous prick test, Multi-Test II (Lincoln Diagnostic, Inc, USA), using a special applicator. The food allergy test was positive in 25 out of the 34 cases with nasal polyps and in 6 out of the 20 controls. The difference between the two groups was statistically significant ($\chi^2 = 0.000$, $p < 0.001$). The number of skin tests with positive results in patients with nasal polyps ranged from 1 to 37 (mean \pm S.D. = 10.0 \pm 7.9), whereas in the control subjects the range was 1 to 10 (mean \pm S.D. = 4.0 \pm 3.3). The difference in the number of food reactions was also statistically significant. Asymptomatic food hypersensitivity, being immunologically mediated, may be a triggering factor for the pathogenesis of nasal polyps. Therefore, treatment of asymptomatic food allergy in patients with nasal polyps may alleviate symptoms, slow the progress of nasal polyps and prolong the disease-free interval after polypectomy.

Dohar J.E. *All that drains is not infectious otorrhea.* Int J Pediatr Otorhinolaryngol. 2003; 67(4) : 417-20.p **Abstract:** It has been said that, 'All that wheezes is not asthma.' Thus, is also so of otorrhea. Bacterial infection most often causes otorrhea which, in turn, generally responds to treatment with ototopical antimicrobial therapy. When it persists, non-infectious etiologies must be considered. Although allergic causes of otorrhea have been described in the literature, inhaled environmental allergens (Type I Allergy) causing eustachian tube dysfunction or ototopical drops, most notoriously neomycin containing formulations, causing contact dermatitis are those usually mentioned. Further, most reports of contact allergic reactions of the ear have involved the external

auditory canal skin or pinna and have been attributed to non-medicinal triggers like shampoos and metals used in ear rings. A search of the literature failed to reveal a reported case of recurrent or chronic otorrhea without cholesteatoma due to an allergic reaction to the components of a tympanotomy tube (TT). Such a case is presented here.

Doherty S. *Evidence-based implementation of evidence-based guidelines.* Int J Health Care Qual Assur Inc Leadersh Health Serv. 2006; 19(1) : 32-41.p Abstract: PURPOSE: There is evidence that some strategies for guideline implementation are more successful than others. This paper aims to describe the process of developing an evidence-based guideline implementation strategy for use in rural emergency departments. DESIGN/METHODOLOGY/APPROACH: Participation in a nationally funded, research fellowship program involved attendance at workshops run by internationally renowned experts in the field of knowledge translation. Attendance at these workshops, associated reading and a literature review allowed those implementation strategies with the most supportive evidence of effectiveness to be determined. FINDINGS: A multi-faceted implementation strategy was developed. This strategy involved the use of an implementation team as well as addressing issues surrounding individual clinicians, the "emergency department team", the physical structure and processes of the ED and the culture of the department as a whole. Reminders, audit and feedback, education, the use of opinion leaders, and evidence-based formatting of guidelines were all integral to the process. PRACTICAL IMPLICATIONS: It is postulated that an evidence-based implementation strategy will lead to greater changes in clinician behaviour than other strategies used in quality improvement projects. ORIGINALITY/VALUE: This is an important article as it describes the concept and development of evidence-based interventions, which, if tailored to the individual hospital (as evidence-based medicine is tailored to the individual patient), has the potential to improve compliance with clinical guidelines beyond that achieved with most QI projects.

Dombkowski K.J. et al. *Pediatric asthma surveillance using Medicaid claims.* Public Health Rep. 2005; 120(5) : 515-24.p Abstract: OBJECTIVE: The purpose of this study was to describe the prevalence of asthma among children using alternative case definitions applied to administrative claims data, and to assess year-to-year classification concordance. METHODS: This study was a retrospective cohort analysis of 357,729 children 0-18 years using 2001-2002 Michigan Medicaid claims. Asthma cases were classified using six alternative definitions based on outpatient, emergency department, inpatient, and pharmacy claims for asthma, including the Health Plan Employer Data Information Set (HEDIS) persistent asthma criteria commonly used for assessments of asthma health care quality: at least one asthma inpatient admission or emergency department visit, four or more asthma medication events, or four asthma outpatient visits and two asthma medication events. RESULTS: Overall, asthma prevalence varied widely between alternative case definitions, ranging from 14.9% based on claims evidence of any type of asthma utilization to 3.7% when restricted to those with four or more asthma medication dispensing events. Among cases meeting HEDIS persistent asthma criteria in 2001, 55.5% met these criteria in 2002. Those with four or more asthma medication dispensing events had the best overall classification concordance between 2001 and 2002. Utilization of asthma services and prevalence estimates were highest among children younger than 5 years old, but year-to-year classification concordance was poorest among these cases ($p < 0.0001$), irrespective of case definition. CONCLUSIONS: While overall asthma prevalence may remain relatively stable from year to year, individuals may not be classified consistently as cases over time, regardless of case definition. Studies that identify asthma cases in one year and assess asthma outcomes in a subsequent year may introduce substantial bias as a result of case misclassification. Among the case definitions considered in this

study, our findings suggest that this bias is minimized among cases classified using the four or more asthma medication dispensing events criterion.

Donato L. et al. [*Viruses protect against asthma*]. Arch Pediatr. 2003; 10 Suppl 1 : 96s-97s.p

Donna M.M. et al. *Low birth weight: a possible risk factor also for liver diseases in adult life?* Med Hypotheses. 2003; 61(4) : 435-8.p Abstract: Birth weight is a popular topic, because it is precisely recorded, a major determinant of infant survival, associated with infant mortality, and health outcomes later in life. Low birth weight (LBW) is a predisposing factor for metabolic abnormalities such as atherosclerosis, renal disease, non-insulin diabetes mellitus, asthma, low IQ, hypertension, obesity, psychological distress. They have all been reported to be more common among those who were small at birth. Due to lack of studies suggesting a linkage between LBW and diseases of liver; evidences, which support the hypothesis on the creation of a link between LBW, an indicator of unfavourable intrauterine environment, and liver diseases emerging in the adult life, and possible direct associations of LBW with liver diseases, e.g., hepatitis, non-alcoholic fatty liver disease, cirrhosis, hepatoblastoma, or hepatocellular carcinoma were discussed. The associations between LBW and hepatitis vaccination as well as paediatric parental nutrition were also noted.

Dougherty J.P. *Asthma in school children: it's important to re recognize the seriousness of this disease.* Nasnewsletter. 2002; 17(2) : 6.p

Dougherty J.P. *Asthma is a serious disease...* Nasnewsletter. 2002; 17(6) : 6.p

Douglass J.A. et al. *Emergency treatment of asthma: how are we doing?* Intern Med J. 2003; 33(9-10) : 401-3.p

Dowdell E.B. *Grandmother caregivers and caregiver burden.* MCN Am J Matern Child Nurs. 2004; 29(5) : 299-304.p Abstract: PURPOSE: To describe the experience of grandmothers who are parenting their grandchildren, and determine the amount of caregiver burden felt by the grandmothers. STUDY DESIGN AND METHODS: This descriptive correlational study had a sample of 104 grandmothers, reporting on 249 custodial grandchildren. Grandmothers completed the Caregiver Reactions Assessment to determine perceived physical health, family support, financial status, and caregiver burden. RESULTS: Overall, grandmothers perceived the health of their grandchildren as excellent. Of the grandchildren who had been born prematurely (30%), the primary health problems were hyperactivity and asthma. Parental drug use was reported as the reason for child placement with the grandmother in 80% of the cases. The range of time grandchildren had been living with the grandmother was 6 months to 15 years. Low ratings of grandchild physical health correlated with low ratings of grandmother physical health, which correlated strongly with low levels of self-esteem, a strong perception of poor family support, and poor financial status, all of which represent measures of caregiver burden. CLINICAL IMPLICATIONS: This study demonstrated that the well being of the grandmother and grandchild are both linked to good physical health. Thus, indicators of poor health for both grandchild and grandmother must be identified early. Grandmothers in this study were surprised at how much had changed in every aspect of child health since they had raised their own children. Nurses working with grandmothers who have custody of grandchildren should understand the dynamics of the relationship, the possibility of caregiver burden, provide anticipatory guidance about the changes in child care and child healthcare in the 21st century, and help link grandmothers who have little support to community programs.

Drake A.J. et al. *Symptomatic adrenal insufficiency presenting with hypoglycaemia in children with asthma receiving high dose inhaled fluticasone propionate.* *BMJ.* 2002; 324(7345): 1081-2.p

Drblik S. et al. *Comparative efficacy of terbutaline sulphate delivered by Turbuhaler dry powder inhaler or pressurised metered dose inhaler with Nebuhaler spacer in children during an acute asthmatic episode.* *Arch Dis Child.* 2003; 88(4): 319-23.p **Abstract:** AIMS: To compare the efficacy of terbutaline sulphate delivered via Turbuhaler with a pressurised metered dose inhaler (pMDI) connected to Nebuhaler spacer in a population of asthmatic children presenting to emergency departments because of an acute episode of asthma. METHODS: Randomised double blind, double dummy, parallel study of acute asthma in the emergency department. A total of 112 children (6-16 years), who had a diagnosis of asthma, a baseline FEV1 of 25-60% of predicted normal value (PNV), and the ability to perform spirometry were studied. Patients received two doses of 0.5 mg/10 kg (maximum 2.0 mg) of terbutaline sulphate at time 0 minutes and time 30 minutes. The two groups were also stratified into subgroups based on FEV1: 25-45% and 45.1-60% PNV. FEV1 before treatment and at two 15-minute intervals after each treatment was the main outcome measure. PIF, PEF, heart rate, SpO2, and tremor were also measured at these times. RESULTS: Both the Turbuhaler and pMDI+Nebuhaler groups showed significant increases from baseline to final value in their FEV1 results, 49% and 50% change from baseline to t = 60 min, respectively (p < 0.001) using last value carried forward. No significant difference was found between the two groups for these results. Subanalysis of the stratified groups revealed similar results. In addition, no significant difference was found in the group and subgroup comparisons for heart rate, SpO2, and tremor. CONCLUSION: Results show that Turbuhaler and pMDI+Nebuhaler are similar in terms of benefit and side effects in the treatment of acute moderate to severe asthma attacks in this study population.

Dubus J.C. et al. *Local side-effects of inhaled corticosteroids in asthmatic children: influence of drug, dose, age, and device.* *Allergy.* 2001; 56(10): 944-8.p **Abstract:** BACKGROUND: The objective was to investigate the local side-effects of inhaled corticosteroids (ICS) in daily life in asthmatic children, particularly the younger ones, by an observational prospective cross-sectional cohort study. METHODS: Asthmatic children (n=639, 75.9+/-48.9 months, 61.3% boys), treated with beclomethasone dipropionate (BDP) (721.0+/-287.3 microg per day) or budesonide (BUD) (835.5+/-684.9 microg per day) for at least 1 month, were recruited at the time of a scheduled visit. Local side-effects were researched by questionnaire (cough during inhalation, hoarseness, dysphonia, and thirsty feeling) and clinical examination (perioral dermatitis, oral candidiasis, and tongue hypertrophy). RESULTS: Exactly 63.3% of the children aged under 6 years and 59.5% of the older ones reported one local side-effect. Cough (39.7%) was dependent on young age, use of BDP, and mainly use of spacer device, with an OR of 4.7 (95% CI: 2.7-8.2). Thirsty feeling (21.9%) and hoarseness (14.1%) occurred in children using ICS and long-acting beta2-agonists. Dysphonia (11.1%) was favored by high doses of BDP and BUD, and by inhalation from spacer devices or nebulizers. No factor favored oral candidiasis (10.7%). Perioral dermatitis (2.9%) and tongue hypertrophy (0.1%) were associated with nebulization. CONCLUSION: Local side-effects of ICS are common in asthmatic children of all ages, and the device used constitutes the most influential factor.

Dubus J.C. et al. *Cough after inhalation of corticosteroids delivered from spacer devices in children with asthma.* *Fundam Clin Pharmacol.* 2003; 17(5): 627-31.p **Abstract:** Children using a spacer device rather than another device for delivering inhaled corticosteroids (ICS) has been identified as a risk factor for cough immediately after inhalation. The aim of this study was to point out the different factors influencing the occurrence of such lateral side-effects. We studied this local side-effect in 402 asthmatic children (55.6 +/- 34.9 months;

65.6% boys) treated for at least 1 month with beclomethasone dipropionate (n = 331), budesonide (n = 47) or fluticasone propionate (n = 24) delivered from pressurized metered-dose inhalers and small (75.1%) or large volume (24.8%) spacer devices mainly used with face mask (90.7%). A total of 219 patients (54.5%), treated with either high doses of ICS or ICS and long-acting beta2-agonist, were considered as having severe asthma. Cough was reported after each inhalation of corticosteroids in 216 patients (53.7%). Among them, about 30% also complained of cough with beta2-agonists. Despite different propellants and dispersants, all corticosteroids induced cough similarly. Cough was not linked with asthma severity, but was significantly related to therapy duration and use of long-acting beta2-agonist. Type and volume of the spacer device, use of a face mask or mouthpiece were not influencing factors. Cough after inhalation of corticosteroids delivered from spacer devices is a frequent local side-effect in children with asthma. This side effect can greatly alter compliance. A practitioner must be sought at each visit.

Ducharme F.M. *Anti-leukotrienes as add-on therapy to inhaled glucocorticoids in patients with asthma: systematic review of current evidence.* *BMJ.* 2002; 324(7353): 1545.p **Abstract:** OBJECTIVES: To examine the evidence for the efficacy and glucocorticoid sparing effect of oral anti-leukotrienes taken daily as add-on therapy to inhaled glucocorticoids in patients with asthma. DESIGN: Systematic review of randomised controlled trials of children and adults with asthma comparing the addition of anti-leukotrienes or placebo to inhaled glucocorticoids. MAIN OUTCOME MEASURES: The rate of exacerbations of asthma requiring rescue systemic glucocorticoids when the intervention was compared to the same or double dose of inhaled glucocorticoids, and the glucocorticoid sparing effect when the intervention was aimed at tapering the glucocorticoid. RESULTS: Of 376 citations, 13 were included: 12 in adult patients and one in children. The addition of licensed doses of anti-leukotrienes to inhaled glucocorticoids resulted in a non-significant reduction in the risk of exacerbations requiring systemic steroids (two trials; relative risk 0.61, 95% confidence interval 0.36 to 1.05). No trials comparing the use of anti-leukotrienes with double the dose of inhaled glucocorticoids could be pooled. The use of anti-leukotrienes resulted in no overall group difference in the lowest achieved dose of inhaled glucocorticoids (three trials; weighted mean difference -44.43 microg/day, -147.87 to 59.02; random effect model) but was associated with a reduction in withdrawals owing to poor asthma control (four trials; relative risk 0.56, 0.35 to 0.89). CONCLUSIONS: The addition of anti-leukotrienes to inhaled glucocorticoids may modestly improve asthma control compared with inhaled glucocorticoids alone but this strategy cannot be recommended as a substitute for increasing the dose of inhaled glucocorticoids. The addition of anti-leukotrienes is possibly associated with superior asthma control after tapering of glucocorticoids, but the glucocorticoids sparing effect cannot be quantified at present.

Ducharme F.M. et al. *Safety profile of frequent short courses of oral glucocorticoids in acute pediatric asthma: impact on bone metabolism, bone density, and adrenal function.* *Pediatrics.* 2003; 111(2): 376-83.p **Abstract:** OBJECTIVE: Our study was designed to establish in children with asthma the safety profile of repeated short courses of oral glucocorticoids on bone mineralization and metabolism and adrenal function. METHODS: This cross-sectional study compared the bone density, bone metabolism, and adrenal function of children who were and were not exposed to bursts of oral glucocorticoids. Children were considered exposed when, in the preceding year, they received >or=2 courses of oral glucocorticoids and were prescribed the same therapy for the index exacerbation. Children were considered unexposed when they had no exposure to oral glucocorticoids and were not prescribed any for the index exacerbation. Indices of bone metabolism were measured during the subsequent month. Cortisol responses to adrenocorticotrophic hormone stimulation and bone density were assessed 30 days after

the index exacerbation. RESULTS: Eighty-three children (48 exposed, 35 unexposed) aged 2 to 17 years were enrolled. The median exposure level was 4 courses (range: 3-11) in the preceding year. Among exposed children, a transient decrease in serum osteocalcin was observed at the end of the 5-day course with a return to baseline by 30 days; no change was observed in urine pyridinoline cross-links. Mean bone density z score was similar in the exposed (-0.61 +/- 1.0 [standard deviation]) and unexposed (-0.67 +/- 0.9) groups. No cases of abnormal response to adrenocorticotropic hormone suggestive of adrenal insufficiency were documented in the exposed (95% confidence interval: 0%-7%) or unexposed (0%-10%) groups. CONCLUSIONS: Repeated short courses of oral glucocorticoids in the treatment of asthma seem to be reasonably safe; this practice was not associated with any lasting perturbation in bone metabolism, bone mineralization, or adrenal function.

Duetsch G. et al. *STAT6 as an asthma candidate gene: polymorphism-screening, association and haplotype analysis in a Caucasian sib-pair study.* Hum Mol Genet. 2002; 11(6) : 613-21.p **Abstract:** The human signal transducer and activator of transcription 6 (STAT6) gene represents one of the most promising candidate genes for asthma and other inflammatory diseases on the chromosomal region 12q13-q24. Therefore we screened all 23 exons, including parts of the neighbouring introns, as well as the promoter region for common polymorphisms and tested them for linkage/association with asthma and related traits (total serum IgE level, eosinophil cell count and SLOPE of the dose-response curve after bronchial challenge) in a Caucasian sib-pair study (108 families with at least two affected children). We could identify 13 single nucleotide polymorphisms (SNPs), which are all non-coding. A recently described dinucleotide (GT) repeat in exon 1 was also examined. Besides the confirmation of the four alleles described elsewhere we could identify a new one, named allele A5. Neither the SNPs nor the GT repeat showed linkage/association to asthma. Two intronic SNPs and one SNP in the 3'untranslated region of the gene showed weak association to total IgE levels (P = 0.0200, 0.0260 and 0.0280, respectively), whereas a significant association was found between a SNP in intron 18 and an increase in total IgE levels (P = 0.0070). However, the most promising effect was seen between allele A4 of the GT repeat polymorphism and an increase in eosinophil cell count (P = 0.0010). From these findings we conclude that the human STAT6 gene is rather involved in the development of eosinophilia and changes in total IgE levels than contributing to the pathogenesis of asthma.

Dufour X. et al. *Diffuse nasal polyposis and endonasal endoscopic surgery: long-term results, a 65-case study.* Laryngoscope. 2004; 114(11) : 1982-7.p **Abstract :** OBJECTIVE: To analyze the efficacy of a standardized surgical procedure in patients with nasal polyposis. STUDY DESIGN: Prospective study of nonrandomized cases from a single institution. METHODS: An inception cohort of 65 consecutive patients with nasal polyposis observed from January 1994 to December 1997. Presence of asthma, allergies, or aspirin intolerance, duration of nasal polyposis, previous surgery, and medical treatment were noted. Clinical symptoms were evaluated with a visual analogue scale (VAS), and a preoperative computed tomography scan was performed before the surgical procedure. At the end of the study, an evaluation was performed to collect all information concerning nasal symptoms, asthma conditions, quality of life, and patient's opinion about this type of surgery. RESULTS: Sixty patients have completed the study. Polyposis was isolated in 29 patients (group A), asthma was present in 21 patients (group B), and aspirin intolerance in 10 patients (group C). Nasal obstruction (n = 53/60, 88.3%) and olfactory disturbances (n = 54/56, 96.4%) were the main preoperative complaints, according to the VAS, with a high degree of severity. No significant difference for nasal symptomatology was found between the three groups. Nasal obstruction and olfactory dysfunction was improved in 37 and 42 patients, respectively, without a statistical significance between the groups. A reduction of the antiasthmatic treatment was observed in

24 of 31 patients. A massive and anteriorly localized recurrence was noted in 3 and 19 patients, respectively. CONCLUSIONS: Endoscopic sphenoidectomy is indicated for nasal polyposis refractory to intensive medical management with a good improvement of patient's quality of life.

Dugmore C.R. et al. *Asthma and tooth erosion. Is there an association?* Int J Paediatr Dent. 2003; 13(6) : 417-24.p **Abstract:** OBJECTIVES: To investigate whether there is an association between asthma and tooth erosion in a representative random sample of adolescents in the East Midlands. METHODS: A random sample of 1753 12-year-old children was examined in all schools in Leicestershire and Rutland. 1308 children were re-examined 2 years later. Tooth erosion was assessed using the index employed in the Children's Dental Health in the UK Survey 1993. Asthma presence was recorded on a self-completed questionnaire at the time of the 12 years examination. Data on asthma prescribing over a one year period was obtained from the Prescription Pricing Authority. RESULTS: Asthma was present in 16.8% of 12-year-olds. Tooth erosion was recorded in 59% of children with asthma and in 59.7% who were asthma free. There was no significant difference in erosion prevalence between asthmatics and asthma free in a cohort of children at age 12 or 14 years, and the incidence of erosion was 12.8% and 12.3%, respectively. 88% of drugs prescribed for treatment of asthma had a pH above the critical pH of 5.5. CONCLUSION: There was no association between asthma and tooth erosion. The majority of drugs prescribed for the treatment of asthma are not potentially erosive.

Duncan P. et al. *Use and misuse of aspirin in rural Ethiopia.* East Afr Med J. 2006; 83(1) : 31-6.p **Abstract:** OBJECTIVES: To investigate ability to distinguish simple analgesics, to document misconceptions about aspirin use, and to identify strategies to diminish potentially harmful aspirin use in Ethiopia. DESIGN: Qualitative study (eight focus group discussions) used to inform cross-sectional survey. SETTING: Butajira, a small town in southern Ethiopia, and surrounding rural areas. PARTICIPANTS: Purposively selected informants for focus groups; random sample of urban and rural residents for cross-sectional survey. MAIN OUTCOME MEASURES: Ability to distinguish aspirin from paracetamol; proportion using aspirin; proportion aware of common risks of aspirin. RESULTS: Questionnaires were completed by 204 of the 250 residents sampled (82% response). Three-quarters of survey participants knew the difference between aspirin and paracetamol. Aspirin was used by 7.3% of respondents, and was mainly taken for headache and fever. In focus group discussions there was a suggestion that aspirin was considered particularly useful for children. There was very low awareness of the risks of using aspirin in children (2.5% unprompted, 18.6% prompted) or in people with asthma (1% unprompted, 5.9% prompted). Aspirin is cheap and widely available in urban and rural areas. CONCLUSION: Awareness of the risks of aspirin use by children and in asthma is extremely low in this rural Ethiopian setting. Medications are purchased with minimal packaging by a population with low literacy. Drug dispensers and vendors must be trained to convey simple verbal warnings about aspirin use.

Dunlop K.A. et al. *Monitoring growth in asthmatic children treated with high dose inhaled glucocorticoids does not predict adrenal suppression.* Arch Dis Child. 2004; 89(8) : 713-6.p **Abstract:** AIMS: To determine whether routine outpatient monitoring of growth predicts adrenal suppression in prepubertal children treated with high dose inhaled glucocorticoid. METHODS: Observational study of 35 prepubertal children (aged 4-10 years) treated with at least 1000 microg/day of inhaled budesonide or equivalent potency glucocorticoid for at least six months. Main outcome measures were: changes in HtSDS over 6 and 12 month periods preceding adrenal function testing, and increment and peak cortisol after stimulation by

low dose tetracosactrin test. Adrenal suppression was defined as a peak cortisol $<$ or $=$ 500 nmol/l. RESULTS: The areas under the receiver operator characteristic curves for a decrease in HtSDS as a predictor of adrenal insufficiency 6 and 12 months prior to adrenal testing were 0.50 (SE 0.10) and 0.59 (SE 0.10). Prediction values of an HtSDS change of -0.5 for adrenal insufficiency at 12 months prior to testing were: sensitivity 13%, specificity 95%, and positive likelihood ratio of 2.4. Peak cortisol reached correlated poorly with change in HtSDS ($\rho = 0.23$, $p = 0.19$ at 6 months; $\rho = 0.33$, $p = 0.06$ at 12 months). CONCLUSIONS: Monitoring growth does not enable prediction of which children treated with high dose inhaled glucocorticoids are at risk of potentially serious adrenal suppression. Both growth and adrenal function should be monitored in patients on high dose inhaled glucocorticoids. Further research is required to determine the optimal frequency of monitoring adrenal function.

Dunn D.W. et al. *A prospective study of teachers' ratings of behavior problems in children with new-onset seizures.* *Epilepsy Behav.* 2003; 4(1) : 26-35.p **Abstract:** The purpose of this study was to explore the association between seizures and behavior problems in children with new-onset seizures using teachers' ratings of behavior. Subjects were 209 children with new-onset seizures and 93 children with asthma. Teacher ratings of behavior were collected prospectively over 24 months to determine differences between children with recurrent seizures, children without recurrent seizures, and children with asthma. During the 2-year period, 155 (74%) children had at least one recurring seizure. Data were analyzed using repeated-measures analysis of variance both with and without covariates. Controlling for covariates, children experiencing recurrent seizures had higher Total ($P=0.002$) and Internalizing ($P=0.018$) Behavior Problems scores across all times than those not experiencing recurrent seizures. Children with asthma were similar to children not experiencing recurrent seizures. The association between seizures and behavioral problems was supported using behavioral ratings from teachers.

Dunn D.W. et al. *Teacher assessment of behaviour in children with new-onset seizures.* *Seizure.* 2002; 11(3) : 169-75.p **Abstract:** RATIONALE: Recent data suggest that children with new-onset seizures may be at increased risk for behaviour problems. Teachers are an excellent source of data about such problems. They do not have the potential bias that a parent worried about a new onset of seizures might have and, furthermore, they are accustomed to comparing performance of children and work in an environment in which the behavioural problems associated with epilepsy may be quite evident. We obtained teachers' reports of behaviour problems in children in the 2 months prior to their first recognized seizure. We also obtained similar data on children with new-onset, moderate severity asthma. In addition to comparing behavioural scores between children with seizures and children with asthma, we compared teachers' assessments of behaviour in children with no prior seizures to those of children with previously unrecognized seizures. METHODS: We evaluated 192 children with new-onset seizures, including 129 children with no prior episodes and 63 children with recognized prior seizure-like episodes. The comparison group consisted of 78 children with new-onset, moderate severity asthma. Behaviour was assessed by the teacher's report form (TRF) of the child behaviour checklist (CBCL) or the caregiver-teacher report form for ages 2-5 (C-TRF). Mean scores were compared by two-sample t -tests and analysis of variance (ANOVA). RESULTS: The children with new-onset seizures had more thought problems than children with asthma. In comparison to children with no prior seizures, the children with prior unrecognized seizures had higher scores in total behaviour problems, internalizing problems, somatic complaints, anxious/depressed, thought problems, and attention problems. CONCLUSIONS: In this sample, children with prior unrecognized seizures were already at increased risk of teacher-rated behaviour problems before starting medication and before any possible stigma effects related to seizures. This sequence suggests

underlying neurological problems causing both behavioural problems and seizures.

Dunson D.B. et al. *Bayesian modeling of time-varying and waning exposure effects.* *Biometrics.* 2003; 59(1) : 83-91.p **Abstract:** In epidemiologic studies, there is often interest in assessing the association between exposure history and disease incidence. For many diseases, incidence may depend not only on cumulative exposure, but also on the ages at which exposure occurred. This article proposes a flexible Bayesian approach for modeling age-varying and waning exposure effects. The Cox model is generalized to allow the hazard of disease to depend on an integral, across the exposed ages, of a piecewise polynomial function of age, multiplied by an exponential decay term. Linearity properties of the model facilitate posterior computation via a Gibbs sampler, which generalizes previous algorithms for Cox regression with time-dependent covariates. The approach is illustrated by an application to the study of protective effects of breastfeeding on incidence of childhood asthma.

Dupont L.J. et al. *Prospective evaluation of the validity of exhaled nitric oxide for the diagnosis of asthma.* *Chest.* 2003; 123(3) : 751-6.p **Abstract:** STUDY OBJECTIVE: Exhaled nitric oxide (NO) levels are significantly elevated in patients with inflammatory airways disorders such as asthma, and the measurement of exhaled NO has been proposed as a noninvasive marker of airways inflammation. The aim of this study was to assess the accuracy of exhaled NO levels for the diagnosis of asthma. METHODS: Two hundred forty consecutive, nonsmoking, steroid-naive patients, who were referred to our outpatient clinic with symptoms suggestive of obstructive airways disease, were investigated. Asthma was diagnosed in 160 patients on the basis of the presence of significant airways reversibility ($\Delta FEV_1 > 12\%$ predicted) and/or airways hyperresponsiveness (provocative concentration of histamine causing a 20% fall in $FEV_1 < \text{or} = 8$ mg/mL). Prior to lung function measurements, exhaled NO was measured during a single-breath exhalation, according to European Respiratory Society and American Thoracic Society guidelines. RESULTS: The measurement of exhaled NO in our study population showed, at a cutoff level of 16 parts per billion, a specificity for the diagnosis of asthma of 90% and a positive predictive value of $> 90\%$. CONCLUSIONS: These findings suggest that the simple and absolutely noninvasive measurement of exhaled NO can be used as an additional diagnostic tool for the screening of patients with a suspected diagnosis of asthma.

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Ebbinghaus S. et al. *Asthma management by an inpatient asthma care team.* *Pediatr Nurs.* 2003; 29(3) : 177-83.p **Abstract:** Recent surveillance data indicates that asthma continues to be a major health problem affecting children and African Americans disproportionately in terms of prevalence, emergency department visits, and hospitalization rates (Centers for Disease Control [CDC], 2002). Death rates due to asthma also remain higher in African Americans as compared to Caucasians. At Children's Hospital of Michigan, the Inpatient Asthma Service manages the majority of children hospitalized for asthma. An allergy/asthma specialist and a pediatric nurse trained in asthma management (asthma nurse specialist [ANS]) direct this service, which provides standardized inpatient asthma management according to current asthma care guidelines and asthma education to patients and their families before discharge, encourages referrals to the outpatient allergy/asthma clinic for further asthma management and education, and addresses other medical or social needs related to asthma care. The positive outcomes measured were a

decreased length of hospital stay (LOS) by 12 hours per hospital admission and average cost savings of \$300,000 annually for the hospital. Other positive outcomes included improved patient and family understanding of asthma and improved coordination of care. The asthma nurse specialists have had the benefit of further developing their pediatric asthma assessment, teaching, and communication skills.

Eder W. et al. *Toll-like receptor 2 as a major gene for asthma in children of European farmers.* J Allergy Clin Immunol. 2004; 113(3) : 482-8.p **Abstract:** BACKGROUND: The finding that the prevalence of asthma and allergies is less frequent in children raised on animal farms has led to the conjecture that exposure to microbial products modifies immune responses. The toll-like receptors (TLRs) represent an evolutionarily conserved family of innate immunity receptors with microbial molecules as ligands. OBJECTIVES: We reasoned that polymorphisms in genes encoding TLRs might modulate the protective effects observed in farming populations. METHODS: Farmers' and nonfarmers' children living in rural areas in Austria and Germany and who were enrolled in the cross-sectional ALEX study were genotyped for single nucleotide polymorphisms in the TLR2 and TLR4 genes. The frequencies of asthma, allergic rhinitis, and atopic sensitization were compared between the genotypes in relation to exposure to farming and endotoxin. RESULTS: Among farmers' children, those carrying a T allele in TLR2-16934 compared with children with genotype AA were significantly less likely to have a diagnosis of asthma (3% vs 13%, P = .012), current asthma symptoms (3% vs 16%, P = .004), atopic sensitization (14% vs 27%, P = .023), and current hay fever symptoms (3% vs 14%, P = .01). The association between TLR2-16934 and asthma among children of farmers was independent of atopy. No such association was found among children from the same rural communities but not living on farms. CONCLUSION: Our results suggest that genetic variation in TLR2 is a major determinant of the susceptibility to asthma and allergies in children of farmers.

Edgren K.K. et al. *Community involvement in the conduct of a health education intervention and research project: Community Action Against Asthma.* Health Promot Pract. 2005; 6(3) : 263-9.p **Abstract:** There is a need for more guidance on how to implement community-based participatory research, particularly on the roles of community members, throughout the process. This article focuses on how a Steering Committee, composed of representatives from community-based organizations, a local health department, an integrated health care system, and academia from the University of Michigan, participated in the design and implementation of a children's asthma study in Detroit, Michigan: Community Action Against Asthma. In addition, this article focuses on the role of community members as data collectors, examining a variety of sophisticated data collection roles. A description and analysis of how community members shaped and participated in the project, the lessons learned, and recommendations for practitioners are also presented.

Edmonds M.L. et al. *Treatment with inhaled flunisolide.* Chest. 2004; 125(5) : 1961-2; author reply 1962-3.p

Edmondson D.A. et al. *Allergy and "toxic mold syndrome".* Ann Allergy Asthma Immunol. 2005; 94(2) : 234-9.p **Abstract:** BACKGROUND: "Toxic mold syndrome" is a controversial diagnosis associated with exposure to mold-contaminated environments. Molds are known to induce asthma and allergic rhinitis through IgE-mediated mechanisms, to cause hypersensitivity pneumonitis through other immune mechanisms, and to cause life-threatening primary and secondary infections in immunocompromised patients. Mold metabolites may be irritants and may be involved in "sick building syndrome." Patients with

environmental mold exposure have presented with atypical constitutional and systemic symptoms, associating those symptoms with the contaminated environment. OBJECTIVE: To characterize the clinical features and possible etiology of symptoms in patients with chief complaints related to mold exposure. METHODS: Review of patients presenting to an allergy and asthma center with the chief complaint of toxic mold exposure. Symptoms were recorded, and physical examinations, skin prick/puncture tests, and intracutaneous tests were performed. RESULTS: A total of 65 individuals aged 1 1/2 to 52 years were studied. Symptoms included rhinitis (62%), cough (52%), headache (34%), respiratory symptoms (34%), central nervous system symptoms (25%), and fatigue (23%). Physical examination revealed pale nasal mucosa, pharyngeal "cobblestoning," and rhinorrhea. Fifty-three percent (33/62) of the patients had skin reactions to molds. CONCLUSIONS: Mold-exposed patients can present with a variety of IgE- and non-IgE-mediated symptoms. Mycotoxins, irritation by spores, or metabolites may be culprits in non-IgE presentations; environmental assays have not been perfected. Symptoms attributable to the toxic effects of molds and not attributable to IgE or other immune mechanisms need further evaluation as to pathogenesis. Allergic, rather than toxic, responses seemed to be the major cause of symptoms in the studied group.

Edwards C.A. et al. *Relationship between birth weight and adult lung function: controlling for maternal factors.* Thorax. 2003; 58(12) : 1061-5.p **Abstract:** BACKGROUND: There is conflicting evidence on the "fetal origins hypothesis" of association between birth weight and adult lung function. This may be due to failure to control for confounding maternal factors influencing birth weight. In the present study access to birth details for adults aged 45-50 years who were documented as children to have asthma, wheezy bronchitis, or no respiratory symptoms provided an opportunity to investigate this association, controlling for maternal factors. METHODS: In 2001 the cohort was assessed for current lung function, smoking status, and respiratory symptoms. Birth details obtained from the Aberdeen Maternity and Neonatal Databank recorded birth weight, gestation, parity, and mother's age and height. RESULTS: 381 subjects aged 45-50 years were traced and tested for lung function; 323 (85%) had birth details available. A significant linear trend (p<0.01) was observed between birth weight and current forced expiratory volume in 1 second (FEV(1)) and forced vital capacity (FVC) values (adjusted for height, age, sex, weight, deprivation category (Depcat), childhood group, and smoking status). This trend remained significant after adjusting birth weight for gestation, parity, sex, mother's height and weight (p = 0.01). The relationship between birth weight and FEV(1) and FVC remained significant when adjusted for smoking history. There was no association between birth weight and current wheezing symptoms. CONCLUSION: There is a positive linear trend between birth weight, adjusted for maternal factors, and lung function in adulthood. The strength of this association supports the "fetal origins hypothesis" that impairment of fetal growth is a significant influence on adult lung function.

Edwards C.A. et al. *Wheezy bronchitis in childhood: a distinct clinical entity with lifelong significance?* Chest. 2003; 124(1) : 18-24.p **Abstract:** BACKGROUND: Historically, clinicians have recognized the existence of the clinical syndrome of childhood wheezy bronchitis. In the late 1960s, children with this syndrome were relabeled as having asthma, and the term wheezy bronchitis was abandoned. In a 1989 study of a cohort that originally had been studied in 1964, we reported that those who had childhood wheezy bronchitis had as adults attained lung function similar to that of healthy control subjects and had less significant symptoms than did those who had experienced childhood asthma, in whom lung function was reduced. In this study, we reexamined these subjects 12 years later to determine whether the improved outcome of the wheezy bronchitis group had been maintained. METHODS: In 2001, we followed up the 283 participants of the 1989 study, who were now

aged 45 to 50 years. In interviews, respiratory symptoms and smoking status were assessed. Spirometry was measured. RESULTS: One hundred seventy-seven subjects (63%) completed the study. After adjusting for age, height, gender, socioeconomic status, smoking status, and number of pack-years smoked, the current FEV(1) in the childhood asthma group (mean, 2.45 L; 95% confidence interval, 2.29 to 2.62) was significantly lower than the wheezy bronchitis group (2.78 L, 95% confidence interval, 2.64 to 2.91; $p < 0.01$) and the control group (2.96 L; 95% confidence interval, 2.83 to 3.1; $p < 0.01$). The difference between the wheezy bronchitis group and the control subjects was not significant ($p = 0.06$). Between 1989 and 2001, both the childhood wheezy bronchitis group ($p < 0.01$) and the childhood asthma group ($p = 0.01$) had greater declines in FEV(1) than did the control group (asthma group decline, - 0.75 L [95% confidence interval, - 0.66 to - 0.84]; wheezy bronchitis group decline, - 0.75 L [95% confidence interval, - 0.68 to - 0.83]; control group decline, - 0.59 L [95% confidence interval, - 0.52 to - 0.67]). In 2001, the asthma group had more symptoms than did the wheezy bronchitis group ($p < 0.01$), who were more symptomatic than the control group ($p < 0.01$). CONCLUSION: Those with childhood wheezy bronchitis, having achieved normal lung function in earlier adulthood, now show a more rapid decline in lung function than did control subjects. If this rate of decline persists, these subjects may develop obstructive airways disease in later life.

Edwards E. et al. *IgA deficiency: clinical correlates and responses to pneumococcal vaccine.* Clin Immunol. 2004; 111(1) : 93-7.p
Abstract: We surveyed historical and laboratory data for 127 IgA-deficient patients (ages 2-67), referred to an immunology clinic; the commonest medical history was recurrent respiratory infections (50%), followed by autoimmunity (28%) asthma and allergy (13%). Fifty-two subjects have been given a pneumococcal vaccination; vaccine responses to 12 serotypes were significantly related to serum IgG2 levels ($P = 0.004$). Six immunized IgA/IgG2-deficient subjects produced insignificant amounts of antibodies to these pneumococcal serotypes; 10 others with normal IgG2 levels also had subnormal vaccine responses. IgA-deficient patients who had at least one B8 allele ($n = 19$) had a significantly greater response to this vaccine than the HLA-B8-negative subjects ($n = 24$) ($P = 0.024$). There was no relationship between a history of recurring infections and pneumococcal vaccine responses; HLA status was not related to a history of autoimmunity.

Edwards E.A. et al. *Nitric oxide levels and ciliary beat frequency in indigenous New Zealand children.* Pediatr Pulmonol. 2005; 39(3) : 238-46.p
Abstract: New Zealand children's morbidity from respiratory disease is high. This study examines whether subclinical ciliary abnormalities underlie the increased prevalence of respiratory disease in indigenous New Zealand children. A prospective study enrolled a group of healthy children who were screened for respiratory disease by questionnaire and lung function. Skin-prick tests were performed to control for atopy. Exhaled and nasal NO was measured online by a single-breath technique using chemiluminescence. Ciliary specimens were obtained by nasal brushings for assessment of structure and function. The ciliary beat frequency (CBF) (median CBF, 12.5 Hz; range, 10.4-16.8 Hz) and NO values (median exhaled NO, 5.6 ppb; range, 2.3-87.7 ppb; median nasal NO, 403 ppb; range, 34-1,120 ppb) for healthy New Zealand European ($n=58$), Pacific Island ($n=61$), and Maori ($n=16$) children were comparable with levels reported internationally. No ethnic differences in NO, atopy, or CBF were demonstrated. Despite an apparently normal ciliary beat, the percentage of ciliary structural defects was 3 times higher than reported controls (9%; range, 3.6-31.3%), with no difference across ethnic groups. In conclusion, it is unlikely that subclinical ciliary abnormalities underlie the increased prevalence of respiratory disease in indigenous New Zealand children. The high percentage of secondary ciliary defects suggests ongoing environmental or infective damage.

Eggleston P.A. et al. *Lessons Learned for the Study of Childhood Asthma from the Centers for Children's Environmental Health and Disease Prevention Research.* Environ Health Perspect. 2005; 113(10) : 1430-6.p
Abstract: The National Children's Study will address, among other illnesses, the environmental causes of both incident asthma and exacerbations of asthma in children. Seven of the Centers for Children's Environmental Health and Disease Prevention Research (Children's Centers), funded by the National Institute of Environmental Health Sciences and the U.S. Environmental Protection Agency, conducted studies relating to asthma. The design of these studies was diverse and included cohorts, longitudinal studies of older children, and intervention trials involving asthmatic children. In addition to the general lessons provided regarding the conduct of clinical studies in both urban and rural populations, these studies provide important lessons regarding the successful conduct of community research addressing asthma. They demonstrate that it is necessary and feasible to conduct repeated evaluation of environmental exposures in the home to address environmental exposures relevant to asthma. The time and staff required were usually underestimated by the investigators, but through resourceful efforts, the studies were completed with a remarkably high completion rate. The definition of asthma and assessment of disease severity proved to be complex and required a combination of questionnaires, pulmonary function tests, and biologic samples for markers of immune response and disease activity. The definition of asthma was particularly problematic in younger children, who may exhibit typical asthma symptoms sporadically with respiratory infections without developing chronic asthma. Medications confounded the definition of asthma disease activity, and must be repeatedly and systematically estimated. Despite these many challenges, the Children's Centers successfully conducted long-term studies of asthma.

Eid N. et al. *Decreased morning serum cortisol levels in children with asthma treated with inhaled fluticasone propionate.* Pediatrics. 2002; 109(2) : 217-21.p
Abstract: OBJECTIVE: In an observational long-term study, we followed 62 children (37 males, 25 females; mean age: 11.6 +/- 2.9 years) with moderate-to-severe asthma for 2 years and studied the effects of fluticasone propionate (176-1320 microg/day) on the function of the hypothalamic-pituitary-adrenal axis. STUDY DESIGN: Morning cortisol levels were monitored after patients had been on fluticasone for a mean of 8.0 +/- 5.2 months. Patients who had abnormal low morning cortisol levels (<5.5 microg/dL) were then switched either to lower fluticasone dosage or to other inhaled steroid formulation. Exact methods based on the binomial distribution were used to construct a 95% confidence interval for the true proportion of abnormal readings among those treated, and the Wilcoxon signed rank test was used to test for a significant difference between cortisol levels taken before and after the switch. RESULTS: Twenty-two patients (36%) had abnormal morning cortisol levels while on fluticasone. Of the patients on a low dose (176 microg/day), 17% had abnormal values, whereas 43% of patients on a high dose (> or =880 microg/day) were abnormal. Patients with abnormal results (17/22) had their morning cortisol levels repeated 3 months after the switch. Thirteen of these patients (77%) had normal levels. A stratified analysis of the difference in morning cortisol levels before and after the switch showed significant increase in morning cortisol levels in the group receiving 440 microg/day or less of fluticasone (median difference: 5.25; confidence interval: 3.60-8.15), as well as in the group receiving 440 microg/day or more (median difference: 3.85; confidence interval: 1.00-7.60). CONCLUSION: Inhaled fluticasone, even at conventional doses, may have greater effects on the adrenal function than previously recognized, but the clinical significance of this suppression still remains to be established.

Eisner M.D. *Environmental tobacco smoke exposure and adult asthma.* Chest. 2002; 121(6) : 2084.p

Eisner M.D. et al. *Passive smoking, lung function, and public health.* Am J Respir Crit Care Med. 2006; 173(11) : 1184-5.p

Ekins-Daukes S. et al. *Burden of corticosteroids in children with asthma in primary care: retrospective observational study.* BMJ. 2002; 324(7350) : 1374.p

El-Mezayen R.E. et al. *In vitro responsiveness to IL-18 in combination with IL-12 or IL-2 by PBMC from patients with bronchial asthma and atopic dermatitis.* Clin Immunol. 2004; 111(1) : 61-8.p
Abstract: Interleukin (IL)-18 is a proinflammatory cytokine and is now recognized as an important regulator of both helper T cells (Th) 1 and 2 cytokine production. An increased IL-18 secretion has been reported in patients with allergic disorders. It is predominantly produced by activated macrophages, and synergizes with IL-12 and IL-2 to induce IFN-gamma synthesis, thereby promoting Th1 cytokine response. Paradoxically, IL-18, by itself, strongly induces immunoglobulin (Ig) E and allergic inflammation, indicating a role for IL-18 in promoting Th2 response. We investigated the inducing effect in vitro of combining IL-18 and IL-12 or IL-2 on Th1- and Th2-type cytokines production by peripheral blood mononuclear cells (PBMC) from patients with allergic diseases. PBMC derived from 44 allergic patients [23 bronchial asthma (BA) and 21 atopic dermatitis (AD)] and 20 healthy controls were cultured with IL-18 in the presence of phytohemagglutinin (PHA) and IL-12 or IL-2. The levels of IFN-gamma, IL-13, and IL-4 in the culture supernatants were measured using enzymatic immunoassaying. IFN-gamma production was detected in all cultures from nonallergic controls stimulated with IL-18 in the presence of IL-12; however, the results for five BA patients and five AD patients were under the detection limit for IFN-gamma. In collaboration with IL-2, IL-18 was able to induce IFN-gamma production by PBMCs from all nonallergic controls and all allergic patients, with the exception of one AD patient. Synergistic induction of IL-13 production was found in cultures with IL-18 + IL-2, and the IL-13 induction was significantly increased in BA patients when compared with that in nonallergic controls (P = 0.006). The stimulation by IL-18, even in combination with IL-2, failed to induce IL-4 production by PBMC from both nonallergic controls and allergic patients. Although the induction of IFN-gamma by IL-18 + IL-12 was impaired in around a quarter of the allergic patients, the impairment of the IFN-gamma production was completely restored by IL-2 in the presence of IL-18. Thus, IL-18 enhances IFN-gamma production through an IL-12-dependent pathway and exhibits synergism when combined with IL-2 in terms of enhanced IL-13 and IFN-gamma production, suggesting the involvement of IL-18/IL-12/IL-2 pathway in modulating Th1/Th2 cytokine response.

El-Mezzein R.E. et al. *Increased secretion of IL-18 in vitro by peripheral blood mononuclear cells of patients with bronchial asthma and atopic dermatitis.* Clin Exp Immunol. 2001; 126(2) : 193-8.p
Abstract: This study was performed to determine whether or not IL-18, formerly called IFN-gamma-inducing factor, is involved in the pathogenesis of allergic disorders. Peripheral blood mononuclear cells (PBMC) were obtained from patients with allergic bronchial asthma (BA), patients with atopic dermatitis (AD) and controls who did not have any allergic disease, and then cultured with lipopolysaccharide (LPS) or phytohaemagglutinin (PHA). The concentrations of IL-18, IFN-gamma and IL-13 in supernatant fluids were determined by enzymatic immunoassaying, and the expression of IFN-gamma messenger (m) RNA in the cells was measured by colorimetric microplate assaying. IL-18 secretion in the BA patients (geometric mean (gm) = 189 pg/ml) and AD patients (gm = 172 pg/ml) was significantly higher than that in non-allergic controls (gm = 118 pg/ml). In contrast, IFN-gamma secretion in the BA patients (gm = 7.3 IU/ml) and AD patients (gm = 6.8 IU/ml) was significantly lower than that in non-allergic controls (gm = 20.7 IU/ml). The amounts of IL-13 in supernatant fluids and IFN-gamma mRNA in cells were not statistically different among the BA patients, AD patients and non-allergic controls. The possible involvement of IL-18 in allergic disorders is discussed.

Eldeirawi K. et al. *Associations of place of birth with asthma and wheezing in Mexican American children.* J Allergy Clin Immunol. 2005; 116(1) : 42-8.p
Abstract: BACKGROUND: There are wide global variations in the prevalence of asthma and wheezing. OBJECTIVES: We examined the associations of place of birth with doctor-diagnosed asthma, wheezing in the past 12 months, and other allergic conditions in Mexican American children. METHODS: The study used data on 4121 Mexican American children age 2 months to 16 years who participated in the Third National Health and Nutrition Examination Survey. RESULTS: The risk of asthma was associated with being born in the United States after adjusting for sex, age, history of ear infection, and having a regular place for health care (odds ratio, 2.19; 95% CI, 1.09-4.40). Among children with no previous history of ear infection, US-born children were more likely to report wheezing in the past 12 months than their peers born in Mexico after controlling for confounding variables (odds ratio, 2.05; 95% CI, 1.09-3.87). Mexican American children born in the United States were more likely to have positive skin reaction to cat, house mite, *Alternaria alternata*, peanut, Bermuda grass, and short ragweed but were less likely to have a positive skin test to German cockroaches after adjusting for sex, age, ear infection, having a regular place for health care, and area of residence. CONCLUSION: Our study indicated significant associations of place of birth with respiratory symptoms and allergic conditions in Mexican American children. These findings highlight the need for further studies to examine environmental factors that change by migration and explain the observed differential in the risk of asthma or wheezing.

Eldeirawi K. et al. *History of ear infections and prevalence of asthma in a national sample of children aged 2 to 11 years: the Third National Health and Nutrition Examination Survey, 1988 to 1994.* Chest. 2004; 125(5) : 1685-92.p
Abstract: METHODS: We analyzed data on 7,538 children aged 2 to 11 years who participated in the Third National Health and Nutrition Examination Survey to examine the cross-sectional associations of history of ear infections with prevalence of ever-diagnosed asthma and the prevalence of wheezing in the last year in US children. RESULTS: History of ear infections was significantly related to the lifetime prevalence of diagnosed asthma (prevalence odds ratio [POR], 1.57; 95% confidence interval [CI], 1.05 to 2.36) and to the prevalence of wheezing in the last year (POR, 1.70; 95% CI, 1.22 to 2.37) after controlling for potential confounding variables. The number of ear infections was linearly and significantly related to the risk of asthma and wheezing in the last year. Among children with no diagnosis of asthma, there was a significant association between a history of ear infections and any wheezing in the last year (adjusted POR, 1.55; 95% CI, 1.07 to 2.25). CONCLUSIONS: Our study indicated strong and significant associations of a history of asthma and wheezing with the frequency of ear infections in a nationally representative sample of 7,538 children aged 2 to 11 years. These findings highlight the need for prospective studies to examine further the relationship between asthma and ear infections.

Elliott K. et al. *The -590C/T and -34C/T interleukin-4 promoter polymorphisms are not associated with atopic eczema in childhood.* J Allergy Clin Immunol. 2001; 108(2) : 285-7.p
Abstract: Susceptibility to the development of asthma and other atopic diseases is known to have a genetic component. To date, several studies have linked chromosome 5q31 to asthma and atopy in human beings. This region harbors a cluster of cytokine and growth factor genes, IL-4 presenting as a prime atopy candidate gene, inasmuch as it plays a pivotal role in the atopy pathway. Our approach was to identify polymorphisms within the promoter regions of IL-4 and test their association with atopic eczema. Polymorphisms were typed in a cohort of 76 small nuclear families and 25 triads with childhood atopic eczema. The genotypes were used to test for linkage in the presence of association with atopic eczema. A new polymorphism, -

34C/T, was identified and studied with a known polymorphism, -590C/T. On its own, each polymorphism showed no association with atopic eczema. The 2 polymorphisms were used to generate haplotypes, and a significant result was found for the -590C/-34C haplotype. However, after Bonferroni correction for multiple testing, the association became nonsignificant. Neither polymorphism predisposes to early-onset atopic eczema by itself, but suggestive linkage was found for the -590C/-34C haplotype in this study.

Ellison-Loschmann L. et al. *Time trends and seasonal patterns of asthma deaths and hospitalisations among Maori and non-Maori.* N Z Med J. 2002; 115(1146) : 6-9.p **Abstract:** AIM: To examine the time trends and seasonal patterns in asthma mortality and hospitalisations in Maori and non-Maori. METHODS: We studied asthma deaths in Maori and non-Maori during 1962-1998 and asthma hospitalisations during 1976-1998 in the 5-34 and 35-74 year age-groups. Average monthly mortality and hospital discharge rates were calculated for 1978-1998 to observe the seasonal patterns. RESULTS: The two asthma mortality epidemics of the 1960s and 1970s affected Maori disproportionately, with the peak rates in 1979 being twice that of non-Maori (7.4 vs 3.7 per 100 000) although the rates are now similar. Hospitalisation rates for Maori were consistently higher than non-Maori with the rates remaining elevated until 1987. The most recent hospitalisation figures show a fall of 61.2% from the 1987 rate. For Maori in the 5-34 year age-group, deaths were highest in spring while hospitalisations peaked in the winter month of May. CONCLUSION: Although asthma mortality and hospitalisation rates for Maori have declined over the period under study, Maori continue to experience more severe asthma and have a higher number of hospital admissions for asthma than non-Maori.

Engelsvold D.H. et al. *Hospital admissions for childhood asthma in Rogaland, Norway, from 1984 to 2000.* Acta Paediatr. 2003; 92(5) : 610-6.p **Abstract:** AIM: The prevalence of childhood asthma is increasing, and it is important to monitor factors related to hospital admissions in order to understand the different aspects of the disease. The aim of this study was to investigate admissions for childhood asthma to Rogaland Central Hospital, Norway, in order to elucidate time trends related to rates of admissions and treatment modalities. METHODS: A population-based study was conducted in which data extracted from the medical records, including number of admissions, length of hospitalization, medication and symptom scores, were recorded for children aged 1 to 14 y admitted to hospital for asthma during four periods, of two years each, from 1984/1985 to 1999/2000. RESULTS: For all the children there was an increase in annual admission rates for asthma from 1984/1985 to 1989/1990 and stabilization thereafter, but there were substantial differences between age groups. For children of 1 or 2 y of age the annual admission rate increased from 43/10000 in the first period to 104/10000 in the last period ($p < 0.001$), with an increase in both primary admissions and re-admissions. For children aged 3 and 4 y, the admission rates increased from the first to the second period, and then declined to an annual admission rate of 40/10000 in 1999/2000. For older children, the admission rate was low and stable. There was a gradual increase in the use of inhaled corticosteroids both prior to admission and at discharge, and the percentage of children receiving systemic corticosteroids at admission increased from 19% to 45% ($p < 0.001$). The average hospital in-days decreased from 3.4 to 1.9 ($p < 0.001$). CONCLUSION: A disturbingly high and increasing rate of both primary admissions and re-admissions for asthma has been observed in children aged 1 and 2 y, which seemed to be unaffected by changes in treatment modalities during the period. The decrease in admissions for children aged 3 and 4 y may have been influenced by the increased use of inhaled corticosteroids.

Enriquez F. *Defining asthma in the preschool-aged child.* Pediatrics. 2003; 112(5) : 1211-2; author reply 1211-2.p

Enriquez R. et al. *The relationship between vaccine refusal and self-report of atopic disease in children.* J Allergy Clin Immunol. 2005; 115(4) : 737-44.p **Abstract:** BACKGROUND: In the last 3 decades, there has been an unexplained increase in the prevalence of asthma and hay fever. OBJECTIVE: We sought to determine whether there is an association between childhood vaccination and atopic diseases, and we assessed the self-reported prevalence of atopic diseases in a population that included a large number of families not vaccinating their children. METHODS: Surveys were mailed to 2964 member households of the National Vaccine Information Center, which represents people concerned about vaccine safety, to ascertain vaccination and atopic disease status. RESULTS: The data included 515 never vaccinated, 423 partially vaccinated, and 239 completely vaccinated children. In multiple regression analyses there were significant ($P < .0005$) and dose-dependent negative relationships between vaccination refusal and self-reported asthma or hay fever only in children with no family history of the condition and, for asthma, in children with no exposure to antibiotics during infancy. Vaccination refusal was also significantly ($P < .005$) and negatively associated with self-reported eczema and current wheeze. A sensitivity analysis indicated that substantial biases would be required to overturn the observed associations. CONCLUSION: Parents who refuse vaccinations reported less asthma and allergies in their unvaccinated children. Although this relationship was independent of measured confounders, it could be due to differences in other unmeasured lifestyle factors or systematic bias. Further research is needed to verify these results and investigate which exposures are driving the associations between vaccination refusal and allergic disease. The known benefits of vaccination currently outweigh the unproved risk of allergic disease.

Epaud R. *[Severe asthma in children].* Arch Pediatr. 2003; 10(5) : 470-3.p

Ericson A. et al. *Hospital care utilization of infants born after IVF.* Hum Reprod. 2002; 17(4) : 929-32.p **Abstract:** BACKGROUND: Infants born after IVF are often twins, and singleton IVF babies have an increased risk for preterm birth. Both conditions are likely to increase morbidity. We examined the frequency and duration of hospitalization required by babies born after IVF, and compared this information with all infants born in Sweden during the same time period. METHODS: We used a nationwide registration of IVF pregnancies from 1984 to 1997 and a nationwide register of all in-patient care up to the end of 1998. We identified 9056 live born infants after IVF treatment and compared them with 1 417 166 non-IVF live born infants. RESULTS: The highest odds ratio (OR approximately 3) was seen for neonatal hospitalization, but an increased OR (1.2-1.3) was noted for children up to 6 years of age. The OR for being hospitalized after IVF was 1.8, but when the analysis was restricted to term infants it was 1.3 and this excess was then explainable by maternal subfertility. Statistically significant increased ORs were seen for hospitalization for cerebral palsy (1.7), epilepsy (1.5), congenital malformation (1.8) or tumour (1.6), but also for asthma (1.4) or any infection (1.4). When information from the Swedish Cancer Registry was used, no excess risk for childhood cancer was found. The average number of days spent in hospital by IVF and non-IVF children was 9.5 and 3.6 respectively. CONCLUSIONS: The increased hospitalization of IVF children is, to a large extent, due to the increased incidence of multiple births. Therefore, the increased costs associated with this may be reduced by the use of single embryo transfers, with the savings in health care costs being offset against the increased number of embryo transfer cycles required to maintain the pregnancy rate.

Ersu R. et al. *Prevalence of snoring and symptoms of sleep-disordered breathing in primary school children in Istanbul.* Chest. 2004; 126(1) : 19-24.p **Abstract:** STUDY OBJECTIVES: Snoring during sleep is an important manifestation of obstructive sleep apnea syndrome (OSAS). Although clinical history is not sufficiently

sensitive and specific to distinguish primary snoring from OSAS, snoring is indicative of upper airway obstruction and may be associated with the presence of diurnal symptoms. Our study aims were to determine the prevalence of snoring in primary school children in Istanbul, and to evaluate the diurnal symptoms and conditions that may be associated with sleep problems. DESIGN, SETTING, AND SUBJECTS: A parental questionnaire was used to assess the sleep and wake behavioral patterns in children. Eight representative schools in each of 9 school districts randomly selected from the 32 school districts in Istanbul were visited. RESULTS: The response rate was 78.1%; 2,147 of 2,746 questionnaires were fully completed, returned, and analyzed. The prevalence of habitual snoring was 7.0%. Habitual snorers had significantly more nighttime symptoms, such as observed apneas (odds ratio [OR], 16.9; 95% confidence interval [CI], 10.0 to 28.8; $p < 0.0001$), difficulty breathing (OR, 17.8; CI, 10.9 to 29.2; $p < 0.0001$), restless sleep, parasomnias, and nocturnal enuresis, compared to occasional and nonsnorers. There were also increased prevalence of daytime symptoms, such as falling asleep while watching television (OR, 1.8; CI, 0.9 to 3.7; $p = 0.01$) and in public places (OR, 2.1; CI, 1.2 to 3.8; $p = 0.03$), and hyperactivity (OR, 2.7; CI, 1.8 to 3.9; $p < 0.0001$). Exposure to cigarette smoke and the presence of asthma and hay fever increased the likelihood of habitual snoring. Children with a higher risk for OSAS (habitual snoring, apnea, and difficulty breathing during sleep) were also compared to nonsnorers. Although nighttime symptoms were more likely in the high-risk group, the risk of daytime symptoms increased as well. CONCLUSIONS: Habitual snoring is a significant problem for children and may be associated with diurnal symptoms. Exposure to cigarette smoke at home and the presence of asthma and hay fever increase the likelihood of habitual snoring.

Erwin E.A. et al. *Quantitative measurement of IgE antibodies to purified allergens using streptavidin linked to a high-capacity solid phase.* J Allergy Clin Immunol. 2005; 115(5) : 1029-35.p **Abstract:** BACKGROUND: Commercially available assays for IgE antibody provide results in international units per milliliter for many allergen extracts, but this is not easily achieved with purified or novel allergens. OBJECTIVE: To develop assays for IgE antibody suitable for purified or novel allergens by using a commercially available immunosorbent. METHODS: Streptavidin coupled to a high-capacity immunosorbent (CAP) was used to bind biotinylated purified allergens from mite (Der p 1 and Der p 2), cat (Fel d 1), and dog (Can f 1). Assays for IgE antibody to these allergens were performed on sera from children (asthma and control) as well as adults with atopic dermatitis. RESULTS: The results were validated by serial dilution of sera with high and low levels of IgE antibody and were quantitated in international units per milliliter by using a standard curve. Values for IgE antibody to Der p 1, Der p 2, and Fel d 1 correlated with values obtained with the allergen extracts ($r^2 = 0.80, 0.84, \text{ and } 0.95$, respectively; $P < .001$ in each case). Furthermore, the values for IgE antibody in sera from children with high exposure to mite and cat allergens demonstrated 10-fold higher levels of IgE antibody to Der p 1 and Der p 2 than to Fel d 1 ($P < .001$). CONCLUSION: The streptavidin immunosorbent technique provides a new method for quantifying IgE antibody to purified proteins. The results provide evidence about the high quantities of IgE antibody to purified inhalant allergens in patients with atopic dermatitis. In addition, the results demonstrate major differences in IgE antibodies specific for mite and cat allergens among children with high exposure to both allergens.

Esamai F. et al. *Prevalence of asthma, allergic rhinitis and dermatitis in primary school children in Uasin Gishu district, Kenya.* East Afr Med J. 2002; 79(10) : 514-8.p **Abstract:** OBJECTIVE: To establish the relative increase in the prevalence of asthma, allergic rhinitis and eczema in primary school children aged 13-14 years over a six year interval. DESIGN: Cross sectional comparative study. Setting: Primary schools in three rural divisions at Uasin Gishu

district in the Rift Valley Province of Kenya. METHODS: Three thousand two hundred and fifty eight children aged 13-14 years from seventy two primary schools in Uasin Gishu district were studied using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. All children in the selected schools in this age range whose parents gave consent were included. RESULTS: There were 47.4% males and 52.6% females as compared to 48.7% and 51.3% respectively in 1995. The cumulative prevalence for wheezing, rhinitis, itchy eyes and dermatitis was 23.6%, 43%, 24.1% and 28.5% respectively which were higher than for 1995 which were 21.2%, 32.4%, 11.8% and 13.8% respectively ($p = 0.001$). The period prevalence rates for wheezing, rhinitis and eczema were 13.8%, 31.4% and 21.3% respectively as compared to 10.2%, 25.3% and 14.4% respectively for 1995 ($p = 0.001$). The prevalence of asthma, allergic rhinitis and eczema was 12.6%, 38.6% and 28.5% respectively in 2001 compared to 6.6%, 14.9% and 13.9% respectively in 1995 ($p = 0.001$). CONCLUSION: There was a significant increase in the prevalence of asthma, allergic rhinitis and eczema in children in the study population over the last six years.

Evans D. et al. *Can children teach their parents about asthma?* Health Educ Behav. 2001; 28(4) : 500-11.p **Abstract:** The Open Airways for Schools (OAS) program has been shown to improve the self-management skills and health outcomes of students with asthma in Grades 3 to 5. This report examines the impact of OAS on students' parents. Because pilot studies showed that parental attendance at school-based sessions was low, the authors held six sessions at school for children and gave children homework assignments to complete with parents at home to teach parents about asthma and build support for children's self-management efforts. Analysis of 1-year follow-up data showed that children's participation in OAS was a significant predictor of parental self-management skills ($p < .03$) and that OAS children's communication was more strongly associated than controls' with parents' self-management ($p = .05$). The findings show that health education activities brought home from school by children can positively influence parents' self-management of a complex chronic disease such as asthma.

Evans D.M. et al. *Major quantitative trait locus for eosinophil count is located on chromosome 2q.* J Allergy Clin Immunol. 2004; 114(4) : 826-30.p **Abstract:** BACKGROUND: Eosinophils are granulocytic white blood cells implicated in asthma and atopic disease. The degree of eosinophilia in the blood of patients with asthma correlates with the severity of asthmatic symptoms. Quantitative trait loci (QTL) linkage analysis of eosinophil count may be a more powerful strategy of mapping genes involved in asthma than linkage analysis using affected relative pairs. OBJECTIVE: To identify QTLs responsible for variation in eosinophil count in adolescent twins. METHODS: We measured eosinophil count longitudinally in 738 pairs of twins at 12, 14, and 16 years of age. We typed 757 highly polymorphic microsatellite markers at an average spacing of approximately 5 centimorgans across the genome. We then used multipoint variance components linkage analysis to test for linkage between marker loci and eosinophil concentrations at each age across the genome. RESULTS: We found highly significant linkage on chromosome 2q33 in 12-year-old twins (logarithm of the odds=4.6; $P=.000002$) and suggestive evidence of linkage in the same region in 14-year-olds (logarithm of the odds=1.0; $P=.016$). We also found suggestive evidence of linkage at other areas of the genome, including regions on chromosomes 2, 3, 4, 8, 9, 11, 12, 17, 20, and 22. CONCLUSION: A QTL for eosinophil count is present on chromosome 2q33. This QTL might represent a gene involved in asthma pathophysiology.

Everden P. et al. *Cost-effectiveness of eformoterol Turbohaler versus salmeterol Accuhaler in children with symptomatic asthma.* Respir Med. 2002; 96(4) : 250-8.p **Abstract:** We conducted an economic evaluation in a UK setting based on a 12-week prospective

randomized open-label parallel-group comparison of eformoterol Turbohaler 12 microg b. i.d. with salmeterol Accuhaler 50 microg b. i.d. in children aged 6-17 with symptomatic asthma receiving inhaled corticosteroids and short-acting beta2-agonists. The principal effectiveness measure was percentage of symptom-free days with no short-acting beta2-agonist use during the study period. Asthma-related medication, unscheduled physician contacts and hospitalizations were collected prospectively and cost to the UK NHS calculated using year 2,000 prices. The economic evaluation included 73 patients in the eformoterol group and 72 patients in the salmeterol group. The mean age of patients was 11.6 years (eformoterol) and 11.8 years (salmeterol). The mean percentage of symptom-free days with no short-acting beta2-agonist use was 39% in the eformoterol group and 30% in the salmeterol group. Mean per patient daily cost was 1.15 pounds in the eformoterol group and 1.39 pounds in the salmeterol group. Both cost and effectiveness differences favoured eformoterol ($P < 0.05$; one-sided). Sensitivity analysis confirmed the results to be robust to changes in effectiveness, price and resource utilisation parameters. Eformoterol delivered by Turbohaler was found to be significantly more effective and less expensive than salmeterol Accuhaler in this study.

Eysink P.E. et al. *Accuracy of specific IgE in the prediction of asthma: development of a scoring formula for general practice.* Br J Gen Pract. 2005; 55(511) : 125-31.p Abstract: BACKGROUND: For the diagnosis of asthma in young children, GPs have to rely on history taking and physical examination, as spirometry is not possible. The additional diagnostic value of specific immunoglobulin E (IgE) to inhalent allergens remains unclear. AIM: To assess the predictive accuracy of specific IgE to cat, dog, and/or house dust mites in young children for the subsequent development of asthma at the age of 6 years. DESIGN OF STUDY: Prospective follow-up study. SETTING: Seventy-two general practices. METHOD: A total of 654 children, aged 1-4 years, visiting their GPs for persistent coughing (≥ 5 days), were tested for IgE antibodies by radio allergosorbent testing (RAST). Parents completed a questionnaire on potential risk indicators. Those children who showed an IgE-positive status (12.7%) and a random sample of those with an IgE-negative status (<0.5 U/ml) were followed up to the age of 6 years when the asthma status was established. The main outcome measure was asthma at the age of 6 years (combination of both symptoms and/or use of asthma medication, and impaired lung function). RESULTS: Addition of RAST results to a prediction model based on age, wheeze, and family history of pollen allergy increased the area under the receiver operating characteristic (ROC) curve from 0.76 to 0.87. Furthermore, RAST improved patient differentiation as indicated by a change in the range of asthma probabilities from 6-75% before the IgE test, to 1-95% after the IgE-test. CONCLUSION: Sensitisation to inhalant allergens in 1-4-year-olds, as shown by RAST, is a useful diagnostic indicator for the presence of asthma at the age of 6 years, even after a clinical history has been obtained. This model should preferably be validated in a new population before it can be applied in practice.

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Fabre Ortiz D. et al. *[Psychological factors contributing to asthma in asthmatic children and adolescents and their parents].* Rev Alerg Mex. 2005; 52(4) : 164-70.p Abstract: INTRODUCTION: Nowadays, psychosocial risk factors may contribute to asthma-related problems among children, adolescents and family members; such disorders are described in this article. METHODS: A descriptive study, which included 50 children and their parents who took part in the educational program of Hospital Pediatrico Universitario Juan Manuel Marquez from 1997 to 1999, was performed. A survey, designed to establish psychological factors in

children during both generally and symptom exacerbations, activities carried out with or without symptoms, and parental attitudes during illness episodes, was given to each one of the participants. Values were expressed in percentages. We used the Crosstabs to explore the relationships among variables. RESULTS: Anxiety, among other psychological stressors, prevailed in children (92%). Day-to-day activities were seriously affected in children with and without symptoms of illness: play 58%, exercise 60%. Children who received less parental support had severe persistent asthma, up to 20%. CONCLUSION: Symptoms severity is associated with child well-being and negative attitudes of parents.

Fadel R. *[Report of the Stallergenes symposium].* Allerg Immunol (Paris). 2004; 36(3) : 104.p

Fageras Bottcher M. et al. *A TLR4 polymorphism is associated with asthma and reduced lipopolysaccharide-induced interleukin-12(p70) responses in Swedish children.* J Allergy Clin Immunol. 2004; 114(3) : 561-7.p Abstract: BACKGROUND: Bacterial signals play an important role in the maturation of the immune system. Polymorphisms in genes coding for receptors to bacterial components can alter the immune responsiveness of the host to microbial agents and may indicate the development of aberrant immune responses that are associated with immune-mediated diseases such as atopic diseases. OBJECTIVE: The study's objective was to investigate the relationship between TLR4 and CD14 gene polymorphisms, the LPS responsiveness of PBMCs, and the presence of asthma and allergic rhinoconjunctivitis in children. METHODS: The TLR4 (Asp299Gly) and CD14/-159 polymorphisms were determined in 115 Swedish children aged 8 and 14 years. LPS-induced IL-12(p70), IL-10, and IFN-gamma responses of PBMCs from 69 of the children were analyzed by means of ELISA. The levels of soluble CD14 in serum samples were analyzed by means of ELISA, and the total IgE levels were analyzed by means of UNICAP Total IgE (Pharmacia Diagnostics, Uppsala, Sweden). RESULTS: Decreased LPS-induced IL-12(p70) and IL-10 responses were associated with the TLR4 (Asp299Gly) polymorphism and independently with asthma, especially atopic asthma. The TLR4 (Asp299Gly) polymorphism was associated with a 4-fold higher prevalence of asthma in school-aged children (adjusted odds ratio 4.5, 95% CI 1.1-17.4) but not to allergic rhinoconjunctivitis. CONCLUSION: A TLR4 polymorphism modifies innate immune responses in children and may be an important determinant for the development of asthma. This may influence the outcome of intervention studies that use microbial stimuli as immune modulators.

Fan R. et al. *Linkage and association studies of QTL for nuclear families by mixed models.* Biostatistics. 2003; 4(1) : 75-95.p Abstract: The transmission disequilibrium test (TDT) has been utilized to test the linkage and association between a genetic trait locus and a marker. Spielman et al. (1993) introduced TDT to test linkage between a qualitative trait and a marker in the presence of association. In the presence of linkage, TDT can be applied to test for association for fine mapping (Martin et al., 1997; Spielman and Ewens, 1996). In recent years, extensive research has been carried out on the TDT between a quantitative trait and a marker locus (Allison, 1997; Fan et al., 2002; George et al., 1999; Rabinowitz, 1997; Xiong et al., 1998; Zhu and Elston, 2000, 2001). The original TDT for both qualitative and quantitative traits requires unrelated offspring of heterozygous parents for analysis, and much research has been carried out to extend it to fit for different settings. For nuclear families with multiple offspring, one approach is to treat each child independently for analysis. Obviously, this may not be a valid method since offspring of one family are related to each other. Another approach is to select one offspring randomly from each family for analysis. However, with this method much information may be lost. Martin et al. (1997, 2000) constructed useful statistical tests to analyse the data for qualitative traits. In this paper, we propose to use mixed models

to analyse sample data of nuclear families with multiple offspring for quantitative traits according to the models in Amos (1994). The method uses data of all offspring by taking into account their trait mean and variance-covariance structures, which contain all the effects of major gene locus, polygenic loci and environment. A test statistic based on mixed models is shown to be more powerful than the test statistic proposed by George et al. (1999) under moderate disequilibrium for nuclear families. Moreover, it has higher power than the TDT statistic which is constructed by randomly choosing a single offspring from each nuclear family.

Farchi S. et al. *Dietary factors associated with wheezing and allergic rhinitis in children.* Eur Respir J. 2003; 22(5) : 772-80.p **Abstract:** The effect of dietary factors on asthma is controversial. This study examined food consumption and the use of fats in relation to wheezing and allergic rhinitis in children. Baseline questionnaire data on individual and family characteristics were recorded by parents of 5,257 children aged 6-7 yrs living in central Italy participating in the International Study on Asthma and Allergies in Childhood study. A total of 4,104 children (78.1%) were reinvestigated after 1 yr using a second parental questionnaire to record occurrence of respiratory symptoms over the intervening 12 months. Consumption of foods rich in antioxidants, such as vitamins C and E, animal fats, and food containing omega-3 fatty acids were investigated using a food-frequency questionnaire. Frequency of use of fats was also evaluated. Wheezing, shortness of breath with wheeze, and symptoms of allergic rhinitis in the past 12 months were considered. Intake of cooked vegetables, tomatoes, and fruit were protective factors for any wheeze in the last 12 months and shortness of breath with wheeze. Consumption of citrus fruit had a protective role for shortness of breath with wheeze. Consumption of bread and margarine was associated with an increased risk of wheeze, while bread and butter was associated with shortness of breath with wheeze. Dietary antioxidants in vegetables may reduce wheezing symptoms in childhood, whereas both butter and margarine may increase the occurrence of such symptoms.

Fasce L. et al. *"Early" cat ownership and the risk of sensitization and allergic rhinitis in Ligurian children with respiratory symptoms.* Ann Allergy Asthma Immunol. 2005; 94(5) : 561-5.p **Abstract:** **BACKGROUND:** Studies on the role of cat ownership in the development of allergy have lead to conflicting results, probably owing to heterogeneity of the populations evaluated. **OBJECTIVE:** To evaluate the possible effect of cat ownership on the frequency of sensitization and asthma or rhinitis in children living in Liguria, Italy, who attended a pediatric clinic for respiratory symptoms. **METHODS:** We enrolled 269 consecutive school-aged children in 12 months. Sensitization to aeroallergens by skin prick testing and the presence of respiratory symptoms (ie, asthma and rhinitis) were evaluated. To analyze the role of different independent variables in association with respiratory symptoms and sensitization, a multiple logistic regression analysis was performed. **RESULTS:** Of 269 children, 81 were exposed to cats at home in the first 2 years of life ("early" cat owners), 65 after the first 2 years of life ("late" cat owners), and 123 never ("never" cat owners). Early cat ownership was significantly associated with a lower risk of cat sensitization compared with never cat ownership (adjusted odds ratio [ORadj], 0.32; 95% confidence interval [CI], 0.14-0.74; P = .01). Early cat ownership was also associated with a significantly lower risk of allergic rhinitis than late cat ownership (ORadj, 0.43; 95% CI, 0.22-0.85) or never cat ownership (ORadj, 0.51; 95% CI, 0.28-0.92). No differences in the frequency of asthma were found among the 3 groups (P = .74) **CONCLUSIONS:** Cat ownership in early childhood can play an important role in preventing sensitization to cat and in lowering the frequency of allergic rhinitis, at least in children with the characteristics of the population studied.

Feenstra T.L. et al. *Cost effectiveness of guideline advice for children with asthma: a literature review.* Pediatr Pulmonol. 2002; 34(6) : 442-54.p **Abstract:** Asthma is an important chronic disease among children. This study reviews the cost effectiveness of interventions in the long-term care of asthmatic children and compares these results with treatment advice in four current guidelines. Cost-effectiveness studies were searched for in Medline, Embase, Healthstar, Biosis, and the Office of Health Economics-Health Economic Evaluations Database (OHE-HEED), and the Cochrane Library was searched for meta-analyses of clinical trials. In the four reviewed guidelines, cost effectiveness is not explicitly used as a criterion. The cost-effectiveness studies show sufficient evidence for the cost effectiveness of treatment with inhaled steroids and for self-management programs for severe asthmatic patients. Inclusion of these results in the guidelines would not lead to significant changes in current treatment advice. The effectiveness of various measures for trigger avoidance is not fully proven, and hence neither is their cost effectiveness. Available information on the cost effectiveness of cromolyn could be used to focus the guidelines. Finally, evidence exists that organizational interventions, e.g., the employment of asthma nurses, can result in cost savings, but it is unclear to what extent these results can be generalized. More cost-effectiveness studies are needed, especially on long-acting bronchodilators and self-management programs for mild and moderate asthma, in order to help make the guidelines more informative and reduce the differences between them.

Feleszko W. et al. *Parental tobacco smoking is associated with augmented IL-13 secretion in children with allergic asthma.* J Allergy Clin Immunol. 2006; 117(1) : 97-102.p **Abstract:** **BACKGROUND:** Exposure to environmental tobacco smoke (ETS) has been shown to increase symptoms of allergic bronchial asthma, but direct effects on the expression of inflammatory markers have not been demonstrated thus far. **OBJECTIVE:** The aim of this study was to assess the correlation of ETS exposure with the expression of proinflammatory mediators in airway secretions, including IFN-gamma and IL-12, as well as IL-5 and IL-13, in allergic asthmatic schoolchildren and healthy control subjects. **METHODS:** By using the nasopharyngeal aspiration technique, airway secretions were collected from 24 atopic children with asthma (age, 6-16 years) and 26 healthy control subjects, and the concentration of cytokines was measured with immunoenzymatic methods. **RESULTS:** IL-13 levels were highly increased in patients with asthma (P < .005), and parental tobacco smoke resulted in a significant increase in airway IL-13 secretion in these children compared with that seen in nonexposed children and healthy control subjects (median, 860 pg/mL vs 242 pg/mL and 125 pg/mL, respectively). Furthermore, a positive correlation between IL-13 levels and serum IgE concentrations (r(s) = 0.55) was found in children with allergic asthma. **CONCLUSIONS:** These results indicate that ETS augments the expression and secretion of IL-13 in allergic asthma and that nasopharyngeal aspiration is a suitable method to assess cytokine measurements in airways in children. Measurements of IL-13 in secretions might be taken into account as a noninvasive marker of airway inflammation and to assess the detrimental effects of ETS.

Felix-Toledo R. et al. *Allergy to sea fishing baits.* J Investig Allergol Clin Immunol. 2005; 15(3) : 216-8.p **Abstract:** We report a new case of rhinitis and asthma caused by sea fishing baits. The results showed exposure to *Sipunculus nudus* (Phylum Sipuncula; order Sipunculida: Sipunculidae) to be the main cause of the allergic symptoms. The intervention of IgE was demonstrated, with the presence of cross-reactions with allergenic extracts from other worm species used as baits, belonging to different orders of Annelida.

Feng Y. et al. *G protein-coupled receptor 154 gene polymorphism is associated with airway hyperresponsiveness to methacholine in a Chinese population.* J Allergy Clin Immunol. 2006; 117(3) : 612-

7.p **Abstract:** BACKGROUND: A new asthma susceptibility gene, the G protein-coupled receptor for asthma susceptibility (GPR154), has recently been identified and the association was replicated in 2 white populations, but not in a Korean population. OBJECTIVE: To test the association between GPR154 gene polymorphisms and airway responsiveness to methacholine in a Chinese population. METHODS: Eight single nucleotide polymorphisms (SNPs) in the GPR154 gene were genotyped in 451 cases and 232 controls in stage I. The association of 1 SNP, rs324981, was tested in an additional 264 case and 241 control subjects in stage II. Both single marker and haplotype associations were tested. RESULTS: In stage I, we found that airway hyperresponsiveness to methacholine was associated with 2 single SNPs, rs324981 and rs324987, but not with the haplotypes of GPR154. The minor allele homozygotes of rs324981 (AA) and rs324987 (TT) were at a significantly lower risk of hyperresponsiveness to methacholine with odds ratios of 0.59 (P=.02) and 0.56 (P=.01), respectively. In stage II, we found a similar trend of association between rs324981 and airway hyperresponsiveness (P=.09). In the pooled analysis, the odds ratio of the AA homozygote of rs324981 was 0.61 (P=.004). The permutation test resulted in a study-wide empirical P value of .023, which meant that the association remained significant after adjustment for multiple tests. CONCLUSIONS: Our study supports a role of the GPR154 gene in asthma susceptibility and suggests that the AA homozygote of rs324981 is a protective factor for airway hyperresponsiveness to methacholine in a Chinese population. CLINICAL IMPLICATIONS: Our findings confirmed a role of GPR154 in the genetic susceptibility of asthma and suggest that GPR154 polymorphism should be taken into consideration to improve the assessment of an individual's risk of asthma.

Fernandes J. et al. *Immunoglobulin E antibody reactivity to the major shrimp allergen, tropomyosin, in unexposed Orthodox Jews.* Clin Exp Allergy. 2003; 33(7) : 956-61.p **Abstract:** BACKGROUND: Assessment of allergic (IgE antibody-mediated) reactions to foods may become complicated by cross-reactivity that can occur among certain food families and between foods and seemingly unrelated allergens. OBJECTIVE: The allergenic properties of tropomyosin (muscle-derived protein) have been recently demonstrated in invertebrates such as cockroaches, dust mites, and shrimp. In view of a possible cross-reactivity between food allergens and related allergens from animal sources, we designed a study to assess IgE antibody reactivity to the major shrimp allergen, Pen a 1, in an unexposed population of Orthodox Jews, who observe Kosher dietary laws that prohibit eating shellfish. METHODS: Nine subjects, who reacted positively by skin tests to shrimp (*Penaeus setiferus*), were selected for the study. Subjects (two females, seven males) ranged in age from 14 to 32 years (mean 20.4). All subjects were strictly observant of Jewish tradition and had no prior exposure to seafood (regarded as a non-Kosher food). Serum was obtained from all the subjects and tested for IgE antibody reactivity to shrimp and dust mite. RESULTS: All subjects reported symptoms of perennial allergic rhinitis, five had history of asthma, atopic dermatitis, and/or sinusitis. All had positive skin prick tests to shrimp and house dust mite (HDM) (*Dermatophagoides farinae*, *D. pteronyssinus*, or both); 2/7 subjects were positive to cockroach mix (*Blattella germanica* and *Periplaneta americana*). Sera of 4/9 subjects demonstrated specific IgE antibodies by RAST to shrimp (7.0-20.0%), 3/9 to Pen a 1 (6.3-24.1%), and 3/9 to shrimp or Pen a 1 by immunoblot. IgE binding to Pen a 1 was inhibited with either mite or cockroach extracts as demonstrated by RAST and/or immunoblot inhibition analysis. CONCLUSIONS: These studies indicate that IgE antibody reactivity to a major food allergen, shrimp, can occur in an unexposed population of individuals; some subjects allergic to HDM and/or cockroach show substantial IgE antibody reactivity to the major shrimp allergen Pen a 1 (tropomyosin). Based on inhibition with cockroach and/or dust mite extracts, this reactivity appears to be due to cross-reacting tropomyosins.

Fernandez-Caldas E. et al. *House dust mite, cat, and cockroach allergen concentrations in daycare centers in Tampa, Florida.* Ann Allergy Asthma Immunol. 2001; 87(3) : 196-200.p **Abstract:** BACKGROUND: Allergen exposure in early childhood is a risk factor for sensitization and the development of asthma. Studies performed in Europe, New Zealand, and Singapore indicated the presence of indoor allergens in childcare centers and schools. However, the importance of indoor allergens in daycare centers in humid and warm regions of the world is not known. OBJECTIVE: To measure total mite counts, Der p 1, Der f 1, Fel d 1, and Per a 1 allergens in dust samples and mite allergen airborne concentrations in daycare centers in Tampa, Florida, United States. METHODS: Twenty daycare centers were surveyed for mite, cat, and cockroach allergens in Tampa, FL. One dust and two air samples (one during the day and one during the night) were collected in each center. Dust samples were extracted and analyzed for mite (Der p 1 and Der f 1), cat (Fel d 1), and cockroach (Per a 1) allergens. Mite airborne concentrations were analyzed by RAST inhibition and expressed in standardized mite allergen units per m³ of air (AU/m³). RESULTS: Mites were identified in 15 samples, and concentrations ranged from 10 to 1,200 mites/g (298 +/- 355.2). The most prevalent mite species was *Dermatophagoides pteronyssinus* (Der p 1). Der p 1 and/or Der f 1 were detected in 10 daycare centers. Der p 1 was detected in eight centers and ranged from 1 to 21.8 microg/g of dust (5.4 +/- 6.9); Der f 1 was detected in 3 centers and ranged from 0.2 to 2.1 microg/g of dust (1.3 +/- 0.9). Per a 1 and Fel d 1 were detected in all centers in small quantities; Per a 1 ranged from 8 to 1,806 ng/g (263.1 +/- 449.7) and Fel d 1 from 0.2 to 120 U/g of dust (16.6 +/- 31.7), respectively. Airborne mite allergen was detected in 18 centers and ranged from 0.01 to 2.7 AU/m³ during the day (0.2 +/- 0.6) and from 0.01 to 0.12 AU/m³ during the night (0.06 +/- 0.03), P = 0.001. CONCLUSIONS: Mite, cat, and cockroach allergens are present in daycare centers in Tampa, FL. Mite allergen concentrations exceeded levels that have been associated with sensitization and symptoms in allergic subjects in 40% of these centers.

Ferrer A. et al. *Occupational allergic rhinoconjunctivitis and asthma to goat and cross-reactivity with cow epithelium.* Ann Allergy Asthma Immunol. 2006; 96(4) : 579-85.p **Abstract:** BACKGROUND: The development of sensitization and symptoms after the inhalation of epithelial allergens is common. OBJECTIVES: To investigate the allergic response (in vivo and in vitro) of 3 individuals clinically sensitive and occupationally exposed to cow and goat and to evaluate the allergenic cross-reactivity between cow and goat epithelium extracts. METHODS: Three patients--a butcher and 2 doctors in veterinary medicine--were evaluated. These patients reported allergic respiratory symptoms after occupational exposure to goats and cows. Extracts were prepared from epithelia of both animals. All the patients underwent organ-specific allergen challenges with cow and goat extracts. Four nasal and 2 bronchial challenges were conducted following standardized procedures. RESULTS: All 3 patients had positive challenge results with the offending allergen extract. Specific IgE to goat allergens was detected in all patients. Several IgE-binding bands were detected. Inhibition assays (enzyme allergosorbent test and immunoblots) confirmed moderate-to-high cross-reactivity between goat and cow extracts. CONCLUSIONS: We confirm clinical sensitivity and specific IgE binding to goat and cow allergens in occupationally exposed individuals. There was good correlation among the clinical history, exposure, and the laboratory findings.

Ferris T.G. et al. *Are minority children the last to benefit from a new technology? Technology diffusion and inhaled corticosteroids for asthma.* Med Care. 2006; 44(1) : 81-6.p **Abstract:** BACKGROUND: Racial and ethnic disparities in health and health care have been well documented, but few studies have addressed how disparities may change over time. OBJECTIVE: We sought to determine the change in relative rates over time of corticosteroid metered dose inhaler (MDI) use in minority and nonminority

populations with asthma. DESIGN AND SETTING: We used a cross-sectional survey for 5 periods of 2 years' each (1989-1990, 1991-1992, 1993-1994, 1995-1996, 1997-1998) using the National Ambulatory Medical Care Surveys (NAMCS). PARTICIPANTS: A total of 3671 visits by adults and children with asthma to U.S. office-based physicians comprised our sample. MAIN OUTCOME MEASURE: We sought to measure differences in inhaled corticosteroid use for minority and nonminority adults and children controlling for gender, specialty, U.S. region, and type of insurance. RESULTS: Minority patients with asthma were less than half as likely as nonminority patients to have had a steroid MDI prescribed during 1989-1990. By 1995-1996, minority and nonminority patients with asthma were equally likely to have had a steroid MDI prescribed. Although differences between black and white patients resolved, differences between white and Hispanic patients persisted even after adjusting for insurance. Children initially were less likely than adults with asthma to have steroid MDI prescribed, and this difference persisted. Minority children had the greatest delay in adoption of steroid MDIs. CONCLUSION: Steroid MDIs diffused into minority and nonminority adult and child populations at different rates.

Fessler D.M. et al. *Infant mouthing behavior: the immunocalibration hypothesis.* Med Hypotheses. 2004; 63(6) : 925-32.p Abstract: Avid mouthing, the propensity of infants to suck objects and put them in their mouths, is a pattern characteristic of the first 2-3 years of life, with its most intensive manifestation occurring during the first year. Although traditional accounts explain infant mouthing as a source of sensual gratification and/or environmental exploration, these proximate hypotheses are inconsistent with the high costs of mouthing, including choking, poisoning, and exposure to pathogens. We propose that mouthing serves to proactively expose the naive gastrointestinal tract to environmental antigens and commensal bacteria while under the sheltering umbrella of breastfeeding. Mouthing functions to accurately calibrate the developing immune system, including antibody production and mucosal immunity, to the local disease ecology. The critical exposure period is not open-ended, as failure to expose the gut to an adequate number of antigens early in life is associated with an increased risk of allergies, asthma, and atopy. Weaning initiates a number of immune changes that may program the neonatal immune system into certain life-long responses.

Field T. et al. *Cortisol decreases and serotonin and dopamine increase following massage therapy.* Int J Neurosci. 2005; 115(10) : 1397-413.p Abstract: In this article the positive effects of massage therapy on biochemistry are reviewed including decreased levels of cortisol and increased levels of serotonin and dopamine. The research reviewed includes studies on depression (including sex abuse and eating disorder studies), pain syndrome studies, research on auto-immune conditions (including asthma and chronic fatigue), immune studies (including HIV and breast cancer), and studies on the reduction of stress on the job, the stress of aging, and pregnancy stress. In studies in which cortisol was assayed either in saliva or in urine, significant decreases were noted in cortisol levels (averaging decreases 31%). In studies in which the activating neurotransmitters (serotonin and dopamine) were assayed in urine, an average increase of 28% was noted for serotonin and an average increase of 31% was noted for dopamine. These studies combined suggest the stress-alleviating effects (decreased cortisol) and the activating effects (increased serotonin and dopamine) of massage therapy on a variety of medical conditions and stressful experiences.

Figueiredo S.D. et al. *[Clinical-epidemiological study of toxocaríasis in a pediatric population].* J Pediatr (Rio J). 2005; 81(2) : 126-32.p Abstract: OBJECTIVE: The variety of toxocaríasis clinic manifestations and its relationship with asthma motivated this study. The aim was to study *T.canis* seropositivity at a public pediatric

service and its association with laboratory, epidemiological and clinical factors. METHODS: This study was cross-sectional and controlled. Two hundred and eight children, from 1 to 14 years old and treated at the University of Santo Amaro Pediatric Department s Immunology and Pneumology clinic between January 2000 and January 2001, underwent serology testing. Antibodies were detected by ELISA testing for the larval excretory-secretory antigen of *T. canis*. We used the chi-square test for *T.canis* seropositivity (titers > or = 1:320) associations with: puppies at home, contact with soil, geophagia, onicophagia, mother's educational level, asthma, chronic cough, repetitive pneumonia, skin manifestations, rhinitis, hepatomegaly, splenomegaly, abdominal pain, anemia, eosinophilia, immunoglobulins, parasitosis and stunted growth. The Kruskal-Wallis variance analysis method was used for mean comparisons between seropositive and seronegative groups. Significance was set at $p < or = 0.05$. RESULTS: Seroprevalence was 54.8%, with a mean age of 6.5 years while for seronegative children the mean age was 5.8 years, showing no significant difference. There was also no difference between sexes. Seropositivity was significantly associated with puppies at home, contact with soil, hepatomegaly, asthma, eosinophilia, increased serum immunoglobulin (Ig) E levels and stunted growth. CONCLUSION: Seroprevalence was elevated in this study. *T.canis* infection must be considered in at-risk children, such as those with puppies at home, who have had contact with soil, who have hepatomegaly and/or asthma with eosinophilia and increased serum IgE.

Figueiredo E. et al. *Clinical characteristics of melon (Cucumis melo) allergy.* Ann Allergy Asthma Immunol. 2003; 91(3) : 303-8.p Abstract: BACKGROUND: Although melon is a frequent allergy-eliciting fruit, allergic reactions to melon have rarely been reported. OBJECTIVE: To evaluate and describe the clinical characteristics of melon allergy in melon-allergic patients. MATERIALS AND METHODS: We evaluated patients allergic to melon and a control group of patients allergic to pollen. The diagnosis of melon allergy was based on a convincing clinical history, positive skin test results (prick-by-prick test), and positive results on oral challenge tests to melon. RESULTS: A total of 161 patients were included in the study: 66 in the melon allergy group and 95 in the pollen control group. The melon allergy group included 35 female and 31 male patients with a mean age of 26.6 +/- 2.7 years (range, 5-61 years). Although all patients had oral symptoms, 13 (19.7%) of the patients had extraoral symptoms and none experienced generalized urticaria or anaphylaxis. Excluding other Cucurbitaceae fruits, peach, fig, and kiwi most frequently elicited positive skin test results and symptoms. Up to 23% of melon-allergic patients had a concomitant latex sensitization. Melon allergy was especially linked to pollen allergy, since all the melon-allergic patients were also allergic to pollen. Some differential features with respect to the pollen allergy control group were a higher prevalence of asthma (odds ratio [OR], 2.13; $P < 0.05$) and a statistical increase in the frequency of sensitization to several tree and weed pollens, including *Ulmus* (OR, 42.8) and *Ambrosia* (OR, 22.4). CONCLUSION: The most important conditions linked to melon allergy are pollen allergy (100%), allergy to other nonrelated fruits, mainly peach (up to 62%), and latex sensitivity (up to 23%). Some differential features of the pollinosis in melon allergy were a higher prevalence of asthma and a higher frequency of sensitization to several weed and tree pollens.

Finkelstein J.A. et al. *Clinical effectiveness research in managed-care systems: lessons from the Pediatric Asthma Care PORT. Patient Outcomes Research Team.* Health Serv Res. 2002; 37(3) : 775-89.p Abstract: OBJECTIVE: To highlight the unique challenges of evaluative research on practice behavior change in the "real world" settings of contemporary managed-care organizations, using the experience of the Pediatric Asthma Care PORT (Patient Outcomes Research Team). STUDY SETTING: The Pediatric Asthma Care PORT is a five-year initiative funded by the Agency for Healthcare Research and Quality to study strategies for asthma care

improvement in three managed-care plans in Chicago, Seattle, and Boston. At its core is a randomized trial of two care improvement strategies compared with usual care: (1) a targeted physician education program using practice based Peer Leaders (PL) as change agents, (2) adding to the PL intervention a "Planned Asthma Care Intervention" incorporating joint "asthma check-tips" by nurse-physician teams. During the trial, each of the participating organizations viewed asthma care improvement as an immediate priority and had their own corporate improvement programs underway. DATA COLLECTION: Investigators at each health plan described the organizational and implementation challenges in conducting the PAC PORT randomized trial. These experiences were reviewed for common themes and "lessons" that might be useful to investigators planning interventional research in similar care-delivery settings. CONCLUSIONS: Randomized trials in "real world" settings represent the most robust design available to test care improvement strategies. In complex, rapidly changing managed-care organizations, blinding is not feasible, corporate initiatives may complicate implementation, and the assumption that a "usual care" arm will be static is highly likely to be mistaken. Investigators must be prepared to use innovative strategies to maintain the integrity of the study design, including: continuous improvement within the intervention arms, comanagement by researchers and health plan managers of condition-related quality improvement initiatives, procedures for avoiding respondent burden in health plan enrollees, and anticipation and minimization of risks from experimental arm contamination and major organizational change. With attention to these delivery system issues, as well as the usual design features of randomized trials, we believe managed-care organizations can serve as important laboratories to test care improvement strategies.

Fiorina A. et al. *Aerobiological diagnosis of respiratory allergy by a personal sampler: two case reports.* J Investig Allergol Clin Immunol. 2003; 13(4) : 284-5.p **Abstract:** We describe two cases of respiratory allergy (asthma), which were difficult to diagnosis from an etiological viewpoint. The routine diagnostic tests were not able to determine the causal allergens, although the clinical history suggested that allergens were confined to restricted environments. Therefore, an aerobiological sampling by means of a battery-powered portable device was carried out. This approach allowed identification of the responsible allergens, which were *Alternaria* spores in one case and thuja pollen in the other. Once a targeted environmental care had been performed, the patients' symptoms rapidly improved and antiasthma therapy could be stepped down or discontinued. We suggest that, in selected cases of difficult diagnosis the presence of proximity allergens is suspected, aerobiological sampling with a portable device should be considered.

FitzGerald J.M. et al. *Adjustable maintenance dosing with budesonide/formoterol reduces asthma exacerbations compared with traditional fixed dosing: a five-month multicentre Canadian study.* Can Respir J. 2003; 10(8) : 427-34.p **Abstract:** BACKGROUND: Adjustable maintenance dosing with budesonide/formoterol in a single inhaler (Symbicort, AstraZeneca, Lund, Sweden) may provide a convenient means of maintaining asthma control with the minimum effective medication level. OBJECTIVES: To compare adjustable and fixed maintenance dosing regimens of budesonide/formoterol in asthma. METHODS: This was an open-label, randomized, parallel-group, multicentre, Canadian study of asthma patients (aged 12 years or older, postbronchodilator forced expiratory volume in 1 s 70% or greater of predicted normal). Following a one-month run-in on budesonide/formoterol (100/6 mg or 200/6 mg metered doses, two inhalations twice daily), 995 patients were randomly assigned either to continue on this fixed dosing regimen or to receive budesonide/formoterol adjustable dosing (step down to one inhalation twice daily if symptoms were controlled or temporarily step up to four inhalations twice daily for seven or 14 days if asthma worsened). The primary efficacy variable was the occurrence of exacerbations (requiring oral or inhaled corticosteroids, emergency

department treatment, serious adverse events or added maintenance therapy because of asthma). RESULTS: With adjustable dosing, significantly fewer patients experienced exacerbations compared with fixed dosing (4.0% versus 8.9%, $P=0.002$; number needed to treat=21 [95% CI 13 to 59]). Patients required 36% fewer overall doses of budesonide/formoterol (2.5 versus 3.9 inhalations/day, $P<0.001$), and total costs per patient were lower (difference over five months -141 Canadian dollars [95% CI -162 Canadian dollars to -116 Canadian dollars]). Asthma symptom severity (modified National Heart, Lung, and Blood Institute stage) was maintained or improved in 97% or greater of patients in both groups (pre-run-in to end of treatment). Both treatments were well tolerated. CONCLUSIONS: Budesonide/formoterol adjustable maintenance dosing provided more effective asthma control than fixed dosing, with a lower overall drug dose and reduced total cost.

Fleming L.E. et al. *Initial evaluation of the effects of aerosolized Florida red tide toxins (brevetoxins) in persons with asthma.* Environ Health Perspect. 2005; 113(5) : 650-7.p **Abstract:** Florida red tides annually occur in the Gulf of Mexico, resulting from blooms of the marine dinoflagellate *Karenia brevis*. *K. brevis* produces highly potent natural polyether toxins, known as brevetoxins, that activate voltage-sensitive sodium channels. In experimental animals, brevetoxins cause significant bronchoconstriction. A study of persons who visited the beach recreationally found a significant increase in self-reported respiratory symptoms after exposure to aerosolized Florida red tides. Anecdotal reports indicate that persons with underlying respiratory diseases may be particularly susceptible to adverse health effects from these aerosolized toxins. Fifty-nine persons with physician-diagnosed asthma were evaluated for 1 hr before and after going to the beach on days with and without Florida red tide. Study participants were evaluated with a brief symptom questionnaire, nose and throat swabs, and spirometry approved by the National Institute for Occupational Safety and Health. Environmental monitoring, water and air sampling (i.e., *K. brevis*, brevetoxins, and particulate size distribution), and personal monitoring (for toxins) were performed. Brevetoxin concentrations were measured by liquid chromatography mass spectrometry, high-performance liquid chromatography, and a newly developed brevetoxin enzyme-linked immunosorbent assay. Participants were significantly more likely to report respiratory symptoms after Florida red tide exposure. Participants demonstrated small but statistically significant decreases in forced expiratory volume in 1 sec, forced expiratory flow between 25 and 75%, and peak expiratory flow after exposure, particularly those regularly using asthma medications. Similar evaluation during nonexposure periods did not significantly differ. This is the first study to show objectively measurable adverse health effects from exposure to aerosolized Florida red tide toxins in persons with asthma. Future studies will examine the possible chronic effects of these toxins among persons with asthma and other chronic respiratory impairment.

Flores G. et al. *Keeping children out of hospitals: parents' and physicians' perspectives on how pediatric hospitalizations for ambulatory care-sensitive conditions can be avoided.* Pediatrics. 2003; 112(5) : 1021-30.p **Abstract:** BACKGROUND: Avoidable hospitalization conditions (AHCs) are hospitalizations that potentially can be avoided with timely, appropriate outpatient care. The specific reasons for avoidability, and parents and physicians' perspectives on the proportion of actually avoidable pediatric AHCs, have not been examined adequately. OBJECTIVES: To identify how pediatric hospitalizations might be avoided, and to determine the proportion of avoidable AHCs according to parents and physicians of hospitalized children. METHODS: Cross-sectional survey of parents, primary care physicians (PCPs), and inpatient attending physicians (IAPs) of a consecutive series of children who were admitted with AHCs to an urban hospital in a 14-month period. RESULTS: The 554 hospitalized children had a median age of 4 years; most were poor (median annual family income: 12,000 dollars), nonwhite (91%), and

had public (73%) or no (16%) health insurance. The most frequent AHC diagnoses were asthma (43%), dehydration/gastroenteritis (16%), pneumonia (11%), seizure disorder (8%), and skin infections (8%). Only 25% of parents said that their child's admission was avoidable, compared with 29% of PCPs and 32% of IAPs. The proportion of AHC hospitalizations assessed as avoidable varied according to the source or combination of sources, from 13% for agreement among all 3 sources to 46% as identified by any 1 of the 3 sources. PCPs (71%) and IAPs (48%) significantly more often than parents (35%) cited parent/patient-related reasons for how hospitalizations could have been avoided, including adhering to and refilling medications, better outpatient follow-up, and avoiding known disease triggers. Parents (48%) significantly more often than PCPs (18%) and IAPs (37%) cited physician-related reasons for how hospitalizations could have been avoided, including better education by physicians about the child's condition, and better quality of care. Multivariate analyses revealed that an age ≥ 11 years, an asthma diagnosis, working poor family income, and having no health insurance were associated with approximately double to triple the odds of an avoidable hospitalization. **CONCLUSIONS:** The proportion of AHCs assessed as avoidable varies from 13% to 46%, depending on the source. Adolescents, children with asthma, children from working-poor families, and uninsured children are at greatest risk for avoidable hospitalizations. Many pediatric hospitalizations might be avoided if parents and children were better educated about the child's condition, medications, the need for follow-up care, and the importance of avoiding known disease triggers. Direct assessment by parents and physicians of hospitalized children can be an informative way to examine the proportion of avoidable pediatric hospitalizations and how they can be prevented.

Flores G. et al. *The health of Latino children: urgent priorities, unanswered questions, and a research agenda.* JAMA. 2002; 288(1) : 82-90.p **Abstract:** Latinos recently became the largest racial/ethnic minority group of US children. The Latino Consortium of the American Academy of Pediatrics Center for Child Health Research, consisting of 13 expert panelists, identified the most important urgent priorities and unanswered questions in Latino child health. Conclusions were drawn when consensus was reached among members, with refinement through multiple iterations. A consensus statement with supporting references was drafted and revised. This article summarizes the key issues, including lack of validated research instruments, frequent unjustified exclusion from studies, and failure to analyze data by pertinent subgroups. Latino children are at high risk for behavioral and developmental disorders, and there are many unanswered questions about their mental health needs and use of services. The prevalence of dental caries is disproportionately higher for Latino children, but the reasons for this disparity are unclear. Culture and language can profoundly affect Latino children's health, but not enough cultural competency training of health care professionals and provision of linguistically appropriate care occur. Latinos are underrepresented at every level of the health care professions. Latino children are at high risk for school dropout, environmental hazards, obesity, diabetes mellitus, asthma, lack of health insurance, nonfinancial barriers to health care access, and impaired quality of care, but many key questions in these areas remain unanswered. This article suggests areas in which more research is needed and ways to improve research and care of Latino children.

Focke M. et al. *Plasma levels of polyunsaturated fatty acids in children with atopic dermatitis and in atopic and nonatopic controls.* Wien Klin Wochenschr. 2005; 117(13-14) : 485-91.p **Abstract:** **BACKGROUND:** Atopic dermatitis has been thought to be associated with a disturbance in n-6 polyunsaturated fatty acid (PUFA) metabolism, but randomized trials investigating the clinical efficacy of oral supplementation with gammalinolenic acid have revealed conflicting results. **AIM OF THE STUDY:** To investigate the proposed linkage between PUFA dysregulation and

atopic dermatitis. **MATERIALS AND METHODS:** Plasma levels of linoleic acid (LA), gammalinolenic acid (GLA), dihomogammalinolenic acid (DGLA) and arachidonic acid (AA) were measured using HPLC in 22 children with atopic dermatitis. Patients were subdivided into those with elevated total serum IgE (group A, n = 15, IgE $> +1$ SD of age-specific normal values) and those with normal IgE (group B, n = 7) and compared with children suffering from allergic rhinitis/asthma (group C, n = 8) and with non-atopic controls (group D, n = 6). **RESULTS:** GLA levels were significantly lower ($p < 0.05$) in eczema patients with elevated IgE (A, 0.19 \pm 0.06%) and in atopic controls (C, 0.23 \pm 0.06%) than in eczema patients with low IgE (B, 0.42 \pm 0.19%) and non-atopic controls (D, 0.43 \pm 0.16%). There were no significant differences between groups for LIN, DGLA and AA, except for lower LIN levels in atopic controls. Correlation of individual LA and GLA values showed significantly steeper regression lines in low-IgE responders (B and D, $k(x) = 0.058$) than in high-IgE responders (A and C, $k(x) = 0.012$; $p < 0.02$), suggesting impaired delta-6-desaturase function in the latter. For the study population as a whole, there was a clear negative correlation between total levels of IgE and GLA ($r(s) = -0.64$) and a moderate negative correlation between total IgE and AA ($r(s) = -0.38$). **CONCLUSIONS:** Dysregulation of n-6 PUFA metabolism is neither consistently found in nor specifically associated with atopic dermatitis but rather appears to be associated with IgE production and atopy in general. The finding of decreased GLA levels in eczema patients with elevated total IgE and in children with allergic rhinitis and asthma but not in eczema patients with normal total IgE questions the proposed pathophysiologic role of fatty acid dysregulation in atopic dermatitis.

Fontan M. et al. *Allergy to freshwater shrimp (Gammarus).* J Invest Allergol Clin Immunol. 2005; 15(2) : 150-2.p **Abstract:** We report three new cases of allergy to Gammarus, two of them involving cutaneous symptoms, and the third one with occupational asthma. The results showed exposure to feed containing Gammarus shrimp to be the main cause of the allergic symptoms in the three patients. In all cases the intervention of IgE was demonstrated, with the absence of cross-reactions with other common allergenic arthropods.

Fotinos C. et al. *Clinical inquiries. Is there a role for theophylline in treating patients with asthma?* J Fam Pract. 2002; 51(9) : 744.p

Franck L.S. et al. *Re-thinking family-centred care across the continuum of children's healthcare.* Child Care Health Dev. 2004; 30(3) : 265-77.p **Abstract:** **BACKGROUND:** The terms family-centred care (FCC) and family-centred services (FCS) are used interchangeably across the continuum of children's healthcare to encompass concepts of: parental participation in children's healthcare; partnership and collaboration between the healthcare team and parents in decision-making; family-friendly environments that normalize as much as possible family functioning within the healthcare setting; and care of family members as well as of children. However, authors from different professional and policy perspectives have used different definitions and literatures when arguing the evidence for FCC and FCS. **METHOD:** A critical literature review and theoretical discussion exploring common concepts and issues forming the basis for a research agenda further strengthening of the evidence base for FCC. A systematic identification of constructs, concepts and empirical indicators is developed and applied to exemplars in pain and asthma that span the continuum of children's healthcare across acute and community settings. **CONCLUSIONS:** The extent to which the concepts are supported by research and applied in practice remains unclear. We propose that re-thinking of FCC is required in order to develop a more coherent programme of research into the application of FCC theory in children's healthcare.

- Franklin P. et al.** *Variability of nitric oxide metabolites in exhaled breath condensate.* *Respir Med.* 2006; 100(1) : 123-9.p **Abstract:** The collection of exhaled breath condensate (EBC) is simple and non-invasive, however, there are few data on the methodological aspects affecting concentrations of compounds in EBC. The aim of this study was to investigate methodological issues for measuring nitric oxide metabolites (NO(x)) in EBC. Twenty-five healthy adults (12 females, age range 23-55 years) and 22 children (11 females, age range 7-6 years) were recruited for studies investigating inter- and intra-day repeatability, repeatability with controlled expiratory flows and temperature, flow dependence, and analytical variability of EBC NO(x). Both intra- and inter-day repeatability was poor with a coefficient of repeatability of 103.4% of the mean difference between intra-day (15 min) measures and 118.6% of inter-day (24 h) differences. Repeatability was not improved when expiratory flow and temperature of the collection device were controlled. However, some of the variability (approximately 50%) may be accounted for by variability in the analytical technique (analytical variability) and this may result from difficulties in controlling for contamination. NO(x) levels were not affected by different expiratory flows in either adults or children but there was still significant variation within individuals. Levels of NO(x) in EBC seem to be highly variable and this needs to be considered if EBC NO(x) is to be used in clinical studies.
- Franklin P.J. et al.** *Exhaled nitric oxide and asthma: complex interactions between atopy, airway responsiveness, and symptoms in a community population of children.* *Thorax.* 2003; 58(12) : 1048-52.p **Abstract:** **BACKGROUND:** Exhaled nitric oxide (FE(NO)) is raised in asthmatic children, but there are inconsistencies in the relationship between FE(NO) and characteristics of asthma, including atopy, increased airway responsiveness (AR), and airway inflammation. The aim of this study was to investigate the relationship between FE(NO) and asthma, atopy, and increased AR in children. **METHODS:** One hundred and fifty five children (79 boys) of mean age 11.5 years underwent an assessment that included FE(NO) measurements, spirometric tests, inhaled histamine challenge, and a skin prick test. Blood was collected for eosinophil count. Current and past asthma like symptoms were determined by questionnaire. **RESULTS:** In multiple linear regression analyses FE(NO) was associated with atopy ($p < 0.001$), level of AR ($p = 0.005$), blood eosinophil count ($p = 0.007$), and height ($p = 0.002$) but not with physician diagnosed asthma ($p = 0.1$) or reported wheeze in the last 12 months ($p = 0.5$). Separate regression models were conducted for atopic and non-atopic children and associations between FE(NO) and AR, blood eosinophils and height were only evident in atopic children. Exhaled NO was raised in children with a combination of atopy and increased AR independent of symptoms. **CONCLUSION:** Raised FE(NO) seems to be associated with an underlying mechanism linking atopy and AR but not necessarily respiratory symptoms.
- Frazier L.M. et al.** *Barriers to smoking cessation initiatives for Medicaid clients in managed care.* *Subst Use Misuse.* 2001; 36(13) : 1875-99.p **Abstract:** In this paper, key barriers to providing smoking cessation services for low income individuals are illustrated using epidemiologic data from a population which was enrolled in a Medicaid managed care plan in Kansas during 1998. The Plan served 623 pregnant women who could potentially benefit from assistance in avoiding tobacco exposure. The prevalence of smoking among adult clients was 44.8%. twice the national average. Only 52.3% of adult smokers were advised by a provider to quit in the previous year. Most individuals in the client population (81.7% of the 10,733 members) were asthma. The adult household member who needed smoking cessation services, however, was unlikely to qualify for health care benefits through Medicaid. The median length of enrollment was only 1.9 months, providing very little client contact time for tobacco control initiatives. The literature suggests that some providers may lack skills in treating tobacco as an addiction. It would be a major task for the managed care organization to train the 2,000 physicians in 68 of the 105 counties of Kansas who cared for this population. Potential solutions include improving reimbursement for smoking prevention and treatment, and developing cheaper smoking cessation services which are effective and acceptable among low-income individuals. The managed care organization could provide patient education materials and staff training for physicians and other members of the office staff.
- Frediani T. et al.** *Allergy and childhood epilepsy: a close relationship?* *Acta Neurol Scand.* 2001; 104(6) : 349-52.p **Abstract:** **OBJECTIVES:** The possibility that certain foods or allergens may induce convulsions has already been reported in the literature. None of the relevant studies has, however, shown a close correlation between allergy and epilepsy, most reports being anecdotal and open to various causal hypotheses. The case-control study reported here was undertaken to test the hypothesis that epilepsy is linked to allergy. **MATERIAL AND METHODS:** Seventy-two epileptic children and a group of 202 controls in the same age bracket were investigated for allergy together with their immediate families. **RESULTS:** The study revealed significantly higher rates of eczema in the mothers and rhinitis in the siblings of the patients studied as well as generally higher incidence of allergic pathologies in both of these groups with respect to the relevant controls. A significantly higher incidence of allergy to cow's milk and asthma was also documented in the epileptic children with respect to the control group. Prick tests gave a significantly higher rate of positive results for cow's milk proteins in the cases examined with respect to the controls. The total serum IgE of a random sample of cases and controls showed no difference in mean values. **CONCLUSION:** The study appears to bear out the hypothesis of a higher incidence of allergy in the children with epilepsy and their immediate families than in the controls and their families.
- Freed G.L. et al.** *Changes in the proportion and volume of care provided to children by generalists and subspecialists.* *J Pediatr.* 2005; 146(1) : 14-9.p **Abstract:** **OBJECTIVE:** To assess whether primary care physicians, via referrals or other mechanisms, are now providing proportionally less care for children with specific common diagnoses, thus driving greater demand for specialist services. **STUDY DESIGN:** Secondary data analysis (1993-2001) from one of the largest commercial healthcare organizations in the United States. **Evaluation and management (E/M) common procedural terminology (CPT) visit codes and International Classification of Diseases (ICD) codes pertaining to asthma, constipation, headache, and heart murmurs were selected. Visits were then assigned to the specialty of physician providing care. Significant differences between and among categories of physicians were tested using logistic regression. RESULTS:** Overall, pediatrician generalists and specialists provided a greater proportion of E/M visits to children in 2001 than in 1993, compared with nonpediatrician providers. However, although the absolute increase in the proportion of all E/M visits by children <18 years of age to pediatrician generalists was greater than that of pediatrician subspecialists (4.77% vs 0.69%; $P < .0001$), the relative increase was much smaller for the generalists (8.9% vs 19.7%; $P < .0001$). Findings were consistent for most of the specific diagnoses examined. **CONCLUSIONS:** The increases in both the proportion and number of visits made to specialists has not been accompanied by a decrease in visits to generalists.
- Frey U. et al.** *Maternal atopic disease modifies effects of prenatal risk factors on exhaled nitric oxide in infants.* *Am J Respir Crit Care Med.* 2004; 170(3) : 260-5.p **Abstract:** In a prospective healthy birth cohort, we determined whether levels of exhaled nitric oxide (eNO) in healthy unselected infants at the age of 1 month were associated with maternal atopic disease and prenatal and early postnatal environmental exposures. Tidal eNO was measured in 98 healthy, unselected infants (35 from mothers with atopy) (mean age

+/- SD, 36.0 +/- 6.2 days) and was compared with histories taken in standardized interviews. eNO was higher in males compared with females (17.7 vs. 14.6 ppb, $p = 0.042$) and infants exposed to postnatal maternal smoking (+4.4 ppb, $p = 0.027$), adjusting for weight and tidal breathing parameters. Prenatal tobacco exposure was associated with higher eNO (+12.0 ppb, $p = 0.01$) in infants of mothers with asthma and lower eNO (-5.7 ppb) in infants of mothers without asthma (p for interaction < 0.0001). Coffee consumption in pregnancy decreased eNO (-6.0 ppb, $p = 0.008$) only in children of mothers with atopy (p for interaction = 0.015). Paternal atopy had no influence. In the early phase of immunologic development, before the onset of infections and allergic disease, the effect of prenatal or early postnatal environmental factors on eNO was modified by the presence of maternal atopic disease. This underlines the complex interaction of maternal and environmental factors in the development of airway disease.

Friedman J.Y. et al. *Parents' reported preference scores for childhood atopic dermatitis disease states.* BMC Pediatr. 2004; 4(1) : 21.p Abstract: BACKGROUND: We sought to elicit preference weights from parents for health states corresponding to children with various levels of severity of atopic dermatitis. We also evaluated the hypothesis that parents with children who had been diagnosed with atopic dermatitis would assign different preferences to the health state scenarios compared with parents who did not have a child with atopic dermatitis. METHODS: Subjects were parents of children aged 3 months to 18 years. The sample was derived from the General Panel, Mommies Sub-Panel, and Chronic Illness Sub-Panel of Harris Interactive. Participants rated health scenarios for atopic dermatitis, asthma, and eyeglasses on a visual analog scale, imagining a child was experiencing the described state. RESULTS: A total of 3539 parents completed the survey. Twenty-nine percent had a child with a history of atopic dermatitis. Mean preference scores for atopic dermatitis were as follows: mild, 91 (95% confidence interval [CI], 90.7 to 91.5); mild/moderate, 84 (95%CI, 83.5 to 84.4); moderate, 73 (95%CI, 72.5 to 73.6); moderate/severe, 61 (95%CI, 60.6 to 61.8); severe, 49 (95% CI, 48.7 to 50.1); asthma, 58 (95%CI, 57.4 to 58.8); and eyeglasses, 87(95%CI, 86.3 to 87.4). CONCLUSIONS: Parents perceive that atopic dermatitis has a negative effect on quality of life that increases with disease severity. Estimates of parents' preferences can provide physicians with insight into the value that parents place on their children's treatment and can be used to evaluate new medical therapies for atopic dermatitis.

Friedman Ross L. *Salmeterol and inhaled corticosteroids in patients with persistent asthma.* JAMA. 2001; 286(24) : 3076; author reply 3077-8.p

Frieri M. et al. *Association between CD62 ligand on naive and memory T cells and history of cow's milk hypersensitivity in atopic patients.* Ann Allergy Asthma Immunol. 2004; 92(5) : 565-72.p Abstract: BACKGROUND: Both IgE and non-IgE cell-mediated reactions can contribute to the immunopathogenesis of food hypersensitivity. OBJECTIVE: To study L-selectin expression in naive (CD45RA+) and memory (CD45RO+) T cells in atopic patients with a history of cow's milk allergy and CD69 expression. METHODS: We evaluated 12 children with a history of cow's milk allergy. All 12 children underwent clinical history, examination, in vivo skin prick testing to inhalants and milk allergen, and in vitro radioallergosorbent testing for milk and total serum IgE levels. L-selectin levels on naive and memory T cells from patients and controls were analyzed by flow cytometry with fluorochrome-conjugated monoclonal antibodies after 4 hours or 7 days of incubation with medium alone, 1 microg/mL of pokeweed mitogen, or 50 microg/mL of casein. RESULTS: The percentage of CD45RA+ 62L+ cells with casein was 56% +/- 11% vs 38% +/- 7.7% in healthy controls ($P < .009$). The percentage of CD45RO- 62L+ cells was 22% +/- 7.1% vs 39% +/- 7.6% in healthy controls ($P < .001$), whereas the expression of CD62L+ in CD45RA+ and CD45RO+ cells decreased 149% +/- 33%

vs 540% +/- 36% for healthy controls ($P < .001$) and 89% +/- 16% vs 402% +/- 103% for healthy controls ($P < .001$), respectively. CONCLUSIONS: The results of the present study demonstrate the presence of CD62 ligand on naive and memory T cells, which might serve as a predictive marker for atopic dermatitis with other overlapping atopic disorders, such as asthma and allergic rhinitis.

Frischer T. et al. *Ambient ozone exposure is associated with eosinophil activation in healthy children.* Clin Exp Allergy. 2001; 31(8) : 1213-9.p Abstract: BACKGROUND: Eosinophil activation is characteristic for allergic airways disease. However, eosinophilic airways inflammation has also been observed subsequent to ambient ozone exposure. METHODS: For a population sample of 877 children living at nine sites with different ozone exposure we measured urinary eosinophil protein X (U-EPX) as a marker of eosinophil activation. U-EPX was determined from a single spot urine sample during autumn 1997. Children were participants in a longitudinal study of ozone effects on lung function. RESULTS: The 5-95% percentiles of ozone exposure (30-day mean before test) were 11.8-51.5 p.p.b. (mean: 31.6 ppb). U-EPX was measured by radioimmunoassay and expressed as ratio to urinary creatinine (microg EPX/mmol creatinine). Log transformation was performed to achieve a normal distribution. LogU-EPX was associated with gender, a diagnosis of asthma and atopy (skin test sensitivity to any of seven aeroallergens). LogU-EPX increased with ozone exposure for all children. The medians of LogU-EPX according to the first-fourth quartiles of ozone exposure were: 1.82, 1.88, 1.95 and 2.03. For 172 non-asthmatic children who had spent the whole summer at their site corresponding figures were 1.57, 1.78, 2.07 and 2.13. In a multivariate model with logU-EPX being the dependent variable and adjusted for gender, site and atopy, ozone was found to be significant (estimate: 0.007 microg/mmol creatinine per ppb ozone; SE:0.02; $P < 0.001$). CONCLUSION: Our observation supports the hypothesis that ozone in healthy children is associated with eosinophil inflammation, most likely in the airways.

Frye C. et al. *Maternal oral contraceptive use and atopic diseases in the offspring.* Allergy. 2003; 58(3) : 229-32.p Abstract: BACKGROUND: This study examined the association of maternal oral contraceptive (OC) use - before and after birth - and atopic manifestations in the offspring. METHODS: A total of 2754 East German children aged 5-14 years participated in a cross-sectional survey in 1998-99. The standardized parental questionnaire in 1998-99 included data on atopic diseases, socio-economic factors, parental atopy and maternal OC use. Specific immunoglobulin E against common inhalant allergens was measured by radioallergosorbent test (RAST). RESULTS: Maternal OC use before birth was associated with a higher risk of atopic diseases in the offspring compared with children of mothers who had never taken OC [asthma: odds ratio (OR) 1.6; 95% confidence interval (CI): 0.9-3.0; allergic rhinitis: OR 1.5; CI: 0.96-2.2; atopic eczema: OR 2.6; CI: 1.6-4.3; atopic sensitization: OR 1.5; CI: 0.97-2.2]. However, the effect estimates for maternal OC use after birth compared with the never users showed quite similar effects for these atopic conditions. No relations were observed between the prevalences of atopic diseases and maternal age at beginning of OC use, the duration of OC use, the type of contraceptive or maternal age at birth. CONCLUSION: This study raises doubts in a true biological association between OC use and atopic diseases.

Fuentes Aparicio V. et al. *Non-occupational allergy caused by the pine processionary caterpillar (Thaumetopoea pityocampa).* Allergol Immunopathol (Madr). 2004; 32(2) : 69-75.p Abstract: Contact with the pine processionary caterpillar induces dermatitis, usually located in exposed areas, and, less frequently, ocular lesions through a toxic-irritative mechanism. Recently, the existence of an immediate hypersensitivity mechanism has been demonstrated, mainly in occupationally exposed patients. OBJECTIVE: To present four

patients who experienced allergic reactions (urticaria-angioedema and rhinitis-asthma) after non-occupational exposure to pine processionary caterpillar. **PATIENTS AND METHODS:** The four patients underwent allergy testing through skin prick tests (SPT), specific IgE detection and SDS-PAGE immunoblotting. One patient also underwent a specific bronchial challenge test with the pine processionary antigen. **RESULTS:** In all patients, both SPT with the caterpillar extract and specific IgE were positive. Western blotting showed several IgE-binding bands with molecular mass values ranging from 18 to 107 kDa. A shift in the electrophoretic mobility of some of the relevant allergens occurred under the presence of a reductive agent (beta -mercaptoethanol). The specific bronchial challenge test with pine processionary antigen performed in one of the patients also produced positive results. **CONCLUSIONS:** The results of this study show an immunologic IgE-mediated immediate hypersensitivity mechanism in these reactions. The processionary caterpillar's airborne urticating hairs or spicules should be considered, at least in some locations, not only as contact and occupational allergens, but also as seasonal aeroallergens.

Fuhlbrigge A.L. et al. *Validity of the HEDIS criteria to identify children with persistent asthma and sustained high utilization.* Am J Manag Care. 2005; 11(5) : 325-30.p **Abstract:** **BACKGROUND:** The most widely used performance measure for asthma, the Health Plan Employer Data and Information Set (HEDIS), has been criticized because the delay between classification (year 1) and assessment of medication dispensing (year 2) may produce a "misalignment" and weaken the validity of the measure. **OBJECTIVE:** To examine whether a previously observed association between the HEDIS performance measure and asthma-related emergency department visits is robust when the period between the classification and outcome assessment is evaluated during a 2-year period as defined. **METHODS:** Children (N = 2766) aged 3 to 15 years enrolled in 1 of 3 managed care organizations with at least 1 asthma diagnosis listed for a hospitalization, an emergency department visit, or an ambulatory encounter and at least 2 consecutive years of data for analysis from July 1996 through June 1999 were identified. **RESULTS:** Children did not consistently meet the HEDIS criteria for persistent asthma, and 24% to 28% of children did not requalify in year 2 of observation. Multivariate regression models showed that a protective relationship between controller medication dispensing and asthma-related emergency department visits was no longer seen among children meeting the HEDIS criteria for persistent asthma when the total period of observation is extended to 2 years (odds ratio, 0.7; 95% confidence interval, 0.4-1.2). **CONCLUSIONS:** Our results suggest that the variable nature of asthma may affect how the HEDIS performance measure should be used for assessing quality of care. The period between identification of the target population and performance assessment should be closely related in time.

Fukai H. et al. *Association between a polymorphism in cysteinyl leukotriene receptor 2 on chromosome 13q14 and atopic asthma.* Pharmacogenetics. 2004; 14(10) : 683-90.p **Abstract:** **OBJECTIVE:** Cysteinyl leukotriene receptor 2 (CYSLTR2) is one of the receptors for the cysteinyl leukotrienes (CYSLTs), which cause bronchoconstrictions, vascular hyperpermeability and mucus hypersecretion in asthmatic patients. CYSLTR1 antagonists have been shown to be effective in the treatment of chronic asthma. CYSLTR2 is located approximately 300 kb from D13S153, which is reportedly linked to asthma in several populations. We characterized the genomic structure of humans CYSLTR2, determined the putative major promoter region and conducted association studies pertaining to polymorphisms in CYSLTR2 and asthma. **METHODS AND RESULTS:** We identified three novel exons in the 5' untranslated region of CYSLTR2 by rapid amplification of cDNA ends and identified eight novel polymorphisms in CYSLTR2 by direct sequencing. A transmission disequilibrium test with 137 Japanese asthmatic families revealed that the -1220A > C polymorphism is associated with the development of asthma (P = 0.0066). In addition,

a polymorphism in the putative promoter region caused different promoter activities in vitro. **CONCLUSION:** Our results suggest that CYSLTR2 is one of the genes that contributes to susceptibility to asthma in the Japanese population.

Fukuda S. et al. *Allergic symptoms and microflora in schoolchildren.* J Adolesc Health. 2004; 35(2) : 156-8.p **Abstract:** We studied 867 junior high school children and administered a questionnaire documenting allergic symptoms and environmental variables, and measured Immunoglobulin E serum levels and the immunoglobulin G titers of serum antibody to microflora. A total of 716 subjects were ultimately used for statistics; those with at least two of the following allergic symptoms: asthma, rhinitis, eczema, or food allergy, showed significantly higher IgG titers to *Bacteroides vulgatus* than other groups. This finding suggests that a species of the *Bacteroides* genus of the intestinal microflora tends to affect the gut issues, but further studies are needed to clarify this.

Fulhan J. et al. *Update on pediatric nutrition: breastfeeding, infant nutrition, and growth.* Curr Opin Pediatr. 2003; 15(3) : 323-32.p **Abstract:** Recent studies continue to point out the critical nature of a patient's nutritional status in helping to determine important health outcomes in pediatrics. We review recent data concerning the composition of breast milk and its adequacy to support infant growth in the first six months of life, as well as trials that support breastfeeding as an important method to delay or reduce the incidence of atopic diseases such as eczema, allergies, and asthma. Studies have also been published that show how physician education and training about breastfeeding can be optimized. Studies showing how nutritional status is measured (using standard anthropometric techniques as well as more modern measures of basal metabolic rate) are highlighted, as well as the role of micronutrient supplementation of patients with the human immunodeficiency virus infection and diarrheal diseases.

Futrakul S. et al. *Risk factors of bronchial hyperresponsiveness in children with wheezing-associated respiratory infection.* Pediatr Pulmonol. 2005; 40(1) : 81-7.p **Abstract:** The objectives of this study were to identify possible risk factors of bronchial hyperresponsiveness (BHR) in children up to 5 years of age with wheezing-associated respiratory infection (WARI), and to study the prevalence of BHR. Children up to 5 years of age with WARI were enrolled in the study. The parents or caregivers of children were asked about their demographic data and clinical histories. Physical examination and clinical score assessment were performed. Pulmonary function tests, i.e., tidal breathing flow volume (TBFV), were performed to measure tidal breathing parameters before and after salbutamol nebulization. If volume at peak tidal expiratory flow/expiratory tidal volume and time to peak expiratory flow/total expiratory time increased > or = 20%, or tidal expiratory flow at 25% of tidal volume/peak tidal expiratory flow increased > or = 20% after nebulization therapy, BHR was diagnosed. The number in the positive BHR group was used to calculate the prevalence of BHR, and clinical features were compared with those of the negative BHR group. Categorical data were analyzed for statistical significance (P < 0.05) by chi-square test or Fisher's exact test, or Student's t-test, as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for those with statistical significance. One hundred and six wheezing children underwent pulmonary function tests before and after salbutamol nebulization. With the aforementioned criteria, 41 cases (38.7%) were diagnosed with BHR. History of reactive airway disease, (OR, 6.31; 95% CI, 1.68-25), maternal history of asthma (OR, 3.45; 95% CI, 1.34-9), breastfeeding less than 3 months (OR, 3.18; 95% CI, 1.26-8.12), and passive smoking (OR, 3; 95% CI, 1.15-7.62) were significant risk factors of BHR. The eosinophil count was significantly higher in the BHR (+) group particularly, in children 1-5 years of age (P < or = 0.01). Patchy infiltrates were more commonly found in patients with negative BHR

but not statistically significant. In conclusion, a history of reactive airway disease, maternal history, breastfeeding less than 3 months, and passive smoking were significant risk factors for BHR.

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Gaby A.R. *Intravenous nutrient therapy: the "Myers' cocktail".* *Altern Med Rev.* 2002; 7(5) : 389-403.p **Abstract:** Building on the work of the late John Myers, MD, the author has used an intravenous vitamin-and-mineral formula for the treatment of a wide range of clinical conditions. The modified "Myers' cocktail," which consists of magnesium, calcium, B vitamins, and vitamin C, has been found to be effective against acute asthma attacks, migraines, fatigue (including chronic fatigue syndrome), fibromyalgia, acute muscle spasm, upper respiratory tract infections, chronic sinusitis, seasonal allergic rhinitis, cardiovascular disease, and other disorders. This paper presents a rationale for the therapeutic use of intravenous nutrients, reviews the relevant published clinical research, describes the author's clinical experiences, and discusses potential side effects and precautions.

Gaffney K.E. et al. *Asthmatic toddler with cough.* *Pediatr Nurs.* 2004; 30(1) : 68-71.p

Gafvelin G. et al. *Cross-reactivity studies of a new group 2 allergen from the dust mite *Glycyphagus domesticus*, *Gly d 2*, and group 2 allergens from *Dermatophagoides pteronyssinus*, *Lepidoglyphus destructor*, and *Tyrophagus putrescentiae* with recombinant allergens.* *J Allergy Clin Immunol.* 2001; 107(3) : 511-8.p **Abstract:** **BACKGROUND:** Dust mites are important inducers of allergic disease. Group 2 allergens are recognized as major allergens in several mite species, including *Dermatophagoides pteronyssinus*, *Lepidoglyphus destructor*, and *Tyrophagus putrescentiae*. No allergens have thus far been characterized on the molecular level from the dust mite *Glycyphagus domesticus*. **OBJECTIVE:** We sought to examine the cross-reactivity among group 2 allergens of *G domesticus*, *L destructor*, *T putrescentiae*, and *D pteronyssinus*. **METHODS:** A group 2 allergen from *G domesticus*, *Gly d 2*, was cloned and expressed as a recombinant protein. Cross-reactivity between *Gly d 2* and 3 other group 2 allergens, *Lep d 2*, *Tyr p 2*, and *Der p 2*, was studied by using individual sera and a serum pool RAST-positive to *G domesticus*, *L destructor*, *T putrescentiae*, and *D pteronyssinus*. Recombinant allergens were used as inhibitors of IgE binding in immunoblotting experiments. Molecular modeling on the basis of the *Der p 2* structure was carried out for *Gly d 2*, *Lep d 2*, and *Tyr p 2*. **RESULTS:** Two cDNAs encoding isoforms of *Gly d 2* were isolated, but only the *Gly d 2.02* isoform was used in this study. Sixteen of 17 subjects had IgE to *Gly d 2*. The protein sequence of *Gly d 2* revealed 79% identity to *Lep d 2* and 46% and 41% identity to *Tyr p 2* and *Der p 2*, respectively. Extensive cross-reactivity was demonstrated among *Gly d 2*, *Lep d 2*, and *Tyr p 2*, but little cross-reactivity was found between these allergens and *Der p 2*. According to the tertiary structure of *Der p 2* and 3-dimensional models of *Gly d 2*, *Lep d 2*, and *Tyr p 2*, differences reside mainly in surface-exposed residues. **CONCLUSION:** *Gly d 2* showed high sequence homology to *Lep d 2*. Cross-reactivity was observed between *Gly d 2*, *Lep d 2*, and *Tyr p 2*, but only limited cross-reactivity was demonstrated between these 3 allergens and *Der p 2*.

Gagro A. et al. *Effect of cysteinyl leukotriene receptor antagonist on *CD11b* and *CD23* expression in asthmatic children.* *Clin Exp Allergy.* 2004; 34(6) : 939-44.p **Abstract:** **BACKGROUND:** Cysteinyl leukotrienes are potent pro-inflammatory mediators that contribute to the pathophysiologic features observed in allergic asthma. Inhibitors of leukotriene receptors represent novel therapy in asthma treatment. In addition to the protection from early asthmatic responses, these drugs have recently been shown to protect from late airway responses too. **METHODS:** We studied the effect of treatment with an oral antagonist of cysteinyl leukotriene receptors on the increased expression of the low-affinity IgE receptor, CD23, on B cells, and of its ligands, CD11b and CD11c, on CD4(+) T cells and monocytes in peripheral blood of patients with allergic asthma. In this uncontrolled open-label study, 14 children with allergic asthma received montelukast, a cysteinyl leukotriene receptor antagonist, for a period of 6 weeks after demonstrating forced expiratory volume in 1 s (FEV₁) of less than 80% of the predicted value. Samples of peripheral heparinized blood and sera were obtained before and after therapy completion. Three-colour immunofluorescence analysis was performed, and expression of CD11b and CD11c on CD4(+) T lymphocytes and monocytes as well as the expression of CD21 and CD23 on B cells were determined (n=12). Peripheral blood eosinophil count, changes in FEV₁ and peak expiratory flow rate (PEFR), asthma exacerbations, and as-needed use of beta-agonist were also monitored. **RESULTS:** Montelukast improved FEV₁ and PEFR, and decreased peripheral eosinophil counts in all study patients. There was no significant change in the expression of CD21 and CD23 on B cells. The expression of CD11c on CD4(+) T cells and of both CD11b and CD11c on monocytes remained similar to the pretreatment expression. However, the percentage of CD11b(+)CD4(+) T lymphocytes significantly decreased after treatment with montelukast. This was accompanied by a significant decrease in the levels of total IgE. **CONCLUSION:** The capacity of 6-week montelukast therapy to reduce the percentage of CD11b CD4(+) T cells might be a mechanism leading to the immune response modulation on this T cell subset interaction with CD23-expressing B cells and subsequent down-regulation of IgE synthesis.

Galassi C. et al. *Environment and respiratory diseases in childhood: the Italian experience.* *Int J Occup Environ Health.* 2005; 11(1) : 103-6.p **Abstract:** To estimate the prevalence of respiratory disorders in children, and to investigate the roles of potential environmental risk factors, including exposure to outdoor air pollution, a large multicenter, population based survey (SIDRIA) was conducted in Italy in 1994-1995. The study enrolled more than 40,000 children. Results allowed international comparisons of the prevalences of asthma and allergies in childhood in the framework of the ISAAC (International Study of Asthma and Allergies in Childhood) study, and supplied further evidence of the adverse respiratory effects of many environmental factors. The methods and main findings of the SIDRIA study are presented, focusing on the role of outdoor risk factors.

Galassi C. et al. *Changes in prevalence of asthma and allergies among children and adolescents in Italy: 1994-2002.* *Pediatrics.* 2006; 117(1) : 34-42.p **Abstract:** **BACKGROUND:** Several studies conducted during the 1990s indicated an increase in the prevalence of symptoms of asthma; more recent investigations suggest that the trend is stabilizing or may even be reversing. **OBJECTIVE:** We compared 2 cross-sectional surveys conducted in 1994 and 2002 in 8 areas in northern and central Italy, to evaluate prevalence changes for asthma, allergic rhinitis, and eczema. **METHODS:** The International Study of Asthma and Allergies in Childhood methods and questionnaires were used to investigate 6- to 7-year-old children (16,115 and 11,287 questionnaires completed by parents in 1994-1995 and 2002, respectively) and 13- to 14-year-old adolescents (19,723 and 10,267 questionnaires completed by adolescents in 1994-1995 and 2002, respectively). In each phase, the overall response rate was >90%. Prevalence changes were calculated as the

absolute difference between the prevalence recorded on the 2 occasions. RESULTS: The prevalence of wheeze (past 12 months) increased slightly among children (change: 0.8%; 95% confidence interval [CI]: 0.0% to 1.6%) and was rather stable among adolescents. Symptoms of allergic rhinitis (children: change: 5.2%; 95% CI: 4.0% to 6.4%; adolescents: change: 4.1%; 95% CI: 1.9% to 6.3%) and symptoms of atopic eczema (children: change: 4.4%; 95% CI: 3.6% to 5.2%; adolescents: change: 2.1%; 95% CI: 1.2% to 3.0%) increased clearly in both age groups. There was some heterogeneity across the centers among adolescents, especially for allergic rhinitis, with larger increases seen in the 3 metropolitan areas. The changes observed paralleled profound family changes, ie, better parental education, higher rates of maternal employment, and lower rates of exposure to parental smoke. These factors, however, do not explain all of the observed changes in prevalence. CONCLUSIONS: The results indicate that the epidemiologic features of asthma and allergies in Italy are changing rapidly, although the causes are still uncertain.

Galea S. et al. *Collaboration among community members, local health service providers, and researchers in an urban research center in Harlem, New York.* Public Health Rep. 2001; 116(6) : 530-9.p **Abstract:** The Urban Research Center at the Center for Urban Epidemiologic Studies brings together community members and researchers working in Harlem, New York. A Community Advisory Board (CAB) composed of community members, service providers, public health professionals, and researchers was formed to assist the Center's research and interventions and to guide community partnerships. Through a collaborative process, the CAB identified three public health problems—substance use, infectious diseases, and asthma—as action priorities. To deal with substance use, the Center created a Web-based resource guide for service providers and a "survival guide" for substance users, designed to improve access to community services. To deal with infectious diseases, the Center is collaborating with local community-based organizations on an intervention that trains injection drug users to serve as peer mentors to motivate behavior change among other injection drug users. To deal with asthma, the Center is collaborating with community child care providers on an educational intervention to increase asthma awareness among day care teaching staff, enhance communication between staff and families, and improve the self-management skills of children with asthma. The Center's experience has demonstrated that active communities and responsive researchers can establish partnerships that improve community health.

Gallagher C. *To bridge a quality chasm: connect with the guidelines.* J Spec Pediatr Nurs. 2002; 7(4) : 137-42.p **Abstract:** ISSUES AND PURPOSE: A wide chasm exists between the care we have and the care we could have. This article will inform nurses about the pediatric quality "chasm" by identifying practice variations from evidence-based guidelines for common childhood conditions. CONCLUSIONS: Nurses are accountable for providing state-of-the-art, evidence-based care to children. The pediatric quality chasm calls for nurses to stand up and speak out for children, to use and develop tools that activate the best scientific knowledge, and to empower parents to make it happen. PRACTICE IMPLICATIONS: Advocacy and patient-centered care are nurses' means to partner with parents and collaborate with colleagues to connect with the guidelines and bridge the quality chasm.

Ganter K. et al. *Association study of polymorphisms within matrix metalloproteinase 9 with bronchial asthma.* Int J Immunogenet. 2005; 32(4) : 233-6.p **Abstract:** Matrix metalloproteinase 9 plays an important role in the development of bronchial asthma. We were interested in whether the polymorphisms -T1702A, -C1562T, R279Q and +C6T within the matrix metalloproteinase 9 (MMP-9) gene were associated with asthma in a population of 231 asthmatic children.

However, we found no association. Thus MMP-9 might not be a major gene for asthma.

García García M.L. et al. *Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: the MOSAIC study.* Pediatrics. 2005; 116(2) : 360-9.p **Abstract:** BACKGROUND: Guidelines recommend daily controller therapy for mild persistent asthma. Montelukast has demonstrated consistent benefit in controlling symptoms of asthma and may be an alternative, orally administered, nonsteroidal agent for treating mild asthma. METHODS: The Montelukast Study of Asthma in Children (MOSAIC study) was a 12-month, multicenter, randomized, double-blind, noninferiority trial to determine the effect of once-daily, orally administered montelukast (5 mg) (n = 495), compared with twice-daily, inhaled fluticasone (100 microg) (n = 499), on the percentage of asthma rescue-free days (RFDs) (any day without asthma rescue medication and with no asthma-related resource use). Patients 6 to 14 years of age had mild persistent asthma (average percentage of predicted forced expiratory volume in 1 second: 87.2%; RFDs at baseline: 64%). Montelukast would be considered not inferior to fluticasone if the upper limit of the 95% confidence interval for the difference in mean percentages of RFDs (fluticasone minus montelukast) was above -7% (a difference of approximately 2 days/month). RESULTS: The mean percentage of RFDs was 84.0% in the montelukast group and 86.7% in the fluticasone group. The least-squares mean difference was -2.8% (95% confidence interval: -4.7% to -0.9%), within the noninferiority limit of -7%. The proportion of patients requiring systemic corticosteroids and the number of patients with an asthma attack were greater in the montelukast group. Both montelukast and fluticasone were well tolerated. CONCLUSIONS: Montelukast was demonstrated to be not inferior to fluticasone in increasing the percentage of RFDs among 6- to 14-year-old patients with mild asthma. Secondary end points, including percentage of predicted forced expiratory volume in 1 second value, days with beta-receptor agonist use, and quality of life, improved in both groups but were significantly better in the fluticasone treatment group.

García-Marcos L. et al. *Childhood asthma knowledge among first year nursing students in three European cities.* Allergol Immunopathol (Madr). 2004; 32(4) : 212-7.p **Abstract:** BACKGROUND: There are no available studies that assess and compare knowledge of childhood asthma among subjects living in different European countries. The objective of this study was to determine knowledge of childhood asthma among first year nursing students during the first week of their training in three European countries. The participants' sources of information and other factors that might influence their asthma knowledge score (AKS) were also evaluated. METHODS: Cross-sectional design using a modified version of a previously validated questionnaire. The study was undertaken in 261 students in Cartagena (Spain), 202 in Manchester (UK) and 94 in Cologne (Germany). RESULTS: AKS (maximum score, 27) was significantly higher in students from Manchester (18.3 +/- 2.6) than in those from Cartagena (15.9 +/- 3.1) and Cologne (15.1 +/- 3.6). In all three cities, more than 70 % of the students answered 10 out of the 27 questions correctly. Knowledge of asthma relievers or preventers was very limited. AKS showed a positive but marginal correlation with student age (r = 0.11, p = 0.07). Only knowledge gained from personal experience was significantly associated (r = 0.27, p < 0.001) with AKS. CONCLUSIONS: This study provides valuable new information about the variations, sources and factors that influence knowledge of asthma among educated individuals living in three European countries. The better AKS of Manchester students might be due to the higher prevalence of asthma in the UK.

García-Marcos L. et al. *BCG immunization at birth and atopic diseases in a homogeneous population of Spanish schoolchildren.* Int Arch Allergy Immunol. 2005; 137(4) : 303-9.p **Abstract:**

BACKGROUND: The role of immunization with bacillus Calmette-Guerin (BCG) in the prevalence of asthma, hay fever and atopic dermatitis is not definitely established and seems to be influenced by ethnic background. The aim of this study was to analyze the relationship between this immunization and the prevalence of those diseases in a homogeneous population of Spanish schoolchildren. **METHODS:** The International Study of Asthma and Allergies in Childhood (ISAAC) core and environmental questionnaires were used in four different centers of the Spanish North Atlantic coast. Bilbao, San Sebastian and Asturias have a universal BCG immunization policy during the first days of life, whereas La Coruna discontinued this practice in 1989. Except for this center, immunization coverage was above 90%. A random sample of schools of Asturias or all schools in the city district (rest of centers) with children 6 and 7 years old was surveyed. **RESULTS:** The participation rate was above 70%. After excluding those children born outside Spain, the numbers were 6,762 immunized and 2,828 nonimmunized. After adjusting for gender, age, smoking habits of the father and mother, truck traffic near the household, older and younger siblings and having a cat or a dog during the first year of the child's life, the adjusted ORs of the BCG-immunized children suffering from asthma, hay fever and atopic dermatitis were respectively 0.87 (95% CI 0.76-1.00), 0.87 (0.75-1.01) and 0.89 (0.76-1.05). **CONCLUSIONS:** BCG immunization offers a weak but significant protection against asthma and hay fever in Spanish schoolchildren.

Garcia-Marcos L. et al. *Validity of parent-reported height and weight for defining obesity among asthmatic and nonasthmatic schoolchildren.* *Int Arch Allergy Immunol.* 2006; 139(2) : 139-45.p **Abstract:** **BACKGROUND:** The relationship between parent-reported and measured height and weight is not well established in schoolchildren. This relationship has never been studied in asthmatic children. The objective of this study is to test the validity of the parent-reported weight and height for defining obesity by BMI and to know whether the perception of this height and weight changes when the child suffers from asthma. **METHODS:** All classes of children of the target ages of 6-8 years (n = 1,672, participation rate 70.2%) of all schools in four municipalities of Murcia (Spain) were included. Parents were asked about their children's weight and height using a questionnaire which included the International Study of Asthma and Allergies in Childhood (ISAAC) core questions on asthma. Parents were not aware that their children were going to be weighed and measured within 1 week's time. Measurements were performed using a rigid stadiometer to the nearest 0.1 cm and a scale to the nearest 0.1 kg. **RESULTS:** The bias (reported minus real) was, respectively, for nonasthmatics and asthmatics: weight +0.42 kg (95% CI +0.24; +0.59 kg) versus +0.97 kg (+0.50; +1.44 kg), height +2.37 cm (+2.06; +2.68 cm) versus +2.87 cm (+1.87; +3.87 cm); BMI -0.39 kg/m(2) (-0.52; -0.23 kg/m(2)) versus -0.23 kg/m(2) (-0.58; +0.13 kg/m(2)). Diagnostic accuracy of obesity calculated from reported measurements was, respectively, for nonasthmatics and asthmatics: sensitivity 78.0 versus 77.8%, specificity 96.2 versus 94.5%, positive predictive value 77.2 versus 73.7% and negative predictive value 96.4 versus 91.7%. **CONCLUSIONS:** Reported weights and heights had large biases, comparable between parents of both asthmatic and those of nonasthmatic children. However, this information could be reasonably valid for classifying children as obese or nonobese in large epidemiological studies.

Garcia-Ortega P. et al. *Isolated chronic conjunctivitis due to storage mite allergy.* *Ann Allergy Asthma Immunol.* 2006; 96(5) : 754-5.p

Garde J. et al. *Tolerance of a Salsola kali extract standardized in biological units administered by subcutaneous route. Multicenter study.* *Allergol Immunopathol (Madr).* 2005; 33(2) : 100-4.p **Abstract:** **BACKGROUND:** Sensitivity to Salsola kali is a frequent cause of allergic respiratory disease in various regions of Spain. However, there are very few articles in which this allergen has been

studied. **METHODS AND RESULTS:** In order to evaluate the tolerance of this extract, a prospective study has been performed. This study was observational, multi-centred and open, involving 88 patients with allergic respiratory disease due to sensitivity to Salsola, aged between 5 and 52 years. The administration of the extract was performed subcutaneously, through one of two treatment schedules: cluster (8 doses in 4 visits) or conventional (13 doses in 12 visits). A total of 42 adverse reactions were registered, in 26 patients (35 local reactions in 21 patients and 7 systemic reactions in 6 patients). Among the 7 systemic reactions, 4 were registered with the cluster protocol and 2 with the conventional protocol (p = 0.329). In no patients were serious adverse reactions registered. **CONCLUSION:** The subcutaneous administration of a Salsola extract is safe and well tolerated, both when administered using a conventional schedule and when using a cluster schedule.

Gauderman W.J. et al. *Childhood asthma and exposure to traffic and nitrogen dioxide.* *Epidemiology.* 2005; 16(6) : 737-43.p **Abstract:** **BACKGROUND:** Evidence for a causal relationship between traffic-related air pollution and asthma has not been consistent across studies, and comparisons among studies have been difficult because of the use of different indicators of exposure. **METHODS:** We examined the association between traffic-related pollution and childhood asthma in 208 children from 10 southern California communities using multiple indicators of exposure. Study subjects were randomly selected from participants in the Children's Health Study. Outdoor nitrogen dioxide (NO₂) was measured in summer and winter outside the home of each child. We also determined residential distance to the nearest freeway, traffic volumes on roadways within 150 meters, and model-based estimates of pollution from nearby roadways. **RESULTS:** Lifetime history of doctor-diagnosed asthma was associated with outdoor NO₂; the odds ratio (OR) was 1.83 (95% confidence interval=1.04-3.22) per increase of 1 interquartile range (IQR=5.7 ppb) in exposure. We also observed increased asthma associated with closer residential distance to a freeway (1.89 per IQR; 1.19-3.02) and with model-based estimates of outdoor pollution from a freeway (2.22 per IQR; 1.36-3.63). These 2 indicators of freeway exposure and measured NO₂ concentrations were also associated with wheezing and use of asthma medication. Asthma was not associated with traffic volumes on roadways within 150 meters of homes or with model-based estimates of pollution from nonfreeway roads. **CONCLUSIONS:** These results indicate that respiratory health in children is adversely affected by local exposures to outdoor NO₂ or other freeway-related pollutants.

Gauvin S. et al. *Contribution of indoor and outdoor environments to PM_{2.5} personal exposure of children--VESTA study.* *Sci Total Environ.* 2002; 297(1-3) : 175-81.p **Abstract:** Several studies among adult populations showed that an array of outdoor and indoor sources of particles emissions contributed to personal exposures to atmospheric particles, with tobacco smoke playing a prominent role (J. Expo. Anal. Environ. Epidemiol. 6 (1996) 57, Environ. Int. 24 (1998) 405, Arch. Environ. Health 54 (1999) 95). The Vesta study was carried out to assess the role of exposure to traffic emissions in the development of childhood asthma. In this paper, we present data on 68 children aged 8-14 years, living in the metropolitan areas of Paris (n = 30), Grenoble (n = 15) and Toulouse (n = 23), France, who continuously carried, over 48 h, a rucksack that contained an active PM_{2.5} sampler. Data about home indoor sources were collected by questionnaires. In parallel, daily concentrations of PM₁₀ in ambient air were monitored by local air quality networks. The contribution of indoor and outdoor factors to personal exposures was assessed using multiple linear regression models. Average personal exposure across all children was 23.7 microg/m³ (S.D. = 19.0 microg/m³), with local means ranging from 18.2 to 29.4 microg/m³. The final model explains 36% of the total between-subjects variance, with environmental tobacco smoke contributing for more than a third to this variability; presence of pets at home, proximity of the home to urban traffic emissions, and concomitant PM₁₀ ambient air

concentrations were the other main determinants of personal exposure.

Gdalevich M. et al. *Breast-feeding and the risk of bronchial asthma in childhood: a systematic review with meta-analysis of prospective studies.* J Pediatr. 2001; 139(2) : 261-6.p Abstract:

BACKGROUND: The protective effect of breast-feeding on the development of childhood asthma remains a matter of controversy. We conducted a systematic review of prospective studies that evaluated the association between exclusive breast-feeding during the first 3 months after birth and asthma. **STUDY DESIGN:** We searched the 1966-1999 MEDLINE database and reviewed reference lists of relevant articles to identify 12 prospective studies that met pre-stated inclusion criteria. Methodological aspects of the studies, duration and exclusivity of breast-feeding, and outcomes were assessed. Effect estimates were abstracted by the investigators, using a standardized approach. **RESULTS:** The summary odds ratio (OR) for the protective effect of breast-feeding was 0.70 (95% CI 0.60 to 0.81). The effect estimate was greater in studies of children with a family history of atopy (OR = 0.52) than in studies of a combined population (OR = 0.73). **CONCLUSIONS:** Exclusive breast-feeding during the first months after birth is associated with lower asthma rates during childhood. The effect, caused by immunomodulatory qualities of breast milk, avoidance of allergens, or a combination of these and other factors, strengthens the advantage of breast-feeding, especially if a family history of atopy is present.

Gehring U. et al. *Traffic-related air pollution and respiratory health during the first 2 yrs of life.* Eur Respir J. 2002; 19(4) : 690-8.p Abstract:

As part of an international collaborative study on the impact of Traffic-Related Air Pollution on Childhood Asthma (TRAPCA), the health effects associated with long-term exposure to particles with a 50% cut-off aerodynamic diameter of 2.5 microm (PM_{2.5}), PM_{2.5} absorbance, and nitrogen dioxide (NO₂) were analysed. The German part of the TRAPCA study used data from subpopulations of two ongoing birth cohort studies (German Infant Nutrition Intervention Programme (GINI) and Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children (LISA)) based in the city of Munich. Geographic information systems (GIS)-based exposure modelling was used to estimate traffic-related air pollutants at the birth addresses of 1,756 infants. Logistic regression was used to analyse possible health effects and potential confounding factors were adjusted for. The ranges in estimated exposures to PM_{2.5}, PM_{2.5} absorbance, and NO₂ were 11.9-21.9 microg m⁻³, 1.38-4.39 x 10⁻⁵ m⁻¹, and 19.5-66.9 microg x m³, respectively. Significant associations between these pollutants and cough without infection (odds ratio (OR) (95% confidence interval (CI)): 1.34 (1.11-1.61), 1.32 (1.10-1.59), and 1.40 (1.12-1.75), respectively) and dry cough at night (OR (95% CI): 1.31 (1.07-1.60), 1.27 (1.04-1.55), and 1.36 (1.07-1.74), respectively) in the first year of life were found. In the second year of life, these effects were attenuated. There was some indication of an association between traffic-related air pollution and symptoms of cough. Due to the very young age of the infants, it was too early to draw definitive conclusions from this for the development of asthma.

Gehring U. et al. *Parental education and children's respiratory and allergic symptoms in the Pollution and the Young (PATY) study.* Eur Respir J. 2006; 27(1) : 95-107.p Abstract:

Inequalities in health between socio-economic groups are a major public health concern. The current authors studied associations between parental socio-economic status (SES) and children's respiratory and allergic symptoms in 13 diverse countries, including the Russian Federation, North America (Canada and the USA), and countries across Eastern and Western Europe. Data of 57,000 children aged 6-12 yrs, originating from eight cross-sectional studies, were analysed. SES was defined by parental education. Respiratory and allergic

symptoms were defined by parental questionnaire reports. Multiple logistic regressions showed that low parental education was associated with a decreased risk of inhalant allergy and itchy rash in school children. Furthermore, low parental education was associated with an increased prevalence of wheeze and nocturnal dry cough. No clear association was found between parental education and prevalence of doctor-diagnosed asthma and bronchitis. Part of the difference between socio-economic groups with regard to their children's symptoms was explained by established risk factors, such as parental allergy, smoking during pregnancy, pet ownership, crowding, mould/moisture in the home, use of gas for cooking, and air pollution (particulate matter with a diameter of <10 microm). However, differences remained after adjusting for these variables. Children's health was associated with parental education. The association could not fully be explained by established risk factors.

Gemou-Engesaeth V. et al. *Expression of activation markers and cytokine mRNA by peripheral blood CD4 and CD8 T cells in atopic and nonatopic childhood asthma: effect of inhaled glucocorticoid therapy.* Pediatrics. 2002; 109(2) : E24.p Abstract:

HYPOTHESIS: Activated CD8 as well as CD4 T cells contribute to the production of asthma-relevant cytokines in both atopic and nonatopic childhood asthma. **OBJECTIVES:** To measure the percentages of peripheral blood CD4 and CD8 T cells expressing naive/memory (CD45RA/CD45RO) and activation (HLA-DR, CD25) markers, as well as mRNA-encoding interleukin-4 (IL-4) and interleukin-5 (IL-5) in atopic and nonatopic childhood asthmatics and in nonasthmatic controls matched for age and atopic status; and to study the effects of inhaled glucocorticoid therapy of the asthmatics on these measurements. **METHODS:** Peripheral blood mononuclear cells were isolated from 17 atopic and 8 nonatopic stable (not acutely ill) asthmatics aged 7 to 16 years with moderate-to-severe disease and from 15 nonasthmatic controls matched for age and atopic status. Activation markers on CD4 and CD8 T cells were measured by flow cytometry, and expression of cytokine mRNA by in situ hybridization with CD4 and CD8 T cells were isolated using magnetic beads. Measurements were repeated in 18 of the asthmatics 4 to 6 months after initiation or escalation of inhaled glucocorticoid therapy for inadequately controlled asthma. **RESULTS:** The percentages of CD4 T cells expressing CD45RO but not CD45RA were elevated in both asthma groups as compared with the relevant controls and were reduced in association with de novo or augmented inhaled glucocorticoid therapy. The percentages of CD8 T cells expressing both markers were not elevated in asthmatics as compared with controls. The percentages of both CD4 and CD8 T lymphocytes expressing HLA-DR and CD25 were elevated in the asthmatics as compared with controls, and significantly reduced in association with de novo or augmented inhaled glucocorticoid therapy. Elevated percentages of CD4 T cells expressing mRNA encoding IL-4 and IL-5, and CD8 T lymphocytes expressing IL-5, were found in asthmatics as compared with the controls. De novo or augmented inhaled glucocorticoid therapy was associated with significant reductions in the percentages of CD4 T cells expressing IL-5 and IL-4 mRNA, as well as improvements in lung function, symptom scores, and bronchial hyperresponsiveness to metacholine (PD₂₀) in both the atopic and nonatopic asthmatics. **CONCLUSIONS:** The data are consistent with the hypothesis that both activated CD4 and CD8 T cells are associated with child asthma, and that CD4 T cells make a greater contribution to IL-4 and IL-5 synthesis. Increased dosages of inhaled glucocorticoid resulted in clinical improvement in the asthmatics along with reduced T-cell activation and cytokine mRNA expression, suggesting a possible causal association.

Gendrel D. et al. *[Mycoplasma pneumoniae, community-acquired pneumonia and asthma].* Arch Pediatr. 2005; 12 Suppl 1 : S7-11.p Abstract:

Mycoplasma pneumoniae is an intracellular pathogen, devoid of cell wall, able to invade airway epithelial cells. Infection may either remain asymptomatic or induce bronchitis and pneumonia. M. pneumoniae is the first-ranking aetiological agent of

community-acquired pneumonias in children over five years of age. Clinical features are usually mild, but this should not preclude the initiation of a treatment, in order to avoid serious sequelae such as impairment of pulmonary gas exchange capacity. In children at high-risk of asthma, infection with *M. pneumoniae* can induce exacerbation. A survey was performed in children admitted to hospital Saint-Vincent-de-Paul (Paris) for an episode of severe asthma exacerbation with persistent hypoxemia. Mycoplasma infection was identified in 26% of children with a history of asthma and 50% of those for whom the exacerbation was the presenting manifestation of the disease. Furthermore, if the Mycoplasma infection was atypical, asthma exacerbation recurred within one month. *M. pneumoniae* should be considered not only as a preeminent agent of respiratory infection in children, but also as a triggering factor in exacerbation and even inception of asthma. As a consequence, it is mandatory to carefully search for and actively treat Mycoplasma infection in children.

Gentile D. et al. *Association between environmental tobacco smoke and diminished dendritic cell interleukin 10 production during infancy.* Ann Allergy Asthma Immunol. 2004; 92(4) : 433-7.p **Abstract:** BACKGROUND: Diminished interleukin 10 (IL-10) production has been documented in children and adults with asthma and atopy. Environmental tobacco smoke (ETS) is recognized as a risk factor for the development of childhood asthma. OBJECTIVE: To determine whether there is an association between ETS and dendritic cell (DC) IL-10 production during infancy. METHODS: ETS was evaluated by questionnaire, and blood samples were obtained at 2 weeks, 3 months, and 5 months of age in 37 healthy infants. DCs were cultured and stimulated, and supernatants were assayed for IL-10 by enzyme immunoassay. RESULTS: Sixteen infants had no history of exposure to ETS, and 21 infants had a history of ETS exposure. The frequency of subjects with detectable IL-10 levels was similar in both groups at 2 weeks and 3 months but significantly different at 5 months ($P < .001$). In those without ETS exposure, the frequency with detectable IL-10 levels increased during the observation period (25% at 2 weeks, 20% at 3 months, and 36% at 5 months; $P = .03$ vs 2 weeks). In contrast, in those with ETS exposure, the frequency with detectable IL-10 levels decreased during the observation period (33% at 2 weeks, 19% at 3 months; $P = .02$ vs 2 weeks; and 7% at 5 months; $P < .001$ vs 2 weeks). CONCLUSIONS: Our study results demonstrate an association between ETS and diminished DC IL-10 production during infancy. Future studies need to expand on these sample sizes and explore whether diminished DC IL-10 production is the mechanism by which ETS predisposes patients to the development of asthma and/or atopy.

Gentile D.A. et al. *Association between TNF-alpha and TGF-beta genotypes in infants and parental history of allergic rhinitis and asthma.* Hum Immunol. 2004; 65(4) : 347-51.p **Abstract:** The development and expression of allergic rhinitis and asthma may be influenced by the elaboration of specific cytokines. Cytokine genotypes moderate illness severity in a variety of inflammatory disorders. Cytokine genotyping was performed on 124 infants (85% white, 57% male) to determine whether specific cytokine genotypes are associated with a parental history of allergic rhinitis and/or asthma. DNA was extracted from buccal brushings and assayed for tumor necrosis factor alpha (TNF-alpha), interferon gamma (IFN-gamma), interleukin (IL)-6, IL-10, and transforming growth factor (TGF)-beta1 genotypes using polymerase chain reaction-sequence specific primer technology. Outcomes consisted of parental history of allergy and asthma, and results were evaluated by logistic regression. TNF-alpha and TGF-beta genotypes were related to maternal and/or paternal history of allergic rhinitis and asthma, respectively. The frequencies of the genotype associated with high production of TNF-alpha were 41% versus 18% in infants with and without a parental history of allergic rhinitis, respectively ($p < 0.01$). The frequencies of the genotype associated with low production of TGF-beta1 were 14% versus 1% in infants with and without a

parental history of asthma, respectively ($p < 0.01$). There were no associations between IFN-gamma, IL-6, and IL-10 genotypes and any of the outcome parameters. These results suggest a role for TNF-alpha and TGF-beta1 genotypes in the pathogenesis of allergic rhinitis and asthma, respectively. If confirmed by future studies, cytokine genotyping may be a useful tool for identifying at-risk infants who may benefit from the selective use of preventative and/or early intervention treatments for these disorders.

Gentile D.A. et al. *Diminished dendritic cell interleukin 10 production in atopic children.* Ann Allergy Asthma Immunol. 2004; 92(5) : 538-44.p **Abstract:** BACKGROUND: Diminished interleukin 10 (IL-10) and/or IL-12 production may contribute to the pathogenesis of asthma and atopy. Dendritic cells (DCs) produce these cytokines and have been implicated in the pathogenesis of these disorders. OBJECTIVE: To determine whether DC IL-10 and/or IL-12 production is diminished in children aged 6 to 12 years with allergic rhinitis (AR) and with or without asthma. METHODS: Monocyte-derived DCs were isolated from 20 subjects without AR or asthma (group 1), 20 subjects with AR without asthma (group 2), and 20 subjects with AR and asthma (group 3). Asthma was defined as a history of physician-diagnosed disease, and AR was defined as a positive history and positive puncture skin test responses (wheal \geq or = 5 mm) to relevant inhalant allergens. DCs were stimulated with either lipopolysaccharide (LPS) or diluent and cultured for 24 hours. Supernatants were assayed for IL-10 and IL-12 levels by enzyme-linked immunosorbent assay. RESULTS: DC IL-10 production was diminished in groups 2 and 3 compared with group 1. Median LPS-induced IL-10 levels were 11.0 pg/mL in group 1, 6.1 pg/mL in group 2, and 1.5 pg/mL in group 3. The frequencies of subjects with detectable IL-10 levels were 85%, 20%, and 20% in groups 1, 2 and 3, respectively. Median LPS-induced IL-12 levels were similar in all groups. CONCLUSIONS: These data support the hypothesis that atopic subjects have an intrinsic inability to up-regulate DC IL-10 production. Future studies in this area could lead to a better understanding of the pathogenesis of atopy.

Georgiou A. et al. *The impact of a large-scale population-based asthma management program on pediatric asthma patients and their caregivers.* Ann Allergy Asthma Immunol. 2003; 90(3) : 308-15.p **Abstract:** BACKGROUND: The consequences of pediatric asthma include missed school attendance, limitations in physical activity, and increased health care utilization and costs. Caregivers of asthmatic children are affected through missed work days and decreased job productivity. In response to these issues, a disease management program encompassing asthmatic children and their caregivers was developed as part of the core services offered to members of a large, national health care plan. OBJECTIVE: To determine the impact of the asthma management program on pediatric asthma patients and their caregivers over a 12-month period. METHODS: In this longitudinal study, 401 randomly selected member households with asthmatic children from 17 regional markets completed surveys before and after 12 months of participation in the asthma management program. Program interventions, which were tailored according to risk and need status, included various staggered educational mailings, reminder aids, videos, a peak expiratory flow rate meter, and telephonic case management. The Asthma Quality Assessment System survey, a battery of self-reported quality indicators, was used to solicit information from parents or caregivers of asthmatic children on issues pertaining to quality of life, asthma management skills and knowledge, and lost work/school days related to asthma. RESULTS: Statistically significant postprogram outcomes were observed in various domains, including a reduction in adverse utilization, symptomatology, and restricted activity days for children and lost work days for adult caretakers. CONCLUSIONS: These findings demonstrate that a large-scale population-based intervention program can produce measurable clinical and economic benefits, thereby lessening the burden of asthma on the family unit.

Ghiro L. et al. *Effect of montelukast added to inhaled corticosteroids on fractional exhaled nitric oxide in asthmatic children.* Eur Respir J . 2002; 20(3) : 630-4.p **Abstract:** The aim of this prospective, self-controlled, single-blind study was to assess the effect of montelukast added to maintenance therapy with inhaled corticosteroids (ICS) on fractional exhaled nitric oxide (FENO) in asthmatic children. Thirty-five children (age 11.2 \pm 0.4 yrs (mean \pm SEM)) with mild-to-moderate persistent asthma treated with low to medium doses of ICS and FENO > 20 parts per billion (ppb) were included. The patients were randomly assigned to two groups: 17 patients continued ICS (group C) and 18 had montelukast added to ICS for 3 weeks (group M). FENO measurements were performed in both groups at baseline (T1) and after 3 weeks (T2), and in group M also after 2 weeks of washout. FENO was measured by a chemiluminescence analyser using an on-line method (50 mL x s(-1)) with nitric oxide-free air. The overall mean daily dose of ICS was equivalent to 530 \pm 58 microg x day(-1) of beclomethasone in group M and to 564 \pm 55 microg x day(-1) of beclomethasone in group C. There were no significant differences in baseline FENO and forced expiratory volume in one second (FEV1) between the two groups. After 3 weeks there was a significant reduction of FENO values in patients of group M (T1 52.2 \pm 7.8 ppb, T2 36.1 \pm 4.6 ppb) but no significant changes in group C (T1 43.5 \pm 6.0 ppb, T2 47.8 \pm 9.4 ppb). In group M after 2 weeks of montelukast withdrawal, FENO rose to baseline values (55.6 \pm 8.7 ppb). In conclusion, after montelukast treatment there is a fractional exhaled nitric oxide reduction in asthmatic children receiving maintenance therapy with inhaled corticosteroids. This suggests an anti-inflammatory effect of montelukast additive to that of inhaled corticosteroids.

Ghose M.K. et al. *Assessment of the status of urban air pollution and its impact on human health in the city of Kolkata.* Environ Monit Assess . 2005; 108(1-3) : 151-67.p **Abstract:** Air pollution has significant effects on exacerbation of asthma, allergy and other respiratory diseases. Like many other magacities in the world the ambient air quality of Kolkata is also being deteriorated day by day. Automobile exhausts and certain industrial pollutants produce O(3) by photochemical reactions. The particulate matter, particularly less than 10 microm in size, can pass through the natural protective mechanism of human respiratory system and plays an important role in genesis and augmentation of allergic disorders. Sources of air pollution in the area and the unique problem arising out of the emission from the vehicles, industries, etc. have been described. Ambient air quality was monitored along with micrometeorological data and the results are discussed. The status of air pollution in the area has been evaluated and a questionnaire survey was conducted to estimate the allergic symptoms and exposure to assess the respiratory disorders. The data are analysed to evaluate the critical situation arising out of the emission of air pollutants and the impact on human health due to respirable diseases (RDs) to middle class sub-population (activity-wise) in the area are assessed. A strategic air quality management plan has been proposed. For the mitigation of air pollution problems in the city, the different measures to be adopted to maintain the balance between sustainable development and environmental management have been discussed.

Gibson P.G. et al. *Migration to a western country increases asthma symptoms but not eosinophilic airway inflammation.* Pediatr Pulmonol. 2003; 36(3) : 209-15.p **Abstract:** The prevalence of asthma symptoms varies markedly throughout the world. However, the asthma mechanisms involved are not defined. Studying the effects of migration can help identify the reasons for this geographic variation. The aims of this study were to examine the prevalence of asthma symptoms, airway hyperresponsiveness (AHR), and induced sputum eosinophils in adolescents who migrate to Australia. The study was conducted in Sydney, Australia, where adolescent students completed a video symptom questionnaire, hypertonic saline

challenge, sputum induction, and allergy skin testing. The 211 students had widely different cultural backgrounds, including Asian, South Pacific, Middle Eastern, European, and African countries. Among adolescents who were migrants to Australia, the prevalence of asthma symptoms was higher than that reported using a similar methodology in their country of origin. Asthma symptom prevalence was related to residence time in Australia. The prevalence of wheeze was 17.2% in recent arrivals, 20.5% in adolescents living in Australia for >2 years, and 36.3% in those living all their lifetime in Australia (P = 0.013). For every year of residence in Australia, there was an 11% increase in prevalence of current wheeze (odds ratio, 1.11; P = 0.02). This effect was not related to atopy, AHR, or eosinophilic airway inflammation. Sputum neutrophils were elevated in recent arrivals. In conclusion, adolescents who migrate to Australia report increased asthma symptoms, compared to their country of origin, and asthma symptoms are further increased for every additional year of residence in Australia. The development of wheeze after migration to Australia was independent of eosinophilic inflammation and consistent with noneosinophilic asthma mechanisms.

Gibson P.G. et al. *Relationship between induced sputum eosinophils and the clinical pattern of childhood asthma.* Thorax. 2003; 58(2) : 116-21.p **Abstract:** BACKGROUND: The relationship between the clinical pattern of asthma and airway inflammation in childhood asthma is poorly characterised, yet underpins the treatment recommendations in current asthma guidelines. A study was undertaken to examine the relationship between airway inflammation and clinical asthma in children. METHODS: Children with asthma (n=146) and healthy controls (C, n=37) were recruited from primary and specialist clinics. Sputum induction and hypertonic saline challenge were performed. RESULTS: As the frequency of asthma episodes in the past 12 months increased, there were significant increases in sputum eosinophils (median; infrequent episodic (IE) 1.5%, frequent episodic (FE) 2.3%, persistent (P) 3.8%, control (C) 1.0%; p=0.002), sputum eosinophil cationic protein (ECP) (IE 113 ng/ml, FE 220, P 375, C 139; p=0.003), and desquamated bronchial epithelial cells (IE 2.0%, FE 6.0%, P 5.0%, C 2.5%; p=0.04). Treatment intensity was also associated with increased sputum eosinophils (p=0.005). The relationships between other severity markers (current symptoms, lung function) were less strong. CONCLUSION: Children with more frequent episodes of clinical asthma exhibit increasing airway inflammation that is characterised by sputum eosinophilia and bronchial epithelial desquamation. The results support clinical assessment by frequency of wheezing episodes over the past 12 months when determining anti-inflammatory treatment requirements, and indicate that current symptoms are determined by mechanisms in addition to sputum eosinophilia.

Gidding S.S. et al. *Severe obesity associated with cardiovascular deconditioning, high prevalence of cardiovascular risk factors, diabetes mellitus/hyperinsulinemia, and respiratory compromise.* J Pediatr. 2004; 144(6) : 766-9.p **Abstract:** OBJECTIVE: To determine the extent and severity of obesity-related cardiorespiratory morbidity in children with body mass index (BMI) \geq 40 kg/m(2). STUDY DESIGN: Cross-sectional analysis of a cohort comprised of 48 boys and girls aged 8 to 17 years with BMI \geq 40 kg/m(2). Cardiorespiratory fitness (graded cycle exercise test), left ventricular (LV) mass (echocardiography), blood pressure, fasting lipid profile, fasting insulin, fasting glucose, HbA1c, and pulmonary function (spirometry and sleep studies) were measured. RESULTS: The cohort averaged 14.2 \pm 2 years of age with mean BMI of 45.5 kg/m(2). Only 2 patients had normal fitness; 37 of 48 had peak oxygen consumption $<$ 20 mL O(2)/minute. Hypertension was present in 10 of 48 patients. Mean lipid values were: triglycerides 103 \pm 48 mg/dL, HDL cholesterol 41 \pm 10 mg/dL, and LDL cholesterol 108 \pm 26 mg/dL. Type II diabetes mellitus was diagnosed in 6 patients. Mean fasting insulin was 31 \pm 19 microU/mL. Asthma treatment, small airways disease by pulmonary function testing, or both were

present in 35 of 48 patients; upper airway obstruction was present in 7 patients. LV hypertrophy was present in 8 patients, with a mean LV mass of 43 +/- 11 g/m(2.7). CONCLUSIONS: Children and adolescents with BMI >or=40 kg/m(2) have substantial cardiorespiratory morbidity including severe physical deconditioning.

Gilberg K. et al. *Analysis of medication use patterns: apparent overuse of antibiotics and underuse of prescription drugs for asthma, depression, and CHF.* J Manag Care Pharm. 2003; 9(3) : 232-7.p Abstract: OBJECTIVE: To assess the appropriateness of prescription medication use based upon widely accepted treatment guidelines. METHODS: We analyzed administrative claims for the period October 1, 1998, through September 20, 1999, supplied by 3 California health plans to determine medication use patterns for outpatient prescriptions. We compared these patterns to those expected in the presence of adherence to treatment guidelines. RESULTS: During the study period, only 27.5% of antidepressant users received the recommended 6 months of continuous therapy, only 49.0% of diagnosed asthma patients received at least one inhaled corticosteroid prescription (compared to 67.1% who received at least one inhaled beta-agonist prescription), and only 54.5% of patients diagnosed with congestive heart failure (CHF) received an angiotensin-converting enzyme (ACE) inhibitor. Of patients who had a diagnosis of common cold or upper respiratory tract infection, 35.7% received antibiotics. CONCLUSION: There is a remarkable degree of apparent overuse and underuse of prescription medications despite the existence of clinical guidelines to support appropriate use in the conditions studied. Effective medications appear to be underused for patients with asthma, CHF, and depression. Antibiotics appear to be overused for the common cold and upper respiratory infections. More effective efforts must be made to address appropriate use of medications. Without these efforts, improved quality of care and decreased total health system costs are unlikely to be realized.

Gilchrist H.K. *Parents' perspectives of asthma crisis hospital management in infants and toddlers: an interpretive view through the lens of attachment theory.* J Pediatr Nurs. 2004; 19(1) : 70-1.p

Gillespie J.A. *Not all that wheezes is asthma.* Nurs BC. 2003; 35(2) : 7.p

Gillespie J.A. *Optimal asthma care.* Nurs BC. 2002; 34(5) : 21-3.p

Gillies J. et al. *PHARMAC and Ventolin in New Zealand.* N Z Med J. 2005; 118(1220) : U1616.p Abstract: Recently, PHARMAC undertook an unfortunate experiment on asthma sufferers when it fundamentally changed its funding support for reliever medications. Ventolin metered dose inhaler (MDI), the backbone of asthma relief for over 30 years, was dropped in favour of Salamol, a post-patent salbutamol in a device which, within the first few weeks of use, has been found to be ineffective by many patients, and thus potentially dangerous. PHARMAC has agreed to reconsider its decision, but how was this decision reached in the first place?

Gilliland F.D. et al. *Effects of early onset asthma and in utero exposure to maternal smoking on childhood lung function.* Am J Respir Crit Care Med. 2003; 167(6) : 917-24.p Abstract: Both in utero exposures to maternal smoking and asthma are associated with chronic deficits in lung function. We hypothesized that in utero exposure affects lung function in children without asthma and synergistically affects children with early onset asthma. To investigate effects of in utero exposure and age at asthma diagnosis on lung function, we examined longitudinal medical history, tobacco smoke exposure, and lung function data from 5,933 participants in the Children's Health Study. We found that children exposed in utero, but without asthma, showed decreased FEV1/FVC, FEF25-75, and FEF25-75/FVC ratio. Among

children without in utero exposure, early asthma diagnosis was associated with larger decreases in FEV1, FEF25-75, and FEV1/FVC ratio compared with later diagnosed asthma. Children with in utero exposure alone and early onset asthma showed deficits in FEV1 (-13.6%; 95% confidence interval [CI], -18.9 to -8.2) and FEF25-75 (-29.7%; 95% CI, -37.8 to -20.5) among boys; and FEF25-75 (-26.6%; 95% CI, -36.4 to -15.1) and FEV1/FVC (-9.3%; 95% CI, -12.9 to -5.4) among girls. The absolute differences in FEF25-75 associated with in utero exposure increased with age in children with early onset asthma. We found little evidence for effects from environmental tobacco smoke exposure alone. In summary, deficits in lung function were largest among children with in utero exposure and early onset asthma.

Gioldassi X.M. et al. *Clara cell secretory protein: determination of serum levels by an enzyme immunoassay and its importance as an indicator of bronchial asthma in children.* J Pharm Biomed Anal. 2004; 34(4) : 823-6.p Abstract: Clara cell secretory protein (CC16) is a 16kDa protein secreted by Clara cells in the lining fluid of bronchiolar and bronchial epithelium. CC16 presents several biologic properties, and has been shown to have immunomodulatory and anti-inflammatory activity. It may play a role in controlling inflammation in the airway. There is some evidence that the CC16 level is primarily lower in adult individuals with bronchial asthma, thus contributing to its pathophysiology. This study was designed to examine CC16 serum levels of children, healthy and with asthma. An enzyme solid phase immunoassay utilizing monoclonal antibody to CC16 was the analytical method to determine the protein concentration in blood sera. The method showed excellent linearity, high sensitivity (detection limit: <50 ng/l) and precision. It was found that asthmatic children appear significantly lower levels (P < 0.001) of CC16 in serum as compared to healthy ones. It is, therefore, concluded that CC16 may be a useful diagnostic index of bronchial asthma in the early child-age.

Girolomoni G. et al. *The epidemiology of atopic dermatitis in Italian schoolchildren.* Allergy. 2003; 58(5) : 420-5.p Abstract: BACKGROUND: Atopic dermatitis (AD) is common in children in industrialized countries. Only one large population study on its prevalence has been conducted in Italy, based on self-report questionnaire. The present study was designed to estimate the prevalence of AD in schoolchildren in Italy by dermatologists' assessment and by UK Working Party criteria, and to investigate associated symptoms and factors. METHODS: Cross-sectional survey on a random sample of 9-year-old schoolchildren from seven Italian cities. Children were examined by experienced dermatologists. Parents and teachers answered standardized questionnaires. RESULTS: Of the 1369 children examined, 88 had a diagnosis of AD, with an estimated point prevalence of 5.8% (95% CI 4.5-7.1) in the reference population. The reported lifetime prevalence was 15.2 (95% CI 12.2-18.2) for AD, 11.9% (95% CI 9.0-14.8) for asthma, and 17.6% (95% CI 14.6-20.7) for rhinoconjunctivitis. The strongest associated factor was the presence of AD in at least one parent. No association of AD with maternal smoking during pregnancy, birth weight, maternal age at the time of the child birth and breast-feeding was observed. The environmental characteristics of the house and the school did not correlate with the prevalence of AD. Episodes of lower respiratory tract infections were associated with asthma, and to a lower extent also with AD and rhinitis. CONCLUSIONS: The prevalence of doctor-diagnosed AD in Italian schoolchildren is comparable to those reported for other developed countries. Family history of atopy was the single most important associated factor, while the complex interplay of environmental factors remains to be elucidated.

Giroux M. et al. *Exhaled NH3 and excreted NH4+ in children in unpolluted or urban environments.* Environ Int. 2002; 28(3) : 197-202.p Abstract: Exhaled ammonia (NH3ex) was measured by

chemiluminescence in a group of healthy children (n = 20) and in two groups of asthmatic children, one (Group 1) residing in a National Park in the mountains (n = 68) and other (Group 2) in an urban area (n = 52). We also determined urinary ammonia, nitrates, urea, sodium and potassium normalized to osmolality. Unlike exhaled nitric oxide (NO_{ex}), NH_{3ex} was not specific to asthma as the children in Group 2 and the controls exhaled more ammonia than did the children in Group 1 (14.3 +/- 10.2 and 14.8 +/- 10.3 vs. 5.6 +/- 4.7 ppb; P < .001, respectively). In the urban environment, all children, including the healthy controls, excreted more ammonia (P < .001) and potassium (P < .001) but less urea (P < .02) than did the children residing in the National Park. These manifestations of moderate metabolic acidosis would favor excretion of ammonia at the expense of urea. In the children residing in the National Park, positive correlations were observed between NH_{3ex} and urinary ammonia, and nitrates, age and morphological parameters. The relationship with the morphological parameters is a reflection of the normal physiological formation of NH_{3ex}. In the children residing in the urban area, the other endogenous source of NH_{3ex} was attributed to a slight disturbance in acid-base balance. In conclusion, the measurement of NH_{3ex} appeared of limited interest, although the higher urinary urea/NH₄⁺ ratio in Group 1 (P < .0001), especially in the treated children, appeared to be linked to the lack of atmospheric pollutants in the National Park. Further experimentation is in progress to confirm these findings.

Glasgow N.J. et al. *Proactive asthma care in childhood: general practice based randomised controlled trial.* BMJ. 2003; 327(7416) : 659.p
Abstract: OBJECTIVES: To assess the feasibility and effectiveness of a general practice based, proactive system of asthma care in children. DESIGN: Randomised controlled trial with cluster sampling by general practice. SETTING: General practices in the northern region of the Australian Capital Territory. PARTICIPANTS: 174 children with moderate to severe asthma who attended 24 general practitioners. INTERVENTION: System of structured asthma care (the 3+ visit plan), with participating families reminded to attend the general practitioner. MAIN OUTCOME MEASURES: Process measures: rates for asthma consultations with general practitioner, written asthma plans, completion of the 3+ visit plan; clinical measures: rates for emergency department visits for asthma, days absent from school, symptom-free days, symptoms over the past year, activity limitation over the past year, and asthma drug use over the past year; spirometric lung function measures before and after cold air challenge. RESULTS: Intervention group children had significantly more asthma related consultations (odds ratio for three or more asthma related consultations 3.8 (95% confidence interval 1.9 to 7.6; P = 0.0001), written asthma plans (2.2 (1.2 to 4.1); P = 0.01), and completed 3+ visit plans (24.2 (5.7 to 103.2); P = 0.0001) than control children and a mean reduction in measurements of forced expiratory volume in one second after cold air challenge of 2.6% (1.7 to 3.5); P = 0.0001) less than control children. The number needed to treat (benefit) for one additional written asthma action plan was 5 (3 to 41) children. Intervention group children had lower emergency department attendance rates for asthma (odds ratio 0.4 (0.2 to 1.04); P = 0.06) and less speech limiting wheeze (0.2 (0.1 to 0.4); P = 0.0001) than control children and were more likely to use a spacer (2.8 (1.6 to 4.7); P = 0.0001). No differences occurred in number of days absent from school or symptom-free day scores. CONCLUSIONS: Proactive care with active recall for children with moderate to severe asthma is feasible in general practice and seems to be beneficial.

Glassroth J. *The role of long-acting beta-agonists in the management of asthma: analysis, meta-analysis, and more analysis.* Ann Intern Med. 2006; 144(12) : 936-7.p

Glauber J.H. et al. *Stratifying asthma populations by medication use: how you count counts.* Ann Allergy Asthma Immunol. 2002; 88(5) : 451-6.p
Abstract: BACKGROUND: Asthma disease management

programs typically use pharmacy data to identify high-risk individuals for outreach. Provider-directed pharmacy profiling seeks to identify physicians whose prescribing of recommended asthma medication is suboptimal. Both strategies require an accurate approach to counting prescribed asthma medication. OBJECTIVE: We compare two methods for counting the use of bronchodilators and inhaled anti-inflammatory medication. One approach uses simple counts of dispensed medication. An alternative, canister-equivalent method standardizes these medications on the basis of variation in both potency and medication-days supplied per prescription. We evaluate whether these alternative methods yield different population risk profiles when applied to managed care enrollees who have asthma and to the physicians treating them. METHODS: Retrospective cohort study of patterns of medication use by asthmatic patients receiving care within a group-model health maintenance organization and prescribing of asthma medications by the physicians treating them. RESULTS: Each method yields a different risk profile of the patient and physician populations, respectively. Relative to simple counts, the canister-equivalent method results in a 40% increase in the population identified as having high bronchodilator use and chronic anti-inflammatory medication use. On the physician-level, the mean anti-inflammatory:bronchodilator ratio (AIF:BD) was 1.50 by the canister-equivalent method compared with 1.08 by the simple-count method. When stratified by each method, 36% of physicians were assigned to different quartiles of anti-inflammatory:bronchodilator ratio. CONCLUSIONS: A novel canister-equivalent method for counting dispensed asthma medications yields different risk profiles compared with simple counts of asthma medications. Asthma disease management programs should consider alternative approaches to improve the accuracy of risk profiling based on patterns of medication use.

Godard P. et al. *[Asthma control in general practice: a cross-sectional survey of 16,580 patients].* Presse Med. 2005; 34(19 Pt 1) : 1351-7.p
Abstract: INTRODUCTION: Little information is available about asthma control in patients followed by general practitioners care in France, although such control is one of the essential aims of their treatment. OBJECTIVES: The ER'Asthme survey sought to assess asthma control among patients visiting their general practitioner (GP) and to determine the factors associated with it. METHODS: This cross-sectional included patients with asthma diagnosed at least 12 months earlier, aged more than 6 years, and followed by a GP. It collected data on self-assessed health status, asthma control (assessed by a 3-level composite score based on the Canadian consensus criteria as adapted by ANAES: optimal, acceptable and unacceptable), and compliance. RESULTS: The study included 16,580 patients; 85% were older than 20 years, and 54% were male. Patients answered the question about their asthma control as follows: 53% "excellent" or "fine", 39% "not very good" and 8% "poor". GPs, however, assessed asthma control as optimal in 21% of patients, acceptable in 7% and unacceptable in 72%. Concordance between these two assessments was thus poor: Kappa coefficient 34.5% (95% CI [33.5%; 35.5%]). Only 59% of patients reported complete compliance with their maintenance treatment. Factors associated with optimal control were: use of fixed combination therapy (inhaled corticosteroid+long-acting beta-agonist) (OR: 3.7; 95%CI [3.5; 4.2]) normal BMI (OR: 2.4; 95%CI [2.0; 2.9]), non-smoker status (OR: 2.4; 95%CI [2.1; 2.8]), age<50 (OR: 2.3; 95%CI [2.1; 2.6]) and good compliance (OR: 1.6; 95%CI [1.5; 1.8]). CONCLUSION: Patients with asthma overestimate their asthma control, which often remains inadequate. Maintenance treatment with a fixed combination, BMI, smoking, age and compliance all influence the level of asthma control.

Gold B.D. *Care at the front line: clinical decisions in the management of pediatric acid-related disorders.* J Pediatr. 2005; 146(3 Suppl) : S1-2.p

Gold D.R. *Less childhood obesity--less persistence of wheeze in teenage girls and boys?* Am J Respir Crit Care Med. 2004; 170(1) : 8-9.p

Gold D.R. et al. *Associations of cord blood fatty acids with lymphocyte proliferation, IL-13, and IFN-gamma.* J Allergy Clin Immunol. 2006; 117(4) : 931-8.p **Abstract:** BACKGROUND: N-3 and n-6 polyunsaturated fatty acids (PUFAs) have been hypothesized to have opposing influences on neonatal immune responses that might influence the risk of allergy or asthma. However, both n-3 eicosapentaenoic acid (EPA) and n-6 arachidonic acid (AA) are required for normal fetal development. OBJECTIVE: We evaluated whether cord blood fatty acid levels were related to neonatal immune responses and whether n-3 and n-6 PUFA responses differed. METHODS: We examined the relation of cord blood plasma n-3 and n-6 PUFAs (n = 192) to antigen- and mitogen-stimulated cord blood lymphocyte proliferation (n = 191) and cytokine (IL-13 and IFN-gamma; n = 167) secretion in a US birth cohort. RESULTS: Higher levels of n-6 linoleic acid were correlated with higher IL-13 levels in response to Bla g 2 (cockroach, P = .009) and Der f 1 (dust mite, P = .02). Higher n-3 EPA and n-6 AA levels were each correlated with reduced lymphocyte proliferation and IFN-gamma levels in response to Bla g 2 and Der f 1 stimulation. Controlling for potential confounders, EPA and AA had similar independent effects on reduced allergen-stimulated IFN-gamma levels. If neonates had either EPA or AA levels in the highest quartile, their Der f 1 IFN-gamma levels were 90% lower (P = .0001) than those with both EPA and AA levels in the lowest 3 quartiles. Reduced AA/EPA ratio was associated with reduced allergen-stimulated IFN-gamma level. CONCLUSION: Increased levels of fetal n-3 EPA and n-6 AA might have similar effects on attenuation of cord blood lymphocyte proliferation and IFN-gamma secretion. CLINICAL IMPLICATIONS: The implications of these findings for allergy or asthma development are not yet known.

Goldberg S. et al. *Can peak expiratory flow measurements estimate small airway function in asthmatic children?* Chest. 2001; 120(2) : 482-8.p **Abstract:** BACKGROUND: Asthma is characterized in part by small airways dysfunction. Peak expiratory flow (PEF) measurement has been suggested by all international guidelines as an important tool in asthma management. The correlation between PEF and FEV(1) but not with forced expired flow at 50% of vital capacity (FEF(50)) is well-established. Study objective: To determine the value of PEF measurement as a predictor of small airways status as expressed by FEF(50). DESIGN: Analysis of the association between PEF and FEF(50) in single and multiple determinations. PATIENTS: One hundred eleven asthmatic children (mean age, 11.8 years), grouped in the following way according to FEV(1) values: within normal range (n = 46); mildly reduced FEV(1) (n = 44); and moderately/severely reduced FEV(1) (n = 21). RESULTS: Overall, FEF(50) and PEF were significantly correlated (r = 0.49; p < 0.0001). However, in 41.6% of the patients, the actual FEF(50) differed by > 20% from the calculated FEF(50). PEF has a high specificity (82.4%) but a poor sensitivity (51.7%) to detect FEF(50) status. PEF was better able to reflect abnormal FEF(50) in the patients with more severe asthma and to reflect normal FEF(50) values in the healthier patients. In patients with multiple measurements (n = 40), the correlation between FEF(50) and PEF was significantly better than that derived from a single determination (multiple measurements r = 0.77; single measurement, r = 0.49). CONCLUSIONS: Although PEF is an important tool in the management of asthmatic patients, it does not yield a complete picture because it is not sensitive in detecting small airways function. It is best used at home along with regular spirometry measurements at the clinic. PEF may serve as a better index of changes in small airways function once an individual regression is determined.

Goldstein A.B. et al. *Bronchodilator responsiveness in normal infants and young children.* Am J Respir Crit Care Med. 2001; 164(3) : 447-54.p **Abstract:** Several studies have demonstrated that normal

infants exhibit bronchoconstriction after inhalation of nonspecific agonists and that the induced airway narrowing can be reversed by the inhalation of a beta-agonist. However, there are very limited data on baseline airway tone and the airway response to a beta-agonist in this subject population. The purpose of our study was to evaluate in normal infants baseline airway responsiveness to the inhaled beta-agonist, albuterol, using changes in maximal expiratory flows. Forty-one healthy infant volunteers with no history of respiratory disease or recurrent wheezing (ages 5.4 to 141.4 wk) were studied. Maximal expiratory flow-volume curves were obtained at baseline and 10 min after inhalation of albuterol (n = 28) or placebo (n = 13) using a metered-dose inhaler with a spacer. The mean percent change was significantly greater (p < 0.05) in the albuterol versus placebo group for FEF(0.5) (2.2% versus -1.5%), FEF(75%) (10.6% versus -3.1%), and FEF(85%) (12.9% versus 0.5%). Six of 28 albuterol-treated infants demonstrated increases in FEF(75%) greater than two standard deviations from the mean change in FEF(75%) seen in the placebo group. These infants were younger and more frequently exposed to maternal smoking during pregnancy. We conclude that normal healthy infants have overall levels of baseline airway tone that are similar to that reported in adults and older children; however, among the infants we evaluated the response to an inhaled bronchodilator was greatest in the youngest infants and in those exposed to tobacco smoking. Keywords: airway responsiveness; asthma; tobacco smoke; infant pulmonary function; bronchodilator.

Gomez-Roman J.J. et al. *[Hormone expression and opioid receptors in fetal and adult lung].* Arch Bronconeumol. 2002; 38(8) : 362-6.p **Abstract:** OBJECTIVES: To describe the cellular distribution and level of expression of certain hormones and opioid receptors during fetal development and in the lung of the healthy adult. METHOD: We sampled lung tissue from fetuses at three stages of development (pseudoglandular, canalicular and saccular) (3 samples per stage), from newborn infants (3), from 10-month-old infants (2) and from adults (3) who had died without lung disease. After specific immunohistochemical staining for hormones (calcitonin, parathormone, serotonin and adrenocorticotrophic hormone - ACTH) and opioid receptors, we assessed the percentage of positive cells for each cell type in each sample. RESULTS: Serotonin is the first to appear (pseudoglandular stage in isolated neuroendocrine cells) and it disappears later. Calcitonin appears in the canalicular stage in neuroendocrine and lung cells. Expression is at its peak at birth and is less in the adult lung. We found no ACTH or parathormone production. Opioid receptors appear in the canalicular stage and peak at birth. In adult lung, bronchiolar muscle and mesothelial cells, only delta-type opioid receptors are present. CONCLUSIONS: Pulmonary hormone secretion is significant during fetal development and peaks at birth. Calcitonin is the main hormone produced in the fetal lung. Opioid receptors are present during fetal development in various types of cells and peak at birth. An understanding of the expression of active substances could have therapeutic relevance in certain conditions, such as bronchial asthma or respiratory distress syndrome in the child.

Gonzalez-Sanchez R. et al. *Furosemide plus albuterol compared with albuterol alone in children with acute asthma.* Allergy Asthma Proc. 2002; 23(3) : 181-4.p **Abstract:** Several reports have shown that inhaled furosemide protects patients with asthma from different bronchoconstrictor agents. However, the effect of this widely used diuretic in acute exacerbation in adults is unproven. There are no reports of furosemide's therapeutic effect in acute asthma in children; thus, the objective of this study was to determine the effectiveness of the combined treatment of furosemide and albuterol in pediatric patients. Using a double-blind design, 20 emergency room patients with an asthmatic exacerbation were studied and randomly assigned to one of the following treatments: (1) furosemide + albuterol (1 and 0.15 mg/kg, respectively) or (2) albuterol (0.15 mg/kg). The forced expiratory volume in one second (FEV1) was measured in each patient before medication and then 30 and 60 minutes after inhalation

of the individual drug or drug combination. Neither group differed in age or baseline FEV1. An increase in FEV1 of 22.8 +/- 4.3% (mean +/- SE) in the drug combination group was noted at 60 minutes, and an increase in FEV1 of 18.0 +/- 2.6% in the albuterol group was obtained at the same time. Although the increase in FEV1 was greater in the first group after 1 hour of treatment, this was not significant. These results suggest that inhaled furosemide does not have a synergistic effect with albuterol in the treatment of asthmatic exacerbations in children.

Goodwin R.D. et al. *Asthma and depressive and anxiety disorders among young persons in the community.* Psychol Med. 2004; 34(8) : 1465-74.p **Abstract:** **BACKGROUND:** The objectives of the study were to examine linkages between asthma and depressive and anxiety disorders in a birth cohort of over 1000 young persons studied to the age of 21 years. Specifically, the study aimed to ascertain the extent to which associations between asthma and depressive and anxiety disorders could be explained by non-observed fixed confounding factors. **METHOD:** Asthma and depressive and anxiety disorders were measured prospectively over the course of a 21-year longitudinal study. Fixed effects logistic regression models were used to determine the relationship between asthma and depressive and anxiety disorders, adjusting for potentially confounding factors. **RESULTS:** Asthma in adolescence and young adulthood was associated with increased likelihood of major depression (OR 1.7, 95 % CI 1.3-2.3), panic attacks (OR 1.9, 95 % CI 1.3-2.8), and any anxiety disorder (OR 1.6, 95% CI 1.2-2.2). Associations between asthma and depressive and anxiety disorders were adjusted for confounding factors using a fixed effects regression model which showed that, after control for fixed confounding factors, asthma was no longer significantly related to major depression (OR 1.1), panic attacks (OR 1.1), or any anxiety disorder (OR 1.2). Additional post hoc analyses suggested that exposure to childhood adversity or unexamined familial factors may account for some of the comorbidity of asthma and depressive and anxiety disorders. **CONCLUSIONS:** These results confirm and extend previous findings by documenting elevated rates of depressive and anxiety disorders among young adults with asthma, compared with their counterparts without asthma, in the community. The weight of the evidence from this study suggests that associations between asthma and depressive and anxiety symptoms may reflect effects of common factors associated with both asthma and depressive and anxiety disorders, rather than a direct causal link. Future research is needed to identify the specific factors underlying these associations.

Goodwin R.D. et al. *Prevalence of probable mental disorders among pediatric asthma patients in an inner-city clinic.* J Asthma. 2005; 42(8) : 643-7.p **Abstract:** **OBJECTIVE:** To determine the screen-positive prevalence of anxiety disorders and depression among pediatric asthma patients in an inner-city asthma clinic and to investigate the association between probable diagnoses of anxiety disorders and depression and medical service use among inner-city pediatric asthma patients. **METHOD:** In this pilot study, a consecutive sample of pediatric asthma patients aged 5-11 in the waiting room of an inner-city asthma clinic was screened for mental disorders using the DISC Predictive Scales (DPS), which produces probable DSM-IV diagnoses. In addition, data on health service use for asthma were collected. Statistical analyses were performed to examine the relationship between probable anxiety disorders and depression and health service use for asthma among pediatric asthma patients. **RESULTS:** Approximately one in four (25.7%) pediatric asthma patients in an inner-city asthma clinic met criteria for a probable diagnosis of current anxiety disorders or depression (past 4-week prevalence). Specifically, childhood separation anxiety disorder was common among 8.1%, panic among 14.9%, generalized anxiety disorder among 4.1%, agoraphobia among 5.4%, and 2.7% had depression. Having more than one anxiety disorder or depression diagnosis was associated with higher levels of inpatient and outpatient medical services, compared with patients who were

negative on screening for anxiety or depressive disorders, although differences failed to reach statistical significance. **CONCLUSIONS:** These findings are the first to provide preliminary evidence suggesting that mental health problems are common among pediatric asthma patients in an inner-city clinic. The results also suggest that mental health problems in pediatric asthma patients may be associated with elevated levels of medical service use for asthma. Replication of this pilot study is needed with a larger sample, more precise diagnostic methodology, and a comparison group with chronic medical illness.

Gordian M.E. et al. *An investigation of the association between traffic exposure and the diagnosis of asthma in children.* J Expo Sci Environ Epidemiol. 2006; 16(1) : 49-55.p **Abstract:** This study investigated whether proximity to traffic at residence location is associated with being diagnosed with asthma as a young child. A survey of parents of children (aged 5-7) in kindergarten and first-grade in 13 schools was completed in Anchorage, Alaska, and Geographical Information System (GIS) mapping was used to obtain an exposure measure based on traffic density within 100 m of the cross streets closest to the child's residence. Using the range of observed exposure values, a score of low, medium or high traffic exposure was assigned to each child. After controlling for individual level confounders, relative to the low referent group, relative risks (95% confidence intervals) of 1.40 (0.77, 2.55) and 2.83 (1.23,6.51) were obtained in the medium and high exposure groups, respectively. For the null hypothesis of no difference in risk, a significance level of 0.056 was obtained, which suggests that further investigation would be worthwhile. Children without a family history of asthma were more likely to have an asthma diagnosis if they resided in a high traffic area than children who had one or more parents with asthma. The relative risk for children without a family history of asthma is 2.43 (1.12, 5.28) for medium exposure and 5.43 (2.08, 13.74) for high exposure. For children with a family history of asthma, the relative risk is 0.66 (0.25, 1.74) for medium exposure and 0.67 (0.12, 3.69) for high exposure. The P-value for the overall "exposure-effect" (i.e. both main effects AND interaction terms) is 0.0097.

Gorelick M.H. et al. *Validity and responsiveness of a brief, asthma-specific quality-of-life instrument in children with acute asthma.* Ann Allergy Asthma Immunol. 2004; 92(1) : 47-51.p **Abstract:** **OBJECTIVE:** To test the validity and short-term responsiveness to change of a pediatric, asthma-specific, health-related quality-of-life (HRQL) instrument. **METHODS:** Children 2 years and older treated in the emergency department (ED) for acute asthma were eligible for this prospective cohort study. A 10-item instrument, the Integrated Therapeutics Group Child Asthma Short Form (ITG-CASF), was administered at the time of the ED visit and again 14 days later (via telephone). At the follow-up call, parents were also asked about the child's current overall asthma status, missed school or limited activities, and persistence of asthma symptoms. **RESULTS:** A total of 121 children were enrolled (mean age, 7.9 years), and follow-up was complete for 96 (79%). Mean +/- SD ITG-CASF scores at follow-up were significantly higher among children reported to have improved overall (61.8 +/- 19.6) than those not improved (41.9 +/- 21.2), and there was a significant correlation between ITG-CASF score at follow-up and the number of days of school missed or limited activities ($r = -0.45$; 95% confidence interval [CI], -0.24 to -0.66). There was also a significant difference in improvement in ITG-CASF score from ED visit to follow-up among those improved (13.7-point improvement) compared with those not improved (3.3-point improvement; difference = 10.4; 95% CI, 1.2 to 19.5). The effect size was 0.68, indicating a large responsiveness to change. **CONCLUSIONS:** The ITG-CASF is a valid and responsive measure of HRQL in children with acute asthma and may be a useful outcome measure in evaluating ED treatment.

Gorelick M.H. et al. *Construct validity and responsiveness of the Child Health Questionnaire in children with acute asthma.* Ann Allergy Asthma Immunol. 2003; 90(6) : 622-8.p Abstract: OBJECTIVE: To examine the validity and responsiveness of the Child Health Questionnaire (CHQ-PF28) in the context of acute exacerbation of asthma in children. DESIGN AND METHODS: This was a prospective cohort study of children age 5 years and older treated for acute asthma at two urban pediatric emergency departments (EDs). At 14 days after the visit, all patients were contacted by telephone and the CHQ-PF28 (modified to have a 2-week recall period) was administered. Poor 14-day outcome was defined as one or more of the following: child or parent missed at least 5 days of school/day care/work; child still having asthma symptoms above baseline at 14 days; or unscheduled care within 7 days after the ED visit. RESULTS: A total of 732 subjects (median age, 9 years) were enrolled; 622 (85%) had successful follow-up at day 14. At the 14-day follow-up, 254 (43%) were classified as having a poor outcome. The mean physical subscale score of the CHQ-PF28 was 48.2 among those with a good outcome, vs 35.9 among the poor outcome group (difference = 12.3; 95% confidence interval, 10.2 to 14.3). For the psychosocial subscale the average difference between groups was 6.9 (95% confidence interval, 5.1 to 8.7). Among the 146 patients at one site who also had a CHQ score obtained at the initial visit, there was a significant improvement in mean physical subscale score among those with good, but not poor, outcome. However, the relative responsiveness was moderate, with an effect size of only 0.37. CONCLUSIONS: Both the physical and psychosocial subscales of the CHQ-PF28 administered 14 days after an ED visit for acute exacerbation of asthma are correlated with poor short-term functional outcome, but scores are only moderately responsive to acute changes in functional status.

Gorelick M.H. et al. *Difficulty in obtaining peak expiratory flow measurements in children with acute asthma.* Pediatr Emerg Care. 2004; 20(1) : 22-6.p Abstract: OBJECTIVE: To determine the frequency with which children ≥ 6 years with acute asthma can perform peak expiratory flow rate measurements (PEFR) in an emergency department (ED). DESIGN/METHODS: Data were obtained from a prospective cohort study of children with acute asthma. All children (age 2-18 years old) treated in an urban pediatric ED for an acute exacerbation during randomly selected days over a 12-month period were prospectively evaluated. According to treatment protocols, PEFR was to be measured in all children age 6 years and older before therapy and after each treatment with inhaled bronchodilators. Registered respiratory therapists obtained PEFR and evaluated whether patients were able to perform the maneuver adequately. RESULTS: Four hundred and fifty-six children, 6 to 18 years old (median 10 years), were enrolled; 291 (64%) had PEFR measured at least once. Of those in whom PEFR was attempted at least once, only 190 (65%) were able to perform adequately. At the start of therapy, 54% (142/262) were able to perform PEFR. Of the 120 who were unable to perform initially, 76 had another attempt at the end of the ED treatment, and 55 (72%) were still unable to perform. A total of 149 patients had attempts at PEFR both at the start and end of treatment, of these, only 71 (48%) provided valid information on both attempts. Patients unable to perform PEFR were younger (mean \pm SD = 8.7 \pm 2.8 years) than those who were able to perform successfully (11.2 \pm 3.2 years) and those with no attempts (10.0 \pm 3.4 years). Children admitted to the hospital were more likely to be unable to perform PEFR (58/126 = 46%) than those discharged from the ED (43/330 = 13%, $P < 0.0001$). CONCLUSION: Adequate PEFR measurements are difficult to obtain in children with acute asthma. Treatment and research protocols cannot rely exclusively on PEFR for evaluation of severity.

Gourgoutis D. et al. *Immune modulator pidotimod decreases the in vitro expression of CD30 in peripheral blood mononuclear cells of atopic asthmatic and normal children.* J Asthma. 2004; 41(3) : 285-7.p Abstract: Recurrent viral infections are frequently observed in

children with atopic asthma. In this study we investigated the ability of the synthetic immunomodulator pidotimod to affect in vitro the phenotype and/or cytokine profile of blood cells in relation to atopic asthma. Peripheral blood mononuclear cells were isolated from 13 atopic asthmatic and 9 normal children and stimulated in culture with mitogen either in the presence or not of the drug. Expression of surface markers was evaluated by flow cytometry, and production of interleukin-4 and interferon-gamma was measured in supernatants. Pidotimod was able to down-regulate the expression of CD30 on cells from both atopic and normal subjects. Because CD30 has been associated with Th-2 cells, this observation supports the possibility of pidotimod being able to affect the Th-1/Th-2 balance in atopic asthma.

Gourgoulis K.I. et al. *The influence of altitude in bronchial asthma.* Arch Med Res. 2001; 32(5) : 429-31.p Abstract: BACKGROUND: Some asthmatic children living in mountain areas experience significant improvement in daily symptoms and in the degree of bronchial obstruction. The aim of this study is to investigate the effect of altitude on the prevalence and morbidity of childhood bronchial asthma. METHODS: A questionnaire regarding the history and symptoms of asthma was distributed to 874 children aged 6-12 years, to be completed by their parents with the help of their pediatrician. A total of 583 children lived at sea level, 180 at an altitude between 501 and 800 meters, and 111 at an altitude between 801 and 1,200 meters. All children with recurrent cough, shortness of breath, wheezing, and a history of bronchial asthma were considered to have bronchial asthma. RESULTS: The prevalence of childhood bronchial asthma in the mountains (800-1,200 meters) was twice as low as that at sea level (15.8% of children) ($p < 0.01$). Parental smoking was more frequent in children who lived at sea level than in the mountains. Additionally, consumption of fish and oranges was more frequent at sea level. Children with asthma who lived in the mountains were absent fewer days from school per year (0.2) and had fewer nights with dyspnea per year (0.5) than asthmatic children who lived at sea level (1.6 days and 25 nights, respectively). CONCLUSIONS: Bronchial asthma in children who live at high altitudes is characterized by low prevalence and low morbidity.

Grasemann H. et al. *Different subgroups of difficult asthma in children.* Thorax. 2001; 56(11) : 895.p

Grech V. et al. *Seasonal variations in hospital admissions for asthma in Malta.* J Asthma. 2002; 39(3) : 263-8.p Abstract: The seasonality of asthma exacerbations may reflect varying exposure to triggers. This study retrospectively analyzes the seasonality of asthma hospital admissions, at all ages, in a population-based study. Analysis of the seasonality of asthma admissions and correlation with temperature was carried out in the setting of a regional hospital covering all acute asthma admissions in an island population. Admissions were divided into pediatric (1994-8) and adult (1989-8) cases. Both pediatric (0-14 years; $n = 2916$) and adult (15-59 years; $n = 1269$) admissions showed a peak in January and a trough in August. The seasonality in pediatric admissions was far more pronounced than in adults. Both cohorts exhibited a second, smaller peak in spring. In school-aged children, the end of school in June was associated with a sharp (91%) drop in admissions, and restarting school in October was associated with an even sharper rise (165%). A negative correlation was found between admissions and mean monthly ambient temperatures, and this was most pronounced in the pediatric age groups. This marked seasonality may indicate that temperature is a proxy for the total time spent indoors. Both the start and end of school had a profound impact on pediatric admission rates. Prospective studies are necessary to establish the role of viral infections and the influence of indoor and outdoor aeroallergens on the seasonality of hospitalization rates for asthma in the local setting.

- Greene J.** *Case management evolves: asthma care points the way.* *AHIP Cover.* 2004; 45(3) : 48-52.p **Abstract:** Case Management was once a simple administrative matter--an insurance adjuster managing a workers' compensation claim. Today, case managers with nursing, social work, or vocational rehabilitation backgrounds work directly with physicians, hospitals, home health agencies, nursing homes, and other organizations. Case managers now coordinate the health care needs of patients with chronic conditions like asthma or diabetes and patients with catastrophic medical problems such as cancer or severe burns.
- Gruber C. et al.** *Is early BCG vaccination associated with less atopic disease? An epidemiological study in German preschool children with different ethnic backgrounds.* *Pediatr Allergy Immunol.* 2002; 13(3) : 177-81.p **Abstract:** We investigated the association of bacille Calmette-Guerin (BCG) vaccination and atopic manifestations among children. Because many children in the study area were from minority ethnic groups, the effect of ethnicity on disease prevalence was also analyzed. A mandatory health survey included all preschool children from Berlin in 1994. Trained medical personnel asked parents whether their child had ever had a diagnosis of atopic dermatitis (AD), bronchial asthma (BA), and hay fever (HF) or symptoms suggestive of these conditions. BCG-vaccination status was recorded from official vaccination documents. Ethnicity of the child was defined by maternal citizenship. We included 38 808 children in our study (20 813 children from former west Berlin), on average aged 6 years. The proportion of children with a foreign family background was 2.1% in East Berlin and 27.5% in West Berlin. BCG vaccination was more common in East Berlin than in West Berlin (94.2% vs. 16.5%) and in West Berlin more common among children with a foreign family background compared with Germans (25.3% vs. 13.2%). The adjusted odds ratio (95% CI) for BA was 0.85 (0.71-1.00) for BCG-vaccinated individuals. BCG vaccination was not significantly associated with AD or HF. Among non-German children, the odds ratios were 0.35 (0.30-0.42) for AD, 0.58 (0.48-0.70) for BA, and 0.72 (0.54-0.92) for HF. The OR for AD among children living in eastern Berlin was 1.19 (1.04-1.36), no significant regional differences were found for BA or HF. This study demonstrated a weak protective effect of BCG vaccination against asthma but a much stronger protective effect of non-German ethnicity against atopic manifestations among preschool children from Germany.
- Gruber W. et al.** *Laser acupuncture in children and adolescents with exercise induced asthma.* *Thorax.* 2002; 57(3) : 222-5.p **Abstract:** BACKGROUND: Laser acupuncture, a painless technique, is a widely used alternative treatment method for childhood asthma, although its efficacy has not been proved in controlled clinical studies. METHODS: A double blind, placebo controlled, crossover study was performed to investigate the possible protective effect of a single laser acupuncture treatment on cold dry air hyperventilation induced bronchoconstriction in 44 children and adolescents of mean age 11.9 years (range 7.5-16.7) with exercise induced asthma. Laser acupuncture was performed on real and placebo points in random order on two consecutive days. Lung function was measured before laser acupuncture, immediately after laser acupuncture (just before cold dry air challenge (CACH)), and 3 and 15 minutes after CACH. CACH consisted of a 4 minute isocapnic hyperventilation of -10 degrees C absolute dry air. RESULTS: Comparison of real acupuncture with placebo acupuncture showed no significant differences in the mean maximum CACH induced decrease in forced expiratory volume in 1 second (27.2 (18.2)% v 23.8 (16.2)% and maximal expiratory flow at 25% remaining vital capacity (51.6 (20.8)% v 44.4 (22.3)%). CONCLUSIONS: A single laser acupuncture treatment offers no protection against exercise induced bronchoconstriction in paediatric and adolescent patients.
- Gruchalla R.S. et al.** *Results of an inner-city school-based asthma and allergy screening pilot study: a combined approach using written questionnaires and step testing.* *Ann Allergy Asthma Immunol.* 2003; 90(5) : 491-9.p **Abstract:** BACKGROUND: A questionnaire alone may not be an adequate screening tool for asthma. OBJECTIVE: To determine whether an asthma questionnaire used in combination with an exercise step test is better than a questionnaire alone in screening for asthma in children and to evaluate the validity of a rhinitis questionnaire in determining atopy. METHODS: The International Study of Asthma and Allergies in Childhood (ISAAC) asthma core questionnaire was used to screen for asthma in 307 inner-city first through third graders. All children who had scores consistent with a diagnosis of asthma underwent step testing, as did a subset of children who had negative overall scores. All children who had inconsistent asthma scores and step test results underwent methacholine challenge testing. The same 307 children underwent rhinitis screening and children who had one or more positive responses on the ISAAC rhinitis questionnaire underwent skin testing as did a subset of children who had all negative responses. RESULTS: Three hundred of 307 asthma and rhinitis questionnaires were returned. Twenty-eight children (9%) had global asthma scores that were considered to be positive (5 or above). Twenty-four of these children underwent step testing as did 34 randomly selected children who had negative global asthma scores. Thirty-one (91%) of the 34 children who had negative global asthma scores had negative step tests. Similarly, 20 of 24 children (83%) of the children who had positive global asthma scores had negative step tests. Only 4 children who had positive global asthma scores were step test-positive or had reversible airway obstruction at baseline. Using a positive methacholine challenge as the gold standard for establishing bronchial hyperresponsiveness, the global asthma score derived from the eight-item ISAAC asthma questionnaire yielded a sensitivity of 64%, a specificity of 11%, a positive predictive value of 47%, and a negative predictive value of 20%. Comparing the six-item ISAAC rhinitis questionnaire results to the gold standard, skin test reactivity, the questionnaire yielded a sensitivity of 76%, a specificity of 21%, a positive predictive value of 56%, and a negative predictive value of 40%. CONCLUSIONS: Step testing was not useful as a screening tool for asthma. In addition, the ISAAC asthma questionnaire may not be a good asthma screening tool for inner-city pediatric populations, especially if the form is self-administered. Investigators should first validate both the ISAAC asthma and rhinitis screening questionnaires in the particular population to be studied before widespread asthma and allergy screening efforts are initiated using these tools.
- Gu H. et al.** *Evaluation of diagnostic criteria for atopic dermatitis: validity of the criteria of Williams et al. in a hospital-based setting.* *Br J Dermatol.* 2001; 145(3) : 428-33.p **Abstract:** BACKGROUND: Surveys of the prevalence of atopic dermatitis (AD) have been carried out world-wide, but the results vary widely. The differences probably result from the use of different diagnostic criteria. Williams et al. proposed minimum, simplified, diagnostic criteria that require no invasive test and are easy to use. Pilot studies in European countries showed their suitability for implementation both in hospitals and in the community, and their high sensitivity and specificity. OBJECTIVES: To evaluate the potential practical value of the criteria of Williams et al. in the Chinese population. METHODS: The criteria of Hanifin and Rajka (gold standard), Williams et al. and Kang and Tian were applied and compared in 111 patients with AD and 121 control subjects with other skin diseases in three out-patient centres in China. RESULTS: The criteria of Williams et al. showed a similar diagnostic efficiency to that of the gold standard, with the sensitivity, specificity and kappa value reaching 95.50%, 97.52% and 0.93, respectively. No significant difference was found between the criteria of Williams et al. and those of Kang and Tian ($\chi^2 = 0.69, P > 0.05$). 'Onset under the age of 2 years', a criterion of Williams et al. could be used in subjects of any age. CONCLUSIONS: The diagnostic efficiency of the criteria of Williams et al. was basically similar to those of Hanifin and Rajka

and of Kang and Tian in our out-patient settings. However, those of Williams et al. were easier to apply and required no invasive tests.

Guendelman S. et al. *Improving asthma outcomes and self-management behaviors of inner-city children: a randomized trial of the Health Buddy interactive device and an asthma diary.* Arch Pediatr Adolesc Med. 2002; 156(2) : 114-20.p **Abstract:** **BACKGROUND:** Asthma is an important cause of morbidity, absence from school, and use of health services among children. Computer-based educational programs can be designed to enhance children's self-management skills and to reduce adverse outcomes. **OBJECTIVE:** To assess the effectiveness of an interactive device programmed for the management of pediatric asthma. **DESIGN:** A randomized controlled trial (66 participants were in the intervention group and 68 were in the control group). **SETTING:** Interventions conducted at home and in an outpatient hospital clinic. **PARTICIPANTS:** Inner-city children aged 8 to 16 years diagnosed as having asthma by a physician. **INTERVENTION:** An asthma self-management and education program, the Health Buddy, designed to enable children to assess and monitor their asthma symptoms and quality of life and to transmit this information to health care providers (physicians, nurses, or other case managers) through a secure Web site. Control group participants used an asthma diary. **MAIN OUTCOME MEASURES:** Any limitation in activity was the primary outcome. Secondary outcomes included perceived asthma symptoms, absence from school, any peak flow reading in the yellow or red zone, and use of health services. **RESULTS:** After adjusting for covariates, the odds of having any limitation in activity during the 90-day trial were significantly ($P = .03$) lower for children randomized to the Health Buddy. The intervention group also was significantly ($P = .01$) less likely to report peak flow readings in the yellow or red zone or to make urgent calls to the hospital ($P = .05$). Self-care behaviors, which were important correlates of asthma outcomes, also improved far more for the intervention group. **CONCLUSION:** Compared with the asthma diary, monitoring asthma symptoms and functional status with the Health Buddy increases self-management skills and improves asthma outcomes.

Guerra S. et al. *Relation of beta2-adrenoceptor polymorphisms at codons 16 and 27 to persistence of asthma symptoms after the onset of puberty.* Chest. 2005; 128(2) : 609-17.p **Abstract:** **BACKGROUND:** It has long been recognized that many children with asthma outgrow the disease after the onset of puberty, but little is known about genetic factors influencing this outcome. **OBJECTIVES:** The aim of the present study was to determine whether the polymorphisms at codons 16 and 27 of the beta2-adrenoceptor are significant predictors of the persistence of asthma during adolescence. **DESIGN AND PARTICIPANTS:** We used data from the prospective Tucson Children's Respiratory Study. Children were genotyped for the polymorphisms at codons 16 and 27. The presence of wheezing/asthma was assessed by questionnaire from age 6 years up to the reported onset of puberty (prepubertal period) and after the onset of puberty up to age 16 years (adolescence). **RESULTS:** Among children who wheezed in the prepubertal period ($n = 168$), subjects homozygous for Gly at codon 16 were at significantly increased risk for persistent wheezing after puberty, as compared with carriers of the other genotypes (relative risk [RR], 1.43; 95% confidence interval [CI], 1.06 to 1.92; $p = 0.019$). This relation was present among boys (RR, 2.17; 95% CI, 1.41 to 3.36) but not girls (RR, 0.85; 95% CI, 0.55 to 1.30), and increased linearly according to the frequency of wheezing episodes after the onset of puberty. These findings persisted after adjusting for ethnicity and other potential confounders and after selecting only white children. The polymorphism at codon 27 showed no relation with risk for persistent wheezing. **CONCLUSIONS:** This study provides evidence for a strong gender-specific effect of the Gly16 polymorphism on the persistence of asthma after the onset of puberty.

Guerra S. et al. *Reduced interferon gamma production and soluble CD14 levels in early life predict recurrent wheezing by 1 year of age.* Am J Respir Crit Care Med. 2004; 169(1) : 70-6.p **Abstract:** It is unknown whether reduced production of IFN γ in early life, before any lower respiratory tract illness, is a risk factor for recurrent wheezing in infancy. We followed 238 infants prospectively from birth to 1 year of age. At birth and at 3 months of age, IFN γ production from polyclonally stimulated peripheral blood mononuclear cells and soluble CD14 (sCD14) levels in plasma were measured. The odds of developing recurrent wheezing (assessed by questionnaire) in the first year of life were up to 4.5 times higher for children in the lowest quartile of IFN γ production at 3 months ($p = 0.0005$) and 3.2 times higher for children in the lowest quartile of sCD14 levels at birth ($p = 0.004$) as compared with children in the other 3 combined quartiles of IFN γ and sCD14, respectively. Findings were confirmed in the multivariate analysis. IFN γ production at 3 months and sCD14 levels at birth were correlated ($r = 0.188$, $p = 0.031$). Our findings from a longitudinal cohort suggest that impaired IFN γ production at 3 months and reduced plasma-sCD14 levels at birth significantly increase the risk of developing recurrent wheezing in the first year of life.

Guevara J.P. *Self-management education of children with asthma: a meta-analysis.* LDI Issue Brief. 2003; 9(3) : 1-4.p **Abstract:** Nearly one in every thirteen children has asthma, making it the most common chronic condition in childhood. For a variety of biological and environmental reasons, the prevalence of childhood asthma has risen dramatically in the past 20 years, with disproportionate effects on low-income populations, minorities, and children living in inner cities. Much of the morbidity associated with childhood asthma, such as activity restrictions, missed school days, and emergency doctor visits, are preventable through appropriate management strategies. This Issue Brief summarizes evidence on the effectiveness of educational programs to improve self-management in children with asthma, and bolsters existing guidelines to include self-management education in the routine care of these patients.

Guevara J.P. et al. *Meta-analytic methods for pooling rates when follow-up duration varies: a case study.* BMC Med Res Methodol. 2004; 4 : 17.p **Abstract:** **BACKGROUND:** Meta-analysis can be used to pool rate measures across studies, but challenges arise when follow-up duration varies. Our objective was to compare different statistical approaches for pooling count data of varying follow-up times in terms of estimates of effect, precision, and clinical interpretability. **METHODS:** We examined data from a published Cochrane Review of asthma self-management education in children. We selected two rate measures with the largest number of contributing studies: school absences and emergency room (ER) visits. We estimated fixed- and random-effects standardized weighted mean differences (SMD), stratified incidence rate differences (IRD), and stratified incidence rate ratios (IRR). We also fit Poisson regression models, which allowed for further adjustment for clustering by study. **RESULTS:** For both outcomes, all methods gave qualitatively similar estimates of effect in favor of the intervention. For school absences, SMD showed modest results in favor of the intervention (SMD -0.14, 95% CI -0.23 to -0.04). IRD implied that the intervention reduced school absences by 1.8 days per year (IRD -0.15 days/child-month, 95% CI -0.19 to -0.11), while IRR suggested a 14% reduction in absences (IRR 0.86, 95% CI 0.83 to 0.90). For ER visits, SMD showed a modest benefit in favor of the intervention (SMD -0.27, 95% CI: -0.45 to -0.09). IRD implied that the intervention reduced ER visits by 1 visit every 2 years (IRD -0.04 visits/child-month, 95% CI: -0.05 to -0.03), while IRR suggested a 34% reduction in ER visits (IRR 0.66, 95% CI 0.59 to 0.74). In Poisson models, adjustment for clustering lowered the precision of the estimates relative to stratified IRR results. For ER visits but not school absences, failure to incorporate study indicators resulted in a different estimate of effect (unadjusted IRR 0.77, 95% CI 0.59 to 0.99). **CONCLUSIONS:** Choice of method among the ones presented had little effect on inference but affected

the clinical interpretability of the findings. Incidence rate methods gave more clinically interpretable results than SMD. Poisson regression allowed for further adjustment for heterogeneity across studies. These data suggest that analysts who want to improve the clinical interpretability of their findings should consider incidence rate methods.

Guevara J.P. et al. *National estimates of health services expenditures for children with behavioral disorders: an analysis of the medical expenditure panel survey.* Pediatrics. 2003; 112(6 Pt 1) : e440.p Abstract: BACKGROUND: Children with attention-deficit/hyperactivity disorder and asthma incur similar health care costs that are greater than those of most children without these conditions. Preliminary findings suggest that children with emotional behavioral disorders, anxiety and depression, incur even greater costs. OBJECTIVE: To determine if children with behavioral disorders have similar health services expenditures as children with physical conditions and to assess whether children with emotional behavioral disorders incur greater expenditures than children with disruptive behavioral disorders. METHODS: Children 2 to 18 years old who were members of households participating in the 1996 Medical Expenditure Panel Survey were eligible for this retrospective cohort study. Children with common behavioral disorders selected a priori were identified by using truncated International Classification of Diseases (Ninth Revision) codes obtained from household interviews. Children with common physical conditions (asthma, epilepsy, and diabetes) and children without these conditions served as controls. Estimates were weighted to reflect the complex sampling scheme. Expenditures for health services were compared. RESULTS: Of 3955 eligible children weighted to represent >44 million, 7.1% were identified with a behavioral disorder: 4.5% with disruptive disorders; 2.1% with emotional disorders; and 0.5% with miscellaneous disorders. Children with behavioral disorders incurred overall expenditures similar to children with physical conditions (adjusted 1492 dollars vs 1245 dollars; $P = .18$) but greater than children without these conditions (adjusted 1492 dollars vs 834 dollars; $P = .001$). Children with behavioral disorders had greater expenditures for office-based visits (adjusted 410 dollars; 95% confidence interval: 146-672 dollars) and prescription medications (adjusted 361 dollars; 95% confidence interval: 72-648 dollars) than those of children in either control group. Among children with behavioral disorders, children with emotional disorders incurred substantially greater overall expenditures (adjusted 2152 dollars vs 1026 dollars; $P = .003$) than children with disruptive disorders. Children with emotional disorders incurred greater hospitalization expenditures (664 dollars vs 43 dollars; $P = .01$) but lower pharmacy expenditures (154 dollars vs 307 dollars; $P = .001$) than children with disruptive disorders. CONCLUSIONS: In this nationally representative sample, children with behavioral disorders incurred overall health care costs similar to children with physical conditions but greater than children without any of these conditions because of increased costs for office-based visits and prescription medications. However, costs were not uniform among children with behavioral disorders. Children with emotional disorders incurred twofold higher costs than children with disruptive disorders. Greater recognition of children with emotional disorders and efforts to address the high rate of hospitalizations in this population are warranted.

Guignon N. et al. [Health status of children 5-6 years old: regional disparities]. Rev Infirm. 2003; (95) : 11-3.p

Guilbert T. et al. *Increased asthma symptoms and healthcare utilization during the fall and winter seasons in children with asthma living in the inner city: opportunity for school-based intervention.* J Pediatr. 2002; 141(5) : 604-5.p

Guill M.F. *Asthma update: clinical aspects and management.* Pediatr Rev. 2004; 25(10) : 335-44.p

Guiney P.A. et al. *Effects of osteopathic manipulative treatment on pediatric patients with asthma: a randomized controlled trial.* J Am Osteopath Assoc. 2005; 105(1) : 7-12.p Abstract: Asthma is a common chronic condition that has long plagued the pediatric patient population. Asthma in children can cause excessive school absenteeism, hospitalizations, and even death. Osteopathic manipulative treatment (OMT) is an underutilized noninvasive treatment method for patients with asthma. The use of OMT may help decrease mortality and morbidity rates among this patient group. The authors conducted a randomized controlled trial attempting to demonstrate the therapeutic relevance of OMT in the pediatric asthma population. With a confidence level of 95%, results for the OMT group showed a statistically significant improvement of 7 L per minute to 9 L per minute for peak expiratory flow rates. These results suggest that OMT has a therapeutic effect among this patient population. The authors suggest that more clinical trials are required to better demonstrate the effectiveness of OMT in patients with asthma.

Guler N. et al. *Leptin: does it have any role in childhood asthma? J Allergy Clin Immunol.* 2004; 114(2) : 254-9.p Abstract: BACKGROUND: Although there is evidence of a positive association between asthma and obesity in adults and children, very little is known about the role of leptin in asthmatic children. OBJECTIVES: The aims of this study were to evaluate the relation between leptin and parameters of atopy and asthma in children. METHODS: Body mass index (BMI) and serum leptin levels were measured in 102 (37 female, 65 male; mean age, 5.9 +/- 3.4 years) asthmatic and 33 (14 female, 19 male; mean age, 6.1 +/- 3.4 years) healthy children. Skin prick tests, total serum IgE, and pulmonary function tests were performed and were completed. RESULTS: A significant difference was observed in serum leptin levels between asthmatic and healthy children. Median (interquartile range) levels were 3.53 (2.06-7.24) ng/mL and 2.26 (1.26-4.71) ng/mL, respectively ($P = .008$). Subgroup analysis revealed that this difference in leptin levels was confined entirely to boys: 3.09 (1.99-7.51) ng/mL in boys with asthma versus 1.52 (1.06-3.17) ng/mL in boys without asthma ($P = .003$). By logistic regression analysis, we found that leptin was a predictive factor for having asthma (odds ratio, 1.98; CI, 1.10-3.55; $P = .021$), whereas sex, age, or BMI were not. In a stepwise multiple regression analysis including sex ($P = .001$), age ($P = .016$), BMI ($P < .001$), and asthma ($P = .022$), all of these variables were found to affect log leptin levels ($R^2 = 0.404$). There was no significant sex difference in serum leptin levels among asthmatic children, whereas healthy boys had significantly lower leptin levels than healthy girls ($P = .019$). Atopic asthmatic subjects had significantly higher leptin levels than nonatopic asthmatic subjects ($P = .038$) with similar BMI. A significant, but weak, correlation was observed between leptin levels and IgE in the overall group of asthmatic children ($r = 0.231$; $P = .019$). Again, this correlation was confined entirely to boys ($r = 0.319$; $P = .010$). There was no relation between leptin levels and skin prick tests, pulmonary function tests, passive smoking, birth weight, and duration of breast-feeding. CONCLUSION: Our findings suggest that leptin may play a role in atopic asthma. High serum leptin levels in asthmatic boys may partly explain the higher prevalence of childhood asthma in male sex.

Guo J.J. et al. *Impact of school-based health centers on children with asthma.* J Adolesc Health. 2005; 37(4) : 266-74.p Abstract: PURPOSE: To quantitatively assess the impact of school-based health centers (SBHCs) on hospitalization and emergency department (ED) visits for children with asthma. METHODS: The study was conducted at four SBHC intervention school districts and two comparable non-SBHC school districts in Greater Cincinnati, Ohio. A longitudinal quasi-experimental time-series repeated measures design was used with a study period from 1997 to 2003.

Children with asthma with at least 2 years of continuous enrollment who had medical claims for asthma diagnosis and antiasthmatic medications were selected. The primary data sources were student enrollment data from the schools and the Ohio Medicaid claims database. Generalized estimating equation (GEE) analysis and analysis of covariance were used to assess the intervention effect before and after the SBHC program. RESULTS: Asthma was one of the major diseases for SBHC encounters. Major prescription drugs that SBHC staff managed for children with asthma included albuterol, montelukast, fluticasone, budesonide, and triamcinolone. Of 273 children (196 in SBHC schools and 77 in non-SBHC schools), 42% were female, 41.7% African-Americans, and the average age was 8.2 years. After the opening of the SBHC, relative risks of hospitalization and ED visits in the SBHC group decreased 2.4-fold and 33.5%, respectively. The cost of hospitalization per child decreased significantly over time for children in SBHC schools ($F = 4.115$, $p = .044$). After SBHCs opened, cost of hospitalization decreased for African-American children ($F = 5.198$, $p = .023$). Costs of ED visits for children in SBHC schools were significantly lower than children in non-SBHC schools ($F = 19.8$, $p < .0001$). CONCLUSIONS: The risk of hospitalization and ED visits for children with asthma decreased significantly with SBHC programs. The potential cost-savings for hospitalization was estimated as 970 dollars per child.

Gupta R.S. et al. *The widening black/white gap in asthma hospitalizations and mortality.* J Allergy Clin Immunol. 2006; 117(2) : 351-8.p **Abstract:** BACKGROUND: Large racial differences in asthma morbidity and mortality have prompted research on new interventions, public awareness, and health policy efforts in the past decade. OBJECTIVE: We sought to characterize recent trends in US asthma hospitalization and mortality for black and white children and adults during the period from 1980 through 2002. METHODS: We conducted a successive representative national cohort study of US residents ages 5 to 34 years using data from the National Hospital Discharge Survey and the US vital statistics system. Outcome measures included black/white (B/W) asthma hospitalization and mortality rates, rate ratios, and rate differences. RESULTS: For asthma hospitalizations from 1980 through 2002, children ages 5 to 18 years had a 50% increase in the B/W rate ratio, and the rate difference increased from 22.8 to 28.3 hospitalizations per 10,000 population. For young adults ages 19 to 34 years, the B/W rate ratio increased from 2.3 to 2.8, and the rate difference decreased from 9.6 to 7.9 hospitalizations per 10,000 population. For asthma mortality from 1980 through 2001, children ages 5 to 19 years had a large increase in the B/W rate ratio from 4.5 to 5.6 and in the rate difference from 5.6 to 8.1 deaths per 1,000,000 population. There did not appear to be a significant change in the B/W differences for adults ages 20 to 34 years. CONCLUSIONS: For children, there have been notable increases in asthma B/W differences in hospitalizations and mortality since 1980, whereas for adults the increase has been smaller. National efforts to improve asthma care over the past decade do not appear to have reduced this B/W gap. When treating children with asthma, it is important to consider the racial-ethnic factors that might lead to avoidable hospitalizations and premature mortality.

Gupta U.K. et al. *Dermatoglyphics: a study of finger tip patterns in bronchial asthma and its genetic disposition.* Kathmandu Univ Med J (KUMJ). 2003; 1(4) : 267-71.p **Abstract:** Finger tip patterns of sixty patients of Bronchial Asthma were compared with that of 50 control cases. Higher frequency of whorls was observed in first digit of both generations of bronchial asthma patients in comparison to controls. In all digits the frequency of arches was reduced in both generations of bronchial asthma patients as compared to controls. These findings proved highly significant statistically (P value: $<.0001$). There was no significant change in finger tip patterns in II, & III digit, but, IV & V digit showed significant reduction in frequency of loops in both generations of bronchial asthma patients as compared to controls. There is scope of more studies in this field

and the significant findings can be included as part of clinical picture of bronchial asthma.

Gurel A. et al. *The Ala-9Val polymorphism in the mitochondrial targeting sequence (MTS) of the manganese superoxide dismutase gene is not associated with juvenile-onset asthma.* Clin Biochem. 2004; 37(12) : 1117-20.p **Abstract:** BACKGROUND: We aimed to investigate the possible association between Mn-SOD polymorphism in the mitochondrial targeting sequence and asthma. METHODS: Alanine or valine polymorphism in the signal peptide of Mn-SOD gene was evaluated using a primer pair to amplify a 107-bp fragment followed by digestion with NgoM IV. RESULTS: No significant difference in genotype frequencies was found between patients and controls. CONCLUSION: These results suggest no major modifying role for the Mn-SOD gene polymorphism in patients with asthma.

Gurkan F. et al. *Serum leptin levels in asthmatic children treated with an inhaled corticosteroid.* Ann Allergy Asthma Immunol. 2004; 93(3) : 277-80.p **Abstract:** BACKGROUND: Recent observations suggest the presence of an interaction between leptin and the inflammatory system; however, there is no adequate knowledge about the role of leptin in atopic states such as asthma. OBJECTIVES: To evaluate the potential role of leptin in relation to bronchial asthma and inhaled corticosteroid therapy. METHODS: Twenty-three children with mild-to-moderate, newly diagnosed asthma enrolled in this 2-period trial. The control group consisted of 20 age- and sex-matched children. Serum leptin levels were measured in patients at initiation and after 4 weeks of budesonide treatment and were compared with control group measurements. RESULTS: Asthmatic children had higher mean \pm SD serum leptin levels at admission (19.3 \pm 5.1 ng/mL) than after budesonide treatment (10.6 \pm 1.6 ng/mL) and vs control group measurements (9.8 \pm 1.6 ng/mL) ($P < .001$). There was a significant correlation between serum leptin levels before and after budesonide treatment ($r = 0.68$; $P = .007$). Mean \pm SD body mass indices in patients and controls were 16.7 \pm 2.1 and 16.9 \pm 2.6 kg/m², respectively. Serum leptin levels did not correlate with body mass indices before budesonide treatment in the study group ($r = -0.13$; $P = .65$) but correlated well after budesonide treatment ($r = 0.58$; $P = .009$) and in the control group ($r = 0.65$; $P = .008$). CONCLUSIONS: The role of leptin elevation in children with asthma might be a regulatory mechanism rather than being etiologic, but a question may be raised whether it is possible that leptin may contribute to poor patient outcomes. Further research, both basic and clinical, is essential to explain the exact mechanism.

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Haagerup A. et al. *Asthma and atopy - a total genome scan for susceptibility genes.* Allergy. 2002; 57(8) : 680-6.p **Abstract:** BACKGROUND: Allergic asthma is an increasingly common disease of complex inheritance. Several studies have suggested candidate regions, but genetic heterogeneity, ethnic differences and varying study designs may in part explain the lack of identified and confirmed susceptibility genes. Investigation of different populations will further clarify the topic. We therefore evaluated allergic asthma and increased total and specific IgE in 39, 45 and 57 sib-pairs from 100 Danish allergy families. METHODS: Affected sib-pairs meeting a narrow phenotype definition were selected for the three phenotypes atopy, allergic asthma and increased total IgE. We performed a total genome scan using 446 microsatellite markers and obtained nonparametric linkage results from the MAPMAKER/SIBS computer program. RESULTS: Our study revealed four candidate regions ($MLS > 2$) on chromosome 1p36, 3q21-q22, 5q31 and 6p24-p22, and 15 candidate regions ($1 < MLS < 2$) that may contain susceptibility genes for asthma and atopy. We did not find linkage to

the candidate genes TNF-beta, FcER1beta and IL4R-alpha, except for weak support for linkage of the asthma phenotype to TNF-beta (MLS = 1.18). CONCLUSIONS: We found evidence for two new asthma and atopy loci, 1p36 and 3q21-q22, and supported linkage in the Danish population to seven previously reported candidate regions.

Haas S.L. et al. -137 (G/C) IL-18 promoter polymorphism in patients with inflammatory bowel disease. *Scand J Gastroenterol.* 2005; 40(12) : 1438-43.p Abstract : OBJECTIVE: There is strong evidence that genetic factors contribute to the susceptibility for inflammatory bowel diseases (IBD). Recently, IL-18 promoter polymorphisms were characterized as risk factors for inflammatory diseases such as sepsis, asthma and adult-onset Still's disease. The aim of this study was to determine whether the -137 (G/C) IL-18 promoter polymorphism was associated with IBD susceptibility. MATERIAL AND METHODS: For association analysis, 470 patients with Crohn's disease (CD), 235 unrelated patients with ulcerative colitis (UC) and 347 controls were enrolled. Furthermore, 233 UC and 470 CD trios were included for segregation analysis. Genotyping was performed by application of the TaqMan MGB biallelic discrimination system. RESULTS: When comparing genotype frequencies of CD and UC patients versus controls, no significant difference was found ($p=0.089$ and $p=0.078$, respectively). However, the Cochran-Armitage trend test revealed a rising probability for CD and UC with increasing number of G alleles ($p=0.030$ and 0.028 , respectively) for the case-control analysis. On the contrary, the family-based transmission disequilibrium test (TDT) did not show an association of the G allele with CD or UC in 470 CD and 233 UC trios ($p=0.53$ and $p=0.79$, respectively). CONCLUSION: The -137 (G/C) IL-18 promoter polymorphism is not a susceptibility factor for IBD in a German cohort.

Haby M.M. et al. Asthma in preschool children: prevalence and risk factors. *Thorax.* 2001; 56(8) : 589-95.p Abstract: BACKGROUND: The prevalence of asthma in children has increased in many countries over recent years. To plan effective interventions to reverse this trend we need a better understanding of the risk factors for asthma in early life. This study was undertaken to measure the prevalence of, and risk factors for, asthma in preschool children. METHODS: Parents of children aged 3-5 years living in two cities (Lismore, $n=383$; Wagga Wagga, $n=591$) in New South Wales, Australia were surveyed by questionnaire to ascertain the presence of asthma and various proposed risk factors for asthma in their children. Recent asthma was defined as ever having been diagnosed with asthma and having cough or wheeze in the last 12 months and having used an asthma medication in the last 12 months. Atopy was measured by skin prick tests to six common allergens. RESULTS: The prevalence of recent asthma was 22% in Lismore and 18% in Wagga Wagga. Factors which increased the risk of recent asthma were: atopy (odds ratio (OR) 2.35, 95% CI 1.49 to 3.72), having a parent with a history of asthma (OR 2.05, 95% CI 1.34 to 3.16), having had a serious respiratory infection in the first 2 years of life (OR 1.93, 95% CI 1.25 to 2.99), and a high dietary intake of polyunsaturated fats (OR 2.03, 95% CI 1.15 to 3.60). Breast feeding (OR 0.41, 95% CI 0.22 to 0.74) and having three or more older siblings (OR 0.16, 95% CI 0.04 to 0.71) decreased the risk of recent asthma. CONCLUSIONS: Of the factors tested, those that have the greatest potential to be modified to reduce the risk of asthma are breast feeding and consumption of polyunsaturated fats.

Haby M.M. et al. Asthma in children: gaps between current management and best practice. *J Paediatr Child Health.* 2002; 38(3) : 284-9.p Abstract: OBJECTIVES: To determine the extent to which steps three to six of the Australian six-step asthma management plan are being implemented in the community and to identify barriers to the adoption of best practice asthma management. METHODS: A cross-sectional descriptive study was conducted at the Royal Children's Hospital and Sunshine Hospital, Melbourne. Two hundred and thirty-

one 2-5-year old children who visited the emergency department for asthma were enrolled in the study. Main outcome measures were frequency of asthma management practices and barriers, as measured by parent-completed questionnaire. RESULTS: Gaps: 51% of parents do not feel they have enough information about asthma triggers, more than 60% of children with persistent or frequent episodic asthma are not using regular preventive medication, 48% do not have a written action plan, 39% have not had their asthma reviewed in the last 6 months, and 38% of parents do not feel that they have enough information about their child's asthma. Areas where current practice was close to best practice: 83% of doctors had talked to parents about what causes or 'triggers' their child's asthma, less than 1% of children are using puffers without a spacer, 83% of parents who had an action plan used it for the current visit to the emergency department. CONCLUSIONS: Large gaps still exist between current management and best practice in this group of emergency department attenders. Improvements in asthma management could be achieved if the child's asthma doctor requested review visits for asthma, provided an action plan and followed best practice in relation to asthma medications.

Hack M. et al. Chronic conditions, functional limitations, and special health care needs of school-aged children born with extremely low-birth-weight in the 1990s. *JAMA.* 2005; 294(3) : 318-25.p Abstract: CONTEXT: Information on the school-age functioning and special health care needs of extremely low-birth-weight (ELBW, <1000 g) children is necessary to plan for medical and educational services. OBJECTIVE: To examine neurosensory, developmental, and medical conditions together with the associated functional limitations and special health care needs of ELBW children compared with normal-birth-weight (NBW) term-born children (controls). DESIGN, SETTING, AND PARTICIPANTS: A follow-up study at age 8 years of a cohort of 219 ELBW children born 1992 to 1995 (92% of survivors) and 176 NBW controls of similar sociodemographic status conducted in Cleveland, Ohio. MAIN OUTCOME MEASURES: Parent Questionnaire for Identifying Children with Chronic Conditions of 12 months or more and categorization of specific medical diagnoses and developmental disabilities based on examination of the children. RESULTS: In logistic regression analyses adjusting for sociodemographic status and sex, ELBW children had significantly more chronic conditions than NBW controls, including functional limitations (64% vs 20%, respectively; odds ratio [OR], 8.1; 95% confidence interval [CI], 5.0-13.1; $P<.001$), compensatory dependency needs (48% vs 23%, respectively; OR, 3.0; 95% CI, 1.9-4.7; $P<.001$), and services above those routinely required by children (65% vs 27%, respectively; OR, 5.4; 95% CI, 3.4-8.5; $P<.001$). These differences remained significant when the 36 ELBW children with neurosensory impairments were excluded. Specific diagnoses and disabilities for ELBW vs NBW children included cerebral palsy (14% vs 0%, respectively; $P<.001$), asthma (21% vs 9%; OR, 3.0; 95% CI, 1.6-5.6; $P = .001$), vision of less than 20/200 (10% vs 3%; OR, 3.1; 95% CI, 1.2-7.8; $P = .02$), low IQ of less than 85 (38% vs 14%; OR, 4.5; 95% CI, 2.7-7.7; $P<.001$), limited academic skills (37% vs 15%; OR, 4.2; 95% CI, 2.5-7.3; $P<.001$), poor motor skills (47% vs 10%; OR, 7.8; 95% CI, 4.5-13.6; $P<.001$), and poor adaptive functioning (69% vs 34%; OR, 6.5; 95% CI, 4.0-10.6; $P<.001$). CONCLUSION: The ELBW survivors in school at age 8 years who were born in the 1990s have considerable long-term health and educational needs.

Hack M. et al. Predictors of internalizing symptoms among very low birth weight young women. *J Dev Behav Pediatr.* 2005; 26(2) : 93-104.p Abstract: As part of a longitudinal study of the outcomes of very low birth weight children (<1.5 kg), we sought to examine the perinatal, childhood, and young adult predictors of internalizing symptoms among very low birth weight young women and their normal birth weight controls. The cohort included 125 very low birth weight and 124 normal birth weight 20-year-old subjects. Perinatal, childhood, and young adult predictors were examined via stepwise multivariate analyses. Results revealed very low birth weight to be a significant

predictor of parent-reported internalizing symptoms of their daughters but only among white subjects who had mothers with high levels of psychological distress. Additional significant predictors of 20-year internalizing symptoms included child I.Q. and internalizing symptoms at age 8 years and family expressiveness. When the results were analyzed according to the young adult self-report, additional predictors of internalizing symptoms included a history of asthma and exposure to violence. Perinatal risk factors were not found to be predictive of internalizing symptoms at age 20 years. Future studies should prospectively examine social and environmental factors associated with the neonatal intensive care experience that might explain the effect of very low birth weight on later psychopathology.

Hadjikoumi I. et al. *Exhaled nitric oxide measurements in childhood asthma: comparison of two sampling techniques.* *Pediatr Res.* 2002; 52(5) : 745-9.p **Abstract:** Nitric oxide (NO) is being increasingly used to assess airway inflammation in childhood. The method recommended by the American Thoracic Society workshop is for a prolonged expiration against a resistance. However, this is very difficult to apply in young children. As a result there have been a number of studies in which mixed expired gas has been collected and analyzed for NO content as this requires very little cooperation. This method has, however, yet to be fully validated. The aims of this study were to compare the two sampling techniques of exhaled NO concentrations in asthmatic and healthy children and to assess the correlation between NO levels and spirometry values in asthmatic children. We studied 25 control children, mean age 11.5 y, and 20 asthmatics, mean age 12 y. The exhaled NO was sampled using both the single breath technique (SB) and by measuring the NO content in mixed expired air after 1 min tidal breathing (ME). Forced expiratory volume in 1 s (FEV(1)) and expiratory flow rates at 25%, 50%, and 75% of vital capacity (FEF(25), FEF(50), FEF(75), respectively) were measured by compact II spirometer (best of three) in the 20 asthmatic children. The NO level was significantly higher in the asthmatics versus the control children when measured by SB ($p = 0.0015$) but not when measured by ME ($p = 0.1913$). The NO results measured by SB were significantly higher than ME results in the asthmatic children ($p = 0.008$). The NO levels were negatively correlated to FEV(1), FEF(25), FEF(50), and FEV(75) when measured by SB ($p < 0.02$) but not when measured by ME. The SB but not the ME method for measuring expired NO discriminates between asthmatic and control children and correlates well with the degree of airway obstruction. The use of the ME technique remains unproven.

Hagendorens M.M. et al. *Flow cytometrical determination of regulatory cytokines (IL-10, IL-12) and circulating dendritic cell cytokines in allergic asthmatic children.* *Cytokine.* 2004; 26(2) : 82-8.p **Abstract:** Interleukin (IL)-10 and IL-12 have been suggested to be key regulators in the pathogenesis of allergic asthma. Several of the secretion products of dendritic cells (DC), such as IL-12, IL-10, IL-1beta and TNF-alpha, are considered to play a role in allergic asthma. This study compares the production of IL-10 and IL-12 in allergic asthmatic children ($n = 17$) and controls ($n = 14$) by measuring their extracellular secretion in whole blood samples after stimulation, using a microsphere-based immunoassay. Additionally, we assessed intracellular production of IL-1beta, TNF-alpha, IL-12 and IL-10 by circulating DC in stimulated whole blood samples of asthmatic and healthy children. The concentration of IL-10 in the supernatants of LPS-stimulated whole blood was significantly lower in allergic asthmatic children as compared to healthy children (463 (207-768) vs 881 (364-2626) pg/mL; $p = 0.005$). When a combined LPS and IFN-gamma stimulation was used, IL-10 production decreased significantly as compared to LPS alone, especially in healthy children. Consequently, no difference in IL-10 production after LPS/IFN-gamma stimulation was found between healthy and allergic children. In contrast to isolated LPS stimulation, stimulation with LPS/IFN-gamma induced higher IL-12 production; allergic asthmatic children showed a significantly lower IL-12 secretion after

LPS/IFN-gamma stimulation as compared to healthy children (20 (5-247) vs 208 (7-775) pg/mL; $p=0.03$). Moreover, the number of IL-12 producing CD11c-positive DC (DC1) tended to be lower in asthmatic children compared to healthy children (0.05 (0.00-0.45) vs 0.27 (0.00-0.83) 10(6)/L) and correlated with the extracellular release of IL-12 in asthmatic children ($r = 0.65$; $p = 0.016$). The number of IL-1beta and TNF-alpha producing CD11c-positive DC (DC1) was comparable between healthy and asthmatic children. We hypothesize that the decreased production of IL-10 and IL-12 is responsible for Th2 polarized responses in allergic asthmatic children.

Hagwall N. et al. *Periventricular leukomalacia and retinopathy in a term infant born to a mother with asthma.* *Dev Med Child Neurol.* 2006; 48(4) : 301-3.p **Abstract:** A male child, born at 37+5 gestational weeks (GWs) (birthweight 2000g) after intrauterine growth retardation (IUG; -3 SD), to a mother treated during pregnancy for asthma, developed periventricular leukomalacia and retinopathy with total retinal detachment in the left eye and partial detachment in the right eye. Apart from basic asthma treatment with terbutalin, budesonid, and fenoterolhydrobromid throughout the pregnancy, she was treated with intravenous or oral cortisone for 6.5 weeks from 28+5 GWs. In addition she developed deep venous thrombosis at 29 GWs and was treated with heparin until delivery. Psychotic symptoms during the 31st GW were treated with diazepam, haloperidol, and levomepromazin. Functional sequelae for the child were visual impairment (visual acuity 5/60), uneven intellectual profile (Wechsler Pre-school and Primary Scale of Intelligence, Verbal IQ 94 and Performance IQ 32 at 8y of age), and autistic-like behaviour. The possibility that pre- and perinatal risk factors (e.g. severe maternal illness, IUGR, and cortisone treatment) in a term infant may create conditions for developing eye and brain pathologies commonly closely related to preterm birth should be considered.

Hahn D.L. *Origins of atopy in pediatric asthma.* *J Allergy Clin Immunol.* 2005; 115(2) : 425-6; author reply 426.p

Hahn D.L. *A theory explaining time trends in asthma prevalence.* *Eur Respir J.* 2006; 27(2) : 434-5; author reply 435-6.p

Hakonarson H. et al. *Allelic frequencies and patterns of single-nucleotide polymorphisms in candidate genes for asthma and atopy in Iceland.* *Am J Respir Crit Care Med.* 2001; 164(11) : 2036-44.p **Abstract:** Numerous asthma and atopy loci have been reported in studies demonstrating associations of the asthma-related phenotypes atopy, elevated IgE levels, and bronchial hyperresponsiveness with alleles of microsatellite markers and single-nucleotide polymorphisms (SNPs) within specific cytokine/chemokine and IgE-regulating genes. Although the studies reporting these observations are compelling, most of them lack statistical power. We assessed the nature, pattern, and frequency of SNPs in 24 candidate genes in Iceland and looked for associations with asthma and atopy. We identified 42 SNPs with an average minor allele frequency of 20.3% (asthma) and 20.7% (control). Twenty SNPs (48%) were within coding sequences and 90% of those led to a predicted change in protein sequence. No differences were detected in the allelic frequencies of SNPs in any of these candidate genes between control subjects and the patients with atopic asthma. Moreover, linkage analysis that included 269 patients with atopic asthma uncovered no evidence of linkage to markers associated with these genes. We conclude that this study has failed to produce evidence in support of the notion that variations within these 24 candidate atopy and asthma genes significantly influence the expression of the atopic asthmatic phenotype or contribute to the susceptibility of atopic asthma.

Halasz A. et al. *Relationship between the tumor necrosis factor system and the serum interleukin-4, interleukin-5, interleukin-8, eosinophil*

cationic protein, and immunoglobulin E levels in the bronchial hyperreactivity of adults and their children. Allergy Asthma Proc. 2003; 24(2) : 111-8.p **Abstract:** The aim of the study was to investigate the activation of inflammatory mediators interleukin (IL)-4, IL-5, and IL-8; immunoglobulin E (IgE); and eosinophil cationic protein (ECP) and to evaluate the regulatory role of the tumor necrosis system (TNF) system in bronchial hyperreactivity. Adults who had suffered from bronchial asthma in childhood but who had been symptom free for at least 3 years were examined together with their children who did not have asthma. The serum concentrations of TNF-alpha, soluble TNF receptor 1 (sTNF-R1), TNF-R2, IL-4, IL-5, IL-8, ECP, and IgE were studied in symptom-free adults (n = 22) and their children (n = 22) with bronchial hyperreactivity. Nonhyperreactive individuals with a similar medical history (adults, n = 17; children, n = 20) served as controls. Significantly elevated serum TNF-alpha (X +/- SD: 5.13 +/- 1.37 pg/mL versus 3.91 +/- 0.61 pg/mL; p < 0.0001), sTNF-R1 (X +/- SD: 1.37 +/- 0.28 ng/mL versus 1.16 +/- 0.13 ng/mL; p = 0.0002), and sTNF-R2 (X +/- SD: 0.78 +/- 0.42 ng/mL versus 0.43 +/- 0.41 ng/mL; p = 0.0001); IL-4 (X +/- SD: 4.05 +/- 1.02 pg/mL versus 3.34 +/- 0.84 pg/mL; p = 0.0016); IgE (X +/- SD: 390.1 +/- 361.4 KU/L versus 130.2 +/- 166.1 KU/L; p = 0.0001); and ECP (X +/- SD: 17.57 +/- 11.03 micrograms/L versus 10.65 +/- 6.01 micrograms/L; p = 0.0016) concentrations were measured in the subjects with bronchial hyperreactivity as compared with the nonhyperreactive group. Significant positive linear correlations were observed for the bronchial hyperreactive group between the concentrations of TNF-alpha and ECP, TNF-alpha and sTNF-R1, TNF-alpha and IL-8, sTNF-R1 and ECP, sTNF-R1 and IL-8, and sTNF-R2 and IL-8. Moreover, the TNF-alpha and sTNF-R2 levels correlated with the airway reactivity in the hyperreactive group. We suggest that the elevated cytokine levels indicate activation of the immune system in individuals who were previously asthmatic, but recovered, and are now symptom free and in their children with nonasthmatic bronchial hyperreactivity. The TNF system may play a key role in the pathomechanism of bronchial hyperreactivity.

Hall J. et al. *Differential prescribing of inhaled corticosteroids in New Zealand general practice.* N Z Med J. 2003; 116(1180) : U563.p **Abstract:** AIM: To determine how inhaled budesonide, beclomethasone and fluticasone are prescribed by general practitioners in New Zealand. METHODS: Retrospective study of computerised clinical records from 42 general practices in New Zealand for the period 1 July 1997 to 30 June 1998. The study population comprised 174 929 consulting patients, of whom 9878 patients were prescribed budesonide, fluticasone, or beclomethasone with full dosing instructions. RESULTS: The mean daily prescribed dose was higher for patients receiving inhaled budesonide (886 microg) than beclomethasone (547 microg), a difference of 339 microg (95% CI 311 microg to 367 microg), and fluticasone (508 microg), a difference of 378 microg (95% CI 344-412). The difference between mean daily prescribed doses of beclomethasone and fluticasone was 39 microg (95% CI 15-63). The overall difference was consistent across age groups and with different types of inhalation device. Evidence of systematic prescribing of higher doses of budesonide to patients with more severe asthma was not found. Patients prescribed fluticasone were more likely to have been prescribed oral steroids in the preceding year. CONCLUSIONS: Conclusions about the relative potencies of inhaled corticosteroids cannot be made with the data presented. However, data presented show that inhaled corticosteroids have not been prescribed in line with their reported relative potencies. This study provides benchmark data for the prescribing of inhaled steroids in New Zealand general practice.

Halpern M.T. et al. *Allergic rhinitis: a potential cause of increased asthma medication use, costs, and morbidity.* J Asthma. 2004; 41(1) : 117-26.p **Abstract:** Allergic rhinitis and asthma each require costly medical resource utilization, and the impact of both conditions

is believed to be even greater. This retrospective cost of illness study evaluated the impact of allergic rhinitis on asthma medical care resource utilization rates and costs for patients with asthma plus allergic rhinitis vs. patients with asthma alone. Patients with one or more claims for asthma (n=27,398) were identified from a medical claims database from a large, northeastern U.S. health insurance plan (1992-1994). A subset of 9226 patients also had at least one visit for allergic rhinitis. Inpatient, professional service, major medical, and pharmaceutical (prescription medications) claims were examined. Patients with asthma and allergic rhinitis had greater medical utilization and costs than individuals with asthma only. The presence of allergic rhinitis was associated with greater frequencies and costs of prescriptions for all asthma-related medications evaluated in the study. Patients with both conditions were also more likely to receive care from medical specialists and less likely to be in managed care. Controlling for these factors, allergic rhinitis was still associated with an increase (P<0.0001) in annual costs of more than dollars 350. Allergic rhinitis in patients with asthma nearly doubles annual medical resource utilization and costs and is associated with increased utilization of asthma-related medications. Based on use of asthma medications, patients with concomitant allergic rhinitis can be regarded as having more severe asthma than do those without allergic rhinitis. Physicians should assess asthma patients for symptoms of allergic rhinitis to improve asthma treatment.

Halterman J.S. et al. *Behavior problems among inner-city children with asthma: findings from a community-based sample.* Pediatrics. 2006; 117(2) : e192-9.p **Abstract:** OBJECTIVE: Previous studies have suggested a relationship between childhood asthma and behavior problems. However, few studies have used community-based samples to assess the prevalence of behavior problems among urban children with asthma symptoms. The objective of this study was to evaluate the relationship between asthma symptoms and behavior among a population-based sample of inner-city children and to determine the prevalence of behavioral comorbidity among children with asthma symptoms. METHODS: In 2003, parents of children who were entering kindergarten in the city of Rochester completed a detailed survey regarding the child's background, medical history (with specific questions about asthma symptoms), and behavior. We compared children with no asthma symptoms, intermittent symptoms, and persistent symptoms with regard to positive peer social skills (eg, makes friends easily), negative peer social skills (eg, fights with other children), task orientation (eg, concentrates well), and shy/anxious behavior (eg, is withdrawn) (validated scales; range: 1-4). We used multivariate regression to determine the independent association between symptom severity and behavioral outcomes. RESULTS: A total of 1619 children were included (response rate: 80%; mean age: 5.1 year), and 15% had asthma symptoms (8% persistent, 7% intermittent). Average negative peer scores were worse for children with persistent asthma symptoms compared with children with intermittent and no symptoms (mean scores: 1.88, 1.70, and 1.65). Children with persistent symptoms also scored worse than children with no symptoms on the assessment of task orientation (2.85 vs 3.03) and shy/anxious behavior (2.11 vs 1.89). Among children with persistent asthma symptoms, >20% scored >1 SD below average on 2 or more scales, compared with 16% of children with intermittent symptoms and 10% with no symptoms. CONCLUSIONS: Urban children with persistent asthma symptoms demonstrate more behavior problems across several domains compared with children with no symptoms. These findings suggest a clear need for an early biopsychosocial approach to care for vulnerable children with asthma.

Halterman J.S. et al. *A randomized trial of primary care provider prompting to enhance preventive asthma therapy.* Arch Pediatr Adolesc Med. 2005; 159(5) : 422-7.p **Abstract:** BACKGROUND: Guidelines recommend preventive medications for all children with persistent asthma, yet young urban children often receive inadequate therapy. This may occur in part because primary care providers are

unaware of the severity of their patients' symptoms. **OBJECTIVE:** To determine whether systematic school-based asthma screening, coupled with primary care provider notification of asthma severity, will prompt providers to take preventive medication action (prescribe a new preventive medication or change a current dose). **DESIGN:** Children aged 3 to 7 years with mild persistent to severe persistent asthma were identified at the start of the 2002-2003 school year in Rochester. Children were assigned randomly to a provider notification group (child's primary care provider notified of asthma severity) or a control group (provider not notified of severity). Primary care providers of children in the provider notification group were sent a facsimile indicating the child's symptoms and recommending medication action based on national criteria. Interviewers blinded to the child's group assignment called parents 3 to 6 months later to determine if preventive actions were taken. **RESULTS:** Of 164 eligible children with mild persistent or more severe asthma, 151 (92.1%) were enrolled. Children in the provider notification group were not more likely to receive a preventive medication action than were children in the control group (21.9% vs 26.0%; $P = .57$). Additional preventive measures, including encouraging compliance with medications (33.3% vs 31.3%; $P = .85$), recommending environmental modifications (39.3% vs 42.4%; $P = .86$), and referrals for specialty care (6.6% vs 6.0%; $P > .99$), also did not differ between the provider notification and control groups. At the end of the study, 52.4% of children in both groups with no medication changes were still experiencing persistent symptoms. **CONCLUSIONS:** School-based asthma screening identified many symptomatic children in need of medication modification. Provider notification, however, did not improve preventive care. Findings suggest that more powerful interventions are needed to make systematic asthma screening effective.

Halterman J.S. et al. *Providers underestimate symptom severity among urban children with asthma.* Arch Pediatr Adolesc Med. 2002; 156(2) : 141-6.p **Abstract:** **BACKGROUND:** Guidelines recommend that children with mild persistent to severe persistent asthma receive maintenance anti-inflammatory medications. However, providers may not be aware of the severity of their patients' symptoms. The underestimation of severity may contribute to poor adherence to asthma care guidelines. **OBJECTIVES:** To describe the use of preventive medications among a group of urban children with mild persistent to severe persistent asthma and to evaluate the degree to which their health care providers are aware of their asthma severity. **DESIGN:** Children (ages 4-6 years) from urban schools in Rochester, NY, were eligible if their parents reported mild persistent to severe persistent asthma symptoms. Each child's health care provider was asked to assess the child's asthma severity and use of medications based both on their knowledge of the child and review of the medical record. Parent and provider assessments were compared. Bivariate and regression analyses were used to identify factors associated with concordant classifications of asthma severity. **RESULTS:** Ninety children with parent-defined mild persistent to severe persistent asthma participated (64% boys, 67% black, 73% receiving Medicaid). Only 40% of the children were described accurately by their providers as having mild persistent to severe persistent asthma, and only 50% of the total had been prescribed maintenance medications. Thirty-six percent of families reported that their child used maintenance medications daily. In contrast, most of the children who were classified by their provider as having mild persistent to severe persistent asthma were prescribed a maintenance medication (83%), and 58% used them daily. Sociodemographic characteristics and asthma severity were not associated with provider accuracy. **CONCLUSIONS:** Most children in this study were not accurately classified by their providers as having mild persistent to severe persistent asthma and had not been prescribed maintenance medications. When providers were aware of their patient's asthma symptoms, most of the children were prescribed maintenance medications. Attempts to improve adherence to asthma guidelines should take into consideration provider underestimations of asthma severity.

Halvorsen T. et al. *Pulmonary outcome in adolescents of extreme preterm birth: a regional cohort study.* Acta Paediatr. 2004; 93(10) : 1294-300.p **Abstract:** **AIMS:** The pulmonary outcome of extreme prematurity remains to be established in adults. We determined respiratory health and lung function status in a population-based, complete cohort of young preterms approaching adulthood. **METHODS:** Forty-six preterms with gestational age $< \text{or} = 28$ wk or birthweight $< \text{or} = 1000$ g, born between 1982 and 1985, were compared to the temporally nearest term-born subject of equal gender. Spirometry, plethysmography, reversibility test to salbutamol and methacholine bronchial provocation test were performed. Neonatal data were obtained from hospital records and current symptoms from validated questionnaires. **RESULTS:** When entering the study at a mean age of 17.7 (SD: 1.2) y, a doctor's diagnosis of asthma and use of asthma inhalers were significantly more prevalent among preterms than controls (one asthmatic control compared to nine preterms, all but one using asthma inhalers). Peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV1) were decreased and the discrepancies relative to controls increased parallel to increased severity of neonatal lung disease. Parameters of increased neonatal oxygen exposure significantly predicted FEV1. Adjusted for height, gender and age, FEV1 was reduced by a mean of 580 ml/s in subjects with a history of bronchopulmonary dysplasia. Fifty-six percent of preterms had a positive methacholine provocation test compared to 26% of controls. **CONCLUSION:** A substantially decreased FEV1, increased bronchial hyperresponsiveness and a number of established risk factors for steeper age-related decline in lung function were observed in preterms. A potential for early onset chronic obstructive pulmonary disease is present in subsets of this group.

Hammerness P. et al. *Reexamining the familial association between asthma and ADHD in girls.* J Atten Disord. 2005; 8(3) : 136-43.p **Abstract:** The objective of this study is to further evaluate the association between asthma and ADHD, addressing issues of familiarity in female probands. A case control study of referred ADHD proband girls, controls, and relatives are used. Participants include 140 ADHD proband girls and 122 non-ADHD comparisons, with 417 and 369 first-degree biological relatives, respectively. Relatives are stratified into four groups according to proband ADHD and asthma status. The authors compare rates of asthma and ADHD in relatives. ADHD does not increase the risk for asthma in probands. Patterns of familial aggregation are mostly consistent with independent transmission of ADHD and asthma in families of girl probands. The results extend to female probands' previously reported findings that asthma and ADHD are independently transmitted in families. These findings further support the conclusion that ADHD symptoms should not be dismissed as part of asthma symptomatology or a consequence of its treatment.

Hancox R.J. et al. *Relationship between socioeconomic status and asthma: a longitudinal cohort study.* Thorax. 2004; 59(5) : 376-80.p **Abstract:** **BACKGROUND:** There is conflicting information about the relationship between asthma and socioeconomic status, with different studies reporting no, positive, or inverse associations. Most of these studies have been cross sectional in design and have relied on subjective markers of asthma such as symptoms of wheeze. Many have been unable to control adequately for potential confounding factors. **METHODS:** We report a prospective cohort study of approximately 1000 individuals born in Dunedin, New Zealand in 1972-3. This sample has been assessed regularly throughout childhood and into adulthood, with detailed information collected on asthma symptoms, lung function, airway responsiveness, and atopy. The prevalence of these in relation to measures of socioeconomic status were analysed with and without controls for potential confounding influences including parental history of asthma, smoking, breast feeding, and birth order using cross sectional time

series models. **RESULTS:** No consistent association was found between childhood or adult socioeconomic status and asthma prevalence, lung function, or airway responsiveness at any age. Having asthma made no difference to educational attainment or socioeconomic status by age 26. There were trends to increased atopy in children from higher socioeconomic status families consistent with previous reports. **CONCLUSIONS:** Socioeconomic status in childhood had no significant impact on the prevalence of asthma in this New Zealand born cohort. Generalisation of these results to other societies should be done with caution, but our results suggest that the previously reported associations may be due to confounding.

Handelman L. et al. *Understanding pediatric inner-city asthma: an explanatory model approach.* *J Asthma.* 2004; 41(2) : 167-77.p **Abstract:** Explanatory models (EMs) for asthma among inner-city school-age children and their families were examined as a means of better understanding health behaviors. Children and parents were interviewed about their concepts of asthma etiology, asthma medications, and alternative therapies. Drawings were elicited from children to understand their beliefs about asthma. Nineteen children with 17 mothers from a variety of cultural backgrounds were interviewed. Among children, contagion was the primary EM for asthma etiology (53%). Twenty-five percent of children reported fear of dying from asthma, while fear of their child dying from asthma was reported by 76% of mothers. Mothers reported a variety of EMs, some culturally specific, but the majority reported biomedical concepts of etiology, pathophysiology, and triggers. Although 76% of mothers knew the names of more than one of their children's medications, 47% thought their child's medications all had similar functions. Thirty-five percent of families used herbal treatments and 35% incorporated religion into asthma treatment. Seventy-one percent of families had discontinued medications and 23% reported currently not giving anti-inflammatory medication. Reasons for discontinuing daily medications included fears of unknown side effects (53%), addiction (18%), tachyphylaxis (18%), and feeling that their child was being given too much medicine (23%). The traditional focus of asthma education is not sufficient to ensure adherence. Asthma education for children should address their views of etiology and fears about dying from asthma. Conversations with parents about their EMs and beliefs about medications and alternative therapies could assist in understanding and responding to parental concerns and choices about medications and help achieve better adherence.

Hansell A. et al. *Validity and interpretation of mortality, health service and survey data on COPD and asthma in England.* *Eur Respir J.* 2003; 21(2) : 279-86.p **Abstract:** The comparability of asthma and chronic obstructive pulmonary disease (COPD) epidemiology in different English routine data sources was examined to explore their use and validity in investigating environmental influences on respiratory health. National data were obtained for mortality, emergency hospital admissions, general practitioner contacts and symptoms in the early 1990s. Age/sex patterns, seasonal variations and regional and urban/rural age/sex standardised event ratios were examined. Spearman rank correlations were used to describe consistency of regional rankings across data sets. Asthma showed inconsistent disease patterns in different data sources and weak correlations for regional rankings but COPD was notably consistent. Unmeasured confounders may partly explain the findings, but individual level adjustment for social class and smoking (possible for symptoms) only partially attenuated the higher COPD rates in northern and urban areas and did not affect findings for asthma. When epidemiological patterns are consistent across data sources as with chronic obstructive pulmonary disease in England, healthcare use is likely to reflect the underlying prevalence and severity of disease and can be used to study environmental influences. When patterns vary, as with asthma, the validity of the data in relation to its intended use must be carefully considered.

Hao K. et al. *Familial aggregation of airway responsiveness: a community-based study.* *Ann Epidemiol.* 2005; 15(10) : 737-43.p **Abstract:** **PURPOSE:** We investigated the familial aggregation of airway hyper-responsiveness (AHR) to methacoline among randomly chosen families in a rural community in Anqing, China. **METHODS:** Airway responsiveness (AR) to methacoline and related risk factors were assessed in each subject. We first modeled the within family correlation in AR and demonstrated the familial aggregation of this trait. Furthermore, we examined the effect size (e.g., odds ratio, OR) of this correlation in a "subsequent offspring model." **RESULTS:** The correlation coefficient is significantly positive for parent-offspring and offspring-offspring pairs, but not significant in father-mother pairs, suggesting a genetic component. The strength of the relationships is in the order of father-offspring < mother-offspring < offspring-offspring. The OR of a positive AHR test for subsequent offspring who had mothers and an eldest sibling with positive AHR is 4.12 (95% CI, 1.72-9.87), compared with subsequent offspring whose mother and eldest sibling were negative in the test. **CONCLUSION:** Our study supports a familial clustering of AHR in a Chinese population, which points to a role for genetic factors.

Harmanci K. et al. *Oral montelukast treatment of preschool-aged children with acute asthma.* *Ann Allergy Asthma Immunol.* 2006; 96(5) : 731-5.p **Abstract:** **BACKGROUND:** Increased amounts of cysteinyl leukotrienes have been demonstrated in urine samples from asthmatic patients, particularly during exacerbations of asthma. Although the use of leukotriene receptor antagonists has been recommended in the treatment of chronic asthma, no guidelines are available regarding their use in the treatment of acute asthma. **OBJECTIVE:** To investigate the safety and effectiveness of a 4-mg tablet of oral montelukast in addition to short-acting beta2-agonist bronchodilator as the initial treatment in mild to moderate asthma exacerbations in children between 2 and 5 years old. **METHODS:** Fifty-one patients who were experiencing mild to moderate asthma exacerbation were included in a randomized, double-blind, placebo-controlled, parallel-group study. Each patient received either a 4-mg tablet of montelukast or placebo in addition to inhaled salbutamol and were followed up for 4 hours. The pulmonary index score, respiratory rate, and pulse were determined at baseline and throughout 4 hours after administration. **RESULTS:** Compared with placebo, the pulmonary index scores and respiratory rates were significantly lower in the montelukast group starting at 90 minutes ($P = .01$). This difference persisted at 120, 180, and 240 minutes of the study ($P = .008$, $P = .02$, and $P = .048$, respectively). At the end of the first hour of treatment, oral steroid need was 20.8% and 38.5% in patients randomized to the montelukast and placebo groups, respectively ($P = .22$). Hospitalization rates were not different between the 2 treatment groups. **CONCLUSION:** A single 4-mg tablet of montelukast had the potential to provide additive clinical benefit in mild to moderate acute asthma in preschool-aged children when administered concomitantly with short-acting beta2-agonist bronchodilators as the initial treatment.

Harris L. *Asthma education for middle school students and staff.* *J Sch Nurs.* 2002; 18(2) : 117-21.p **Abstract:** In recent years, the number of middle school students identified with asthma has increased dramatically. In addition, physical education teachers were concerned about the lack of class participation among many of these students. Students with asthma had little knowledge about the respiratory system or how to control their asthma. After overcoming certain barriers, an asthma education program was developed for the middle school students. The primary objective was to promote self-management of asthma and provide resources as needed. In addition, an asthma education program was presented to school personnel to enhance their ability to assist students with asthma and allergies in the school setting. Included in this article is an extensive list of resources about asthma.

Harrison R.M. et al. *Personal exposure monitoring of particulate matter, nitrogen dioxide, and carbon monoxide, including susceptible groups.* *Occup Environ Med.* 2002; 59(10) : 671-9.p **Abstract:** AIMS: To investigate the relation between personal exposures to nitrogen dioxide, carbon monoxide, and PM(10), and exposures estimated from static concentrations of these pollutants measured within the same microenvironments, for healthy individuals and members of susceptible groups. METHODS: Eleven healthy adult subjects and 18 members of groups more susceptible to adverse health changes in response to a given level of exposure to nitrogen dioxide, carbon monoxide, and/or PM(10) than the general population (six schoolchildren, six elderly subjects, and six with pre-existing disease-two with chronic obstructive pulmonary disease (COPD), two with left ventricular failure (LVF), and two with severe asthma) were recruited. Daytime personal exposures were determined either directly or through shadowing. Relations between personal exposures and simultaneously measured microenvironment concentrations were examined. RESULTS: Correlations between personal exposures and microenvironment concentration were frequently weak for individual subjects because of the small range in measured concentrations. However, when all subjects were pooled, excellent relations between measured personal exposure and microenvironment concentration were found for both carbon monoxide and nitrogen dioxide, with slopes of close to one and near zero intercepts. For PM(10), a good correlation was also found with an intercept of personal exposure (personal cloud) of 16.7 (SD 10.4) micro g/m³. Modelled and measured personal exposures were generally in reasonably good agreement, but modelling with generic mean microenvironment data was unable to represent the full range of measured concentrations. CONCLUSIONS: Microenvironment measurements of carbon monoxide and nitrogen dioxide can well represent the personal exposures of individuals within that microenvironment. The same is true for PM(10) with the addition of a personal cloud increment. Elderly subjects and those with pre-existing disease received generally lower PM(10) exposures than the healthy adult subjects and schoolchildren by virtue of their less active lifestyles.

Harrop M. *Self-management plans in childhood asthma.* *Nurs Stand.* 2002; 17(10) : 38-42.p **Abstract:** Current literature supports the use of self-management plans in childhood asthma. The aim of this article is to describe the purpose of such plans. It gives step-by-step advice on how to prepare an individualized management plan and discusses important considerations on how they can best be implemented in clinical practice.

Hartert T.V. et al. *Antibiotics for asthma?* *Clin Infect Dis.* 2004; 38(10) : 1347-9.p

Hartl D. et al. *Pulmonary chemokines and their receptors differentiate children with asthma and chronic cough.* *J Allergy Clin Immunol.* 2005; 115(4) : 728-36.p **Abstract:** BACKGROUND: Cough is a frequent symptom in children, but the differentiation of asthmatic cough from cough of other origins can be difficult. Chemokines recruit T lymphocytes to inflamed tissues, and the corresponding chemokine receptors are differentially expressed on T H 1 and T H 2 cells. OBJECTIVE: We sought to determine whether levels of T H 1/T H 2-related chemokines and their receptors differ in bronchoalveolar lavage fluid (BALF) from 12 children with allergic asthma, 15 nonatopic children with chronic cough, and 10 children without airway disease. METHODS: The T H 1-related (IFN-gamma-inducible protein of 10 kd [IP-10], IFN-gamma-inducible T cell alpha chemoattractant [ITAC], monokine induced by IFN-gamma [Mig], and IFN-gamma) and T H 2-related (thymus- and activation-regulated chemokine [TARC], macrophage-derived chemokine [MDC], IL-5, and IL-4) chemokines and cytokines were

quantified in BALF by ELISA and a particle-based multiplex array. Percentages of pulmonary lymphocytes expressing CXCR3 + and CCR5 + (T H 1) and CCR4 + and CCR3 + (T H 2) chemokine receptors were determined in BALF by flow cytometry. RESULTS: Pulmonary CCR4 + CD4 + cells and levels of TARC and MDC were significantly increased in asthmatic children versus children with chronic cough or without airway disease. In asthmatic children CCR4 + CD4 + cells correlated positively with levels of TARC, MDC, and serum IgE levels and negatively with FEV₁. In contrast, CXCR3 + CD8 + cells and levels of ITAC were significantly increased in children with non-atopic chronic cough compared with the other groups. In children with chronic cough, CXCR3 + CD8 + cells correlated with levels of ITAC and IFN-gamma. CONCLUSION: Pulmonary CCR4 + CD4 + and CXCR3 + CD8 + cells and their ligands TARC, MDC, and ITAC clearly differentiate asthmatic children from nonatopic children with chronic cough. The analysis of these markers could facilitate the diagnostic discrimination of asthma versus other reasons for chronic cough in children.

Hartl D. et al. *A role for MCP-1/CCR2 in interstitial lung disease in children.* *Respir Res.* 2005; 6 : 93.p **Abstract:** BACKGROUND: Interstitial lung diseases (ILD) are chronic inflammatory disorders leading to pulmonary fibrosis. Monocyte chemoattractant protein 1 (MCP-1) promotes collagen synthesis and deletion of the MCP-1 receptor CCR2 protects from pulmonary fibrosis in ILD mouse models. We hypothesized that pulmonary MCP-1 and CCR2+ T cells accumulate in pediatric ILD and are related to disease severity. METHODS: Bronchoalveolar lavage fluid was obtained from 25 children with ILD and 10 healthy children. Levels of pulmonary MCP-1 and Th1/Th2-associated cytokines were quantified at the protein and the mRNA levels. Pulmonary CCR2+, CCR4+, CCR3+, CCR5+ and CXCR3+ T cells were quantified by flow-cytometry. RESULTS: CCR2+ T cells and MCP-1 levels were significantly elevated in children with ILD and correlated with forced vital capacity, total lung capacity and ILD disease severity scores. Children with lung fibrosis had significantly higher MCP-1 levels and CCR2+ T cells in bronchoalveolar lavage fluid compared to non-fibrotic children. CONCLUSION: The results indicate that pulmonary CCR2+ T cells and MCP-1 contribute to the pathogenesis of pediatric ILD and might provide a novel target for therapeutic strategies.

Hasbargen U. et al. *Growth and development of children to 4 years of age after repeated antenatal steroid administration.* *Eur J Pediatr.* 2001; 160(9) : 552-5.p **Abstract:** It is common practice to repeat antenatal steroid administration after 7 to 10 days in women who continue to be at risk for preterm delivery. However, safety and efficacy of repeated courses have not been established. Mothers of singleton infants who had more than five courses of betamethasone (80-120 mg cumulative dose) were eligible for this cohort study. Index patients (IP) were compared to concurrent controls who had < or = 1 course but were matched for sex and gestational age. Of 35 IP born between 1986 and 1995 in a single perinatal centre, 28 were available for follow-up and could be matched. There was no difference between groups with respect to maternal age and gestational age at delivery. Median gestational age at initial treatment was 26.3 weeks (25th percentile 25.1 weeks, 75th percentile 27.2 weeks) in IP. There was no significant difference between groups in head circumference, length and body weight at birth and at age 4 years. The ability to sit and to walk without assistance and to use two-word phrases was attained at similar ages. The use of glasses or hearing aids, allergies, asthma or recurrent upper respiratory infections were not reported more frequently in IP. CONCLUSION: This study failed to ascertain adverse long-term effects of repeated antenatal steroid administration in infants and children to the age of 4 years. In contrast to a similar Australian study, we were unable to demonstrate a lower birth size in exposed infants even though our sample size for women with more than five courses and their cumulative doses were larger.

Hasegawa K. et al. *Variations in the C3, C3a receptor, and C5 genes affect susceptibility to bronchial asthma.* Hum Genet. 2004; 115(4) : 295-301.p **Abstract:** Bronchial asthma (BA) is a common chronic inflammatory disease characterized by hyperresponsive airways, excess mucus production, eosinophil activation, and the production of IgE. The complement system plays an immunoregulatory role at the interface of innate and acquired immunities. Recent studies have provided evidence that C3, C3a receptor, and C5 are linked to airway hyperresponsiveness. To determine whether genetic variations in the genes of the complement system affect susceptibility to BA, we screened single nucleotide polymorphisms (SNPs) in C3, C5, the C3a receptor gene (C3AR1), and the C5a receptor gene (C5R1) and performed association studies in the Japanese population. The results of this SNP case-control study suggested an association between 4896C/T in the C3 gene and atopic childhood BA (P = 0.0078) as well as adult BA (P = 0.010). When patient data were stratified according to elevated total IgE levels, 4896C/T was more closely associated with adult BA (P = 0.0016). A patient-only association study suggested that severity of childhood BA was associated with 1526G/A of the C3AR1 gene (P = 0.0057). We identified a high-risk haplotype of the C3 gene for childhood (P = 0.0021) and adult BA (P = 0.0058) and a low-risk haplotype for adult BA (P = 0.00011). We also identified a haplotype of the C5 gene that was protective against childhood BA (P = 1.4 x 10(-6)) and adult BA (P = 0.00063). These results suggest that the C3 and C5 pathways of the complement system play important roles in the pathogenesis of BA and that polymorphisms of these genes affect susceptibility to BA.

Hauache A.G. et al. *IGF-I, IGF-BP3, and GH serum levels after stimulation tests in prepubertal allergic boys.* J Investig Allergol Clin Immunol. 2003; 13(4) : 266-71.p **Abstract:** The prevalence of short stature (SS, < 3rd percentile NCHS) among children with respiratory allergy (asthma and/or rhinitis) varies from 2% to 10%. In spite of several studies, the etiology of SS in those patients remains unknown. We evaluated growth hormone (GH) serum levels in response to two stimulating tests (standardized exercise and clonidine) in prepubertal boys (GIP1, Tanner; 8 years and 5 months to 14 years) with SS, 14 of them with respiratory allergy (A, positive skin prick test to D. pteronyssinus) and 5 nonallergic children (NA). Other causes of SS were excluded in both groups. Patients had mild asthma and/or rhinitis, and they had never received inhaled or systemic corticosteroid at any time. Tests were performed on different days, at least 1 week apart. [To prevent exercise-induced asthma, 30 min before the exercise test, allergic children inhaled disodium cromoglycate (2 mg)]. GH serum levels (Immunoassay, AIA-PACK HGH, Tosoh Co, Japan) were determined at the following times: exercise (E)--basal, 5, 15, and 30 min after exercising for 6 min; clonidine (C)--basal, 30, 60, and 90 min after clonidine (0.15 mg/m² body surface) ingestion. A response was considered positive when GH serum levels reached the minimum of 10 ng/ml. Among (the allergic) A patients, four responded to both tests, five to C (clonidine) alone, four to E (exercise) alone and one had no response. Among NA, four had a positive response to both tests and one to C (clonidine) alone. The serum levels of insulin-like growth factor I (IGF-I) (DSL-5600 Active TM IGF-I Coated-Tube IRMA [DSL Lab Inc, USA]) and its binding protein (IGF-BP3) (DSL-6600 Active TM IGF-BP3 Coated-Tube IRMA [DSL Lab Inc, USA]) were within the normal range except for one A child. Bone age was delayed in relation to chronological age in all children, but adequate for height age. All children had delayed skeletal age in relation to chronological age, but bone age was normal for height. We concluded that in the children studied a deficiency of GH does not seem to be responsible for SS.

Hayashi K. et al. *Oxatomide for stable asthma in adults and children.* Cochrane Database Syst Rev. 2003; (2) : CD002179.p **Abstract:** BACKGROUND: Oxatomide is a histamine H1-receptor antagonist. As an oral agent, oxatomide may be useful in managing asthma. Some guidelines recommend oxatomide for long-term prophylaxis of

asthma in children. There is no clear evidence whether children or adults with asthma benefit from oxatomide. OBJECTIVES: To determine whether oxatomide alone, or in combination with other interventions, results in better disease control in people with asthma. SEARCH STRATEGY: The Collaborative Airway Group register and Collaborations trial register CENTRAL were searched using terms: oxatomide* OR Cellect OR Pinset OR KW-4354 OR Tinct. Reference lists of all relevant trials or review articles were checked. Enquiries were made of authors of included studies and relevant pharmaceutical companies. A search of 'Igaku Chuo Zasshi' and 'J-Medicine' were made using the following terms: oxatomide (also in Japanese) or Cellect (also in Japanese) or KW-4354. SELECTION CRITERIA: Studies were randomised, placebo-controlled trials and the interventions were oxatomide or matched placebo given alone or in combination with other asthma-medication for at least 4 weeks. DATA COLLECTION AND ANALYSIS: Four independent reviewers performed assessments of methodological quality and extracted relevant data. MAIN RESULTS: Six studies are included in this review. Three studies were mainly conducted in adults, two were conducted in older children (5-16 years) and one in infants (18-25 months). Trial duration was 4 to 52 weeks. Doses of oxatomide varied between studies, ranging from 1 mg/kg/day for infants to 180 mg/day for adults. Only data on adverse events was suitable for meta-analysis. Although PEF did not change significantly in any of the studies, the FVC and FEV1 improved significantly in two. There was no uniform change in symptom scores. There was no significant difference between oxatomide and placebo treatment in use of inhaled corticosteroid or bronchodilator. Two studies showed significant improvement with oxatomide as judged subjectively by physicians. Adverse events, analysed using data from 4 parallel and one cross over study, showed oxatomide to be associated with a significantly higher risk of any adverse event (OR: 2.97, 95%CI: 1.69 to 5.22) and drowsiness (OR: 5.22,95%CI: 2.53 to 10.74). REVIEWER'S CONCLUSIONS: There is no evidence to show that oxatomide has a significant effect on the control of stable asthma. Some studies reported significant benefits in subjective parameters. There was improvement in some lung function outcomes reported, but this were not consistent across measures or studies and may represent reporting bias. Adverse events, including drowsiness, were significantly greater with oxatomide than placebo.

Hayday K. et al. *In children hospitalized for asthma exacerbations, does adding ipratropium bromide to albuterol and corticosteroids improve outcome?* J Fam Pract. 2002; 51(3) : 280.p

Haynes J.M. et al. *Use of heliox to avoid intubation in a child with acute severe asthma and hypercapnia.* Am J Crit Care. 2003; 12(1) : 28-30.p

Heap E. et al. *Emergency asthma inhalers in schools.* Arch Dis Child. 2004; 89(6) : 590.p

Heaton T. et al. *Staphylococcal enterotoxin induced IL-5 stimulation as a cofactor in the pathogenesis of atopic disease: the hygiene hypothesis in reverse?* Allergy. 2003; 58(3) : 252-6.p **Abstract:** BACKGROUND: The incidence of Staphylococcus aureus (S. aureus) colonization on the skin of patients with atopic eczema/dermatitis syndrome (AEDS) is approximately 90% and a variety of evidence implicates epidermal staphylococcal infection as a pathogenic factor in atopic dermatitis. However, the mechanism(s) underlying the effects of this organism in the disease process are unclear. The cellular responses of AEDS sufferers and asymptomatic atopic individuals to bacterial superantigens (SAg) were investigated in an attempt to elucidate the role of staphylococcal enterotoxin B (SEB) in atopic disease. METHODS: Peripheral blood mononuclear cells (PBMC) were isolated from normal nonatopic adults, asymptomatic atopic individuals, patients with active AEDS and patients with active allergic asthma. The cells were cultured for 24 or 96 h with house dust mite (HDM), SEB and phytohaemagglutinin

(PHA), and the supernatants were assayed for cytokine levels. RESULTS: Staphylococcal enterotoxin B selectively stimulates the production of interleukin (IL)-5 in AIDS sufferers but not in asymptomatic atopics or nonatopics. Additionally, we observed comparable susceptibility to the IL-5-stimulatory effects of SEB in allergic asthmatics. CONCLUSIONS: Given the central role of IL-5-driven eosinophilia in progression from mild atopy to severe disease, these findings provide a plausible mechanism for the AIDS-promoting effects of staphylococcal SA_g. Staphylococcal enterotoxin B may also have a similar role in atopic respiratory disease.

Heaton T. et al. *An immunoepidemiological approach to asthma: identification of in-vitro T-cell response patterns associated with different wheezing phenotypes in children.* Lancet. 2005; 365(9454) : 142-9.p **Abstract:** BACKGROUND: Increasing evidence suggests that patterns of T-cell immunity to inhaled allergens in genetically diverse human populations are more heterogeneous than previously assumed, and that covert differences in expression patterns might underlie variations in airway disease phenotypes. We tested this proposition in a community sample of children. METHODS: We analysed data from 172 individuals who had been recruited antenatally to a longitudinal birth cohort study. Of the 194 birth cohort participants, data from the 147 probands (age range 8.6-13.5 years) who consented to blood collection were included along with data from 25 consenting siblings (mean age 11 years [range 7.4-17.4]). We ascertained clinical phenotypes related to asthma and allergy. We measured T-cell responses to allergens and mitogens, together with blood eosinophils and IgE/IgG antibodies, and assessed associations between these indices and clinical phenotypes. FINDINGS: Atopy was associated with allergen-specific T-helper (Th)2 responses dominated by interleukin 4, interleukin 5, interleukin 9, interleukin 13, whereas interleukin 10, tumour necrosis factor alpha, and interferon gamma responses were common to both atopics and non-atopics. The wheal size from skin prick with allergen was positively associated with in-vitro interleukin 5 and interferon gamma responses, and negatively associated with interleukin 10. Asthma, especially in atopics, was strongly associated with eosinophilia/interleukin 5, and bronchial hyper-responsiveness (BHR) was associated with eosinophilia plus polyclonal interferon gamma production. BHR in non-atopics was associated with elevated allergen-specific and polyclonal interleukin 10 production. INTERPRETATION: Parallel immunological and clinical profiling of children identified distinctive immune response patterns related to asthma and wheeze compared with BHR, in atopics non-atopics. Immunological hyper-responsiveness, including within the Th1 cytokine compartment, is identified as a hallmark of BHR. RELEVANCE TO PRACTICE: These findings highlight the heterogeneity of immune response patterns in asthmatic children, including those with seemingly homogeneous Th2-driven atopic asthma. Further elucidation of the covert relationships between wheezing phenotypes and underlying immunophenotypes in this age group will potentially lead to more effective treatments for what is an unexpectedly heterogeneous collection of disease subtypes.

Heinig M.J. *Risk, research, and infant feeding recommendations.* J Hum Lact. 2002; 18(1) : 5-6.p

Heinzmann A. et al. *Association of uteroglobin-related protein 1 with bronchial asthma.* Int Arch Allergy Immunol. 2003; 131(4) : 291-5.p **Abstract:** BACKGROUND: Chromosomal region 5q31 harbours a number of genes associated with atopic phenotypes, for example the genes coding for interleukin (IL) 4, IL13 and the beta(2)-adrenoreceptor. A new gene within this region was identified only very recently. The encoded protein - uteroglobin-related protein 1 (UGRP1) - is thought to act as an anti-inflammatory agent and is mainly expressed in the lung and trachea. The functional promoter polymorphism A-112G in UGRP1 was shown to be associated with bronchial asthma in a Japanese population. We were thus interested in finding out whether the polymorphism so far identified or others

within UGRP1 were associated with bronchial asthma in a German Caucasian population. METHODS: We performed direct genomic sequencing of the promoter and coding region of UGRP1 in 15 asthmatic children and 15 controls. The identified polymorphisms were genotyped by means of RFLP. Statistical analysis was performed with the Armitage trend test. RESULTS: We identified 5 non-coding variants, 4 of which being described for the first time. Three polymorphisms were common and typed in 182 asthmatic children and 270 controls. None of the polymorphisms were associated with bronchial asthma in our population. CONCLUSIONS: We conclude from our data that UGRP1 does not play a major role in the development of bronchial asthma in our Caucasian population.

Heinzmann A. et al. *Promoter polymorphisms of the CD14 gene are not associated with bronchial asthma in Caucasian children.* Eur J Immunogenet. 2003; 30(5) : 345-8.p **Abstract:** Several studies have investigated the association of a promoter polymorphism in CD14 with atopic phenotypes. We screened this and another polymorphism in 182 asthmatic children and found no association with asthma. Furthermore, there was substantial linkage disequilibrium of the polymorphisms. Thus CD14 does not play a major role in the development of asthma in our population of Caucasian children.

Heinzmann A. et al. *Association study of polymorphisms within interleukin-18 in juvenile idiopathic arthritis and bronchial asthma.* Allergy. 2004; 59(8) : 845-9.p **Abstract:** BACKGROUND: Interleukin-18 (IL-18) plays an important role in the regulation of TH1 as well as TH2 immunologic responses and thus in the development of chronic inflammatory diseases. Positive association studies of polymorphisms in IL-18 with different diseases have underlined the involvement of IL-18 in the pathogenetic processes. Our interest was to test polymorphisms of IL-18 for association with a typical TH1-mediated disease--juvenile idiopathic arthritis--and the TH2-mediated disease bronchial asthma in Caucasian children. METHODS: We genotyped five polymorphisms that were in association with chronic inflammatory diseases (-607C, -137C, 113G, 127T, and -133G). This was performed by restriction fragment length polymorphism in populations of asthmatic children, control individuals, and children with antinuclear antibodies (ANA)-positive juvenile idiopathic arthritis. Statistical analysis was performed by the Armitage trend test; haplotypes were calculated by the Arlequin program. RESULTS: No significant association was found between any single nucleotide polymorphism or any haplotype and bronchial asthma or ANA-positive juvenile idiopathic arthritis. CONCLUSION: We conclude that the effect of IL-18 in the immunologic context of diseases like bronchial asthma or juvenile arthritis might be too complex to be reflected in a simple one-way association study. Furthermore, the polymorphisms under investigation might be nonfunctional.

Heinzmann A. et al. *Association study of the IL13 variant Arg110Gln in atopic diseases and juvenile idiopathic arthritis.* J Allergy Clin Immunol. 2003; 112(4) : 735-9.p **Abstract:** BACKGROUND: It has previously been shown that various inflammatory diseases, such as diabetes mellitus, bronchial asthma, chronic inflammatory bowel diseases, and rheumatoid arthritis, are in some circumstances genetically linked to the same chromosomal regions. Consequently, common genes underlying the pathogenetics of these diseases have been proposed. Chronic inflammatory disorders can be subdivided by their predominant immune response, either TH1 or TH2. For example, juvenile idiopathic arthritis (JIA) is a TH1 disease, and bronchial asthma is a TH2 disease. OBJECTIVES: The present study investigated the polymorphism Arg110Gln within the IL13 gene, a strong TH2 cytokine. We attempted to determine whether it is associated with these 2 diseases and whether this would reflect the TH1/TH2 paradigm. METHODS: Arg110Gln was typed in 4

different populations: asthmatic children, atopic children, children with JIA, and a control population. Statistical analysis was performed by using logistic and linear regression analysis of serum IgE levels and the Armitage trend test. RESULTS: The variant Gln110 was shown to be associated with increased total serum IgE levels in our atopic population ($P = .006$) and was weakly associated with bronchial asthma ($P = .04$). There was no association of the variant with JIA when compared with the control population. However, the variant Gln110 was significantly less frequent in children with JIA compared with its presence in children with bronchial asthma ($P = .007$). CONCLUSION: This is the first study to compare the same gene variant in TH1 and TH2 chronic inflammatory diseases. The results suggest that the same gene variant might protect from one disease and make an individual susceptible to the other.

Hellman C. et al. *Down-regulated IL-5 receptor expression on peripheral blood eosinophils from budesonide-treated children with asthma.* Allergy. 2002; 57(4) : 323-8.p Abstract: BACKGROUND: The expression and function of cytokine receptors on peripheral blood eosinophils (PBE) from healthy and asthmatic children are poorly characterized. METHODS: The PBE count and expression of IL-5 receptor (R) and GM-CSF positive PBE was analyzed in nonsteroid-treated asthmatic children ($n = 13$), budesonide-treated asthmatic children ($n = 24$) and healthy children ($n = 16$) by flow cytometry. Alterations in intracellular EG2-epitope expression were used to measure the in vitro responsiveness of PBE to recombinant IL-5 and GM-CSF. RESULTS: The PBE count was increased ($P < 0.05$) in both asthmatic groups, independent of treatment, as compared to healthy children. The IL-5R expression on PBE, as well as the in vitro responsiveness of PBE to recombinant IL-5, was reduced ($P < 0.05$), in budesonide-treated asthmatic children compared to nonsteroid-treated asthmatic children and healthy children. The proportion of GM-CSFR positive PBE and in vitro responsiveness of PBE to recombinant GM-CSF were not different between the groups. In vitro treatment with budesonide did not down-regulate the proportion of IL-5R positive PBE. CONCLUSIONS: Budesonide-treatment of asthmatic children induces a selectively reduced IL-5R expression on PBE, concomitant with a reduced in vitro responsiveness of PBE to IL-5. We suggest that this budesonide-related down-regulation of the IL-5R might be a mechanism by which steroid treatment inhibits the action of IL-5 on eosinophil accumulation and activation in vivo.

Helm T.J. *Advancing asthma management: asthma care education and improved outcomes.* Minn Med. 2005; 88(7) : 45-7.p Abstract: According to the American Lung Association, the National Center for Health Statistics, and the Centers for Disease Control and Prevention, an estimated 15 million to 20 million Americans have asthma. Those numbers include approximately 5 million to 6 million children younger than 18 years of age. Asthma is the most common chronic illness among children, and it is one of the main causes of emergency room visits, inpatient admissions, and school absenteeism, especially among those younger than 15 years of age. In Minnesota, approximately 8% of middle school students have asthma, and another 18% may have the disease. The highest rates are found in the Twin Cities metro area. This article describes an educational program to help physicians make more accurate diagnoses and improve asthma care by providing evidence-based treatment.

Helms P.J. et al. *Utility of routinely acquired primary care data for paediatric disease epidemiology and pharmacoepidemiology.* Br J Clin Pharmacol. 2005; 59(6) : 684-90.p Abstract: BACKGROUND: The majority of medicines prescribed for children are prescribed in primary care for common acute and chronic conditions. This is in contrast to prescribing in secondary care where the population of children admitted is small but where a large number of different medicines are prescribed to treat more serious

and less common conditions. METHODS: Data on prescribing was extracted from the General Practice Administration System for Scotland (GPASS) for the year November 1999 to October 2000 and prescribing patterns for children aged 0-16 years expressed as percentages. A comparison of age specific consultations for asthma, as an example of a common paediatric condition, was also made between two separate general practice data sets, the General Practice Research Database (GRPD) and the continuous morbidity recording (CMR) subset of GPASS. RESULTS: Of 214 medicines investigated for unlicensed and off-label prescribing no unlicensed prescribing was identified. Off-label prescribing due to age was most common among younger and older children. The most common reasons for off-label prescriptions were, in order of frequency, lower than recommended dose, higher than recommended dose, below the recommended age, and unlicensed formulation. Age and gender specific consultations for asthma were similar in the two representative databases, GPRD and CMR, both showing disappearance of the male predominance in the teenage years. CONCLUSIONS: Large primary care data sets available within a unified health care system such as the UK National Health Service (NHS) are likely to be broadly compatible and produce similar results. The prescribing of off-label medicines to children is common in primary care, most commonly due to prescribing out with the recommended dosage regimen.

Hendrika J.M. et al. *The parenting competency framework: learning to be a parent of a child with asthma.* Int J Nurs Pract. 2003; 9(6) : 368-73.p Abstract: Every parent who faces an illness in their child might doubt their competence to care. When a chronic illness is diagnosed, competence can be severely challenged because of the sustained and multiple disruptions to daily life. A conceptual framework entitled 'Learning to be a Parent of a Child with Asthma' was developed from the results of a descriptive phenomenological study completed in Perth, Western Australia. It describes the stages of challenges to competency that parents experience as they learn to care for their asthmatic children. The impact of this illness on parents and the extent to which they are able to help their children respond to the demands of asthma are critical components in understanding the effect of this disease on parental competency. Insight into parental competency and the relationship to chronic illness will help health professionals provide the support and information needed by parents to manage asthma in their children.

Henry R.L. *Invasive monitoring of airway inflammation.* Med J Aust. 2002; 177 Suppl : S57-8.p Abstract: What we know: Ethical concerns have limited research involving invasive bronchoscopy techniques in young children. No longitudinal studies have been conducted to compare the findings of bronchial biopsy or bronchoalveolar lavage in young children with transient episodic wheeze versus asthma. Children with atopic asthma have more airway eosinophils and mast cells than children with viral-associated wheeze. Both neutrophilic and eosinophilic patterns of inflammation are present in asthma. What we need to know: Can we establish robust normal values for tissue and fluid samples obtained at bronchoscopy or bronchoalveolar lavage? Do biopsy specimens taken at the carina tell us about the pathological processes occurring in asthma? Can we use invasive procedures to predict which children with wheeze will continue to wheeze and develop a classical asthma phenotype? Can we use invasive procedures to guide asthma therapy? Can we expect airway inflammation to resolve with anti-inflammatory medication? Can we correlate invasive with non-invasive measures of inflammation? Can we use our understanding of pro- and anti-inflammatory pathways to develop new therapeutic interventions? Is there a presymptomatic phase of inflammation?

Hensley M.J. et al. *Symptoms of asthma: comparison of a parent-completed retrospective questionnaire with a prospective daily symptom diary.* Pediatr Pulmonol. 2003; 36(6) : 509-13.p Abstract:

In a study of the effects of indoor air pollution on the respiratory health of children in Newcastle, Australia, parental reports of symptoms experienced by children over the previous 12 months were compared with a prospective record of symptoms of cough and wheeze. Parents of 390 children aged 8-11 years completed a questionnaire about child and family respiratory health, which was used to assign children to one of four symptom groups: Wheeze (two or more attacks of wheezing in the last 12 months), Chest-Colds (two or more chest-colds in the last 12 months without wheezing), Cough Alone (a dry cough at night, without a cold or chest infection, that lasted for more than 2 weeks), or Control (none). A balanced sample of children (n=139) was invited to participate further by completing lung function tests, atopy testing, and keeping a daily diary of peak expiratory flow (PEF) and symptoms of cough and wheeze over a 7-week period. Valid data for the daily diary were provided by 66/85 (77.6%) of participants who commenced this stage (47.5% of the 139 invited to participate). The Wheeze group reported significantly more subsequent wheeze (median 16.8% of days) than the other three groups (median 0% of days). Parent reports of asthma-like symptoms over the previous 12 months were consistent with the subsequent experience of symptoms recorded in a daily diary.

Herjavec I. et al. *Cost, morbidity, and control of asthma in Hungary: The Hunair Study.* J Asthma. 2003; 40(6) : 673-81.p Abstract: OBJECTIVE: To assess asthma-related morbidity, symptom control, and societal cost of asthmatic patients in Hungary. Secondary objective was to assess the relationship between asthma symptom control and costs incurred. METHODS: Three hundred seventy-eight pediatric asthma patients (6-14 years of age) and 711 adult asthma patients (18-55 years of age) in 19 pulmonary clinics were interviewed by their physicians regarding asthma-related drug therapy and recent (past 2 weeks) asthma morbidity (daytime asthma symptoms, nocturnal symptoms, limitation in daily activities resulting from asthma and asthma exacerbation). Physicians estimated patients' level of asthma control based on the Global Initiative of Asthma guidelines. Direct and indirect costs for asthma-related resources were determined based on patient reported 6 months' data except for drug costs that were based on patient reported 2 weeks of data. All cost data were annualized. RESULTS: Patients in the study were mostly prescribed inhaled controller medications for asthma symptom management (76.2% pediatric and 92.3% adult) during the 2 weeks preceding the survey. Asthma-related morbidity was experienced by 15% of pediatric patients and 30% of the adult patients at least once during the 2 weeks preceding the survey. Physician classified 69% of pediatric patients as having good control, 27.5% as having moderate control, and 2.8% as having poor control of their asthma. In the adult population, 50.7% were classified as having good control, 36.6% as having moderate control, and 12.7% as having poor control. The average total annual costs (direct and indirect costs) per patient were 833 EUR (897 USD) for pediatric patients and 632 EUR (681 USD) for adult patients. In both pediatric and adult patients the total costs were highest for patients with poor asthma control. The total cost per patient increased in the ratios of 1 to 1.4 to 2.4 for pediatric patients and 1 to 1.5 to 2.9 for adult patients with good, moderate, and poor control of asthma, respectively. CONCLUSION: Inhaled corticosteroids was the most frequent treatment prescribed for asthma patients in the study. However, patients reported substantial asthma-related morbidity. Children used more resources than adults, despite being classified as having better control. Patients with poor control of asthma symptoms incurred the highest societal cost, improving patient control may reduce cost to society by 40% or more.

Hermann C. et al. *A comparison of risk factors for wheeze and recurrent cough in preschool children.* Am J Epidemiol. 2005; 162(4) : 345-50.p Abstract: In a study of 2,978 Danish children aged 5 years from two suburban counties of Copenhagen, carried out in 1998, the authors compared risk factor profiles for wheeze and recurrent cough without wheeze by using polytomous logistic regression to clarify

whether the two conditions are likely to have the same etiology. Data were obtained 1) by a mailed parental questionnaire (International Study of Asthma and Allergies in Childhood questions and supplementary questions on cough, sociodemography, perinatal factors, and environmental exposure); 2) through general practitioners (familial allergic disease); and 3) from the National Medical Birth Register (birth weight). Wheeze (WH) was defined as more than one episode of wheeze within the last 12 months (irrespective of cough status) and recurrent cough without WH (RC) as cough occurring outside colds and usually lasting for periods of more than 1 week in children with no more than one attack of wheeze within the last 12 months. Risk factors for comparison were selected as those that, after repeated stepwise logistic regression, remained significant for children with WH or RC. Significant differences were found for gender (p = 0.003), gestational age (p = 0.0002), maternal history of asthma (p = 0.0008), and standard of housing condition (p = 0.04)-all risk factors for WH but not RC. Results may suggest that the two conditions have different etiologies.

Hernando S.V. et al. *Montelukast in early childhood asthma. Predict value of IgG in clinical reply in children 2 to 5 years old?* Allergol Immunopathol (Madr). 2004; 32(4) : 204-11.p Abstract: BACKGROUND: According to current knowledge, asthma is basically an inflammatory process. Its causes and physiopathological mechanisms are various. The final result is a recurrent obstructive bronchial process, with sibilants and/or dyspnea, which causes an upset in functional respiratory tests, among which the maximum respiratory peak flow meter diminished for the age, sex, and height of patient. AIMS: Our aim is to evaluate if response to treatment with Montelukast has any link with immunoglobulin values (IgG, IgA, IgM, IgE) at start of treatment. MATERIALS AND METHODS: Included in the study were 32 children, of whom 2 did not begin and 1 who did not provide personal data. There were 29 patients in total, 11 girls and 18 boys. Each made three visits: first where they were instructed, together with their parents, in how to manage the meter and where they received the peak flow meter, Vitalograph, and personal data sheet, where personal and family medical history were noted. The second visit was after 4 weeks, for a clinical assessment and the third visit after 8 weeks. The value register of the PEF would be made morning and night, noting the highest value of three measurements. IgG, IgA, IgM, IgA values were quantified before treatment began. The statistic package STATA 2001 was used in the treatment of data statistics. RESULTS: Our between the value reached by the PEF after treatment and the IgG values at the beginning of treatment (0.712). In lesser measurement for IgA values (0.660). For each 100 mg/ml of increase in the value of IgG, an increase of 10 l/min in the PEF measurement before and following treatment with Montelukast was produced. CONCLUSIONS: IgG values increase with age. Children with a greater IgG value at the beginning of treatment reached higher PEF values after same. It is not known if the results would be similar with another type of treatment and the way in which IgG influences the results. What appears to be confirmed by available studies is that this relation is found in a group of small children, the aim of our study.

Hertzman P.A. et al. *Chronic illness care in Russia: a pilot project to improve asthma care in a "closed city".* Chest. 2005; 127(3) : 861-5.p Abstract: CONTEXT: In Russia, where health status has deteriorated since the late 1960s, asthma is a growing medical and public health problem. OBJECTIVE: To create a model for improving care and outcomes of patients with asthma through altering the culture of health care, physician behavior, and public policy in a Russian community. DESIGN: A 6-month, nonrandomized, before-and-after intervention evaluation. SETTING: Outpatients of Medical-Sanitary Unit No. 50, the central health authority in Sarov, Russia, a "closed" nuclear city. PARTICIPANTS: A consecutive sample of 85 adult patients with severe-persistent or moderate-persistent asthma. INTERVENTIONS: A comprehensive asthma-care program that emphasized patient education and self-

management with treatment based on internationally accepted guidelines modified for local resources. **MAIN OUTCOME MEASURES:** Missed work or school, patients requiring emergency department visits, number of patients hospitalized, daytime symptoms, nighttime symptoms, rescue inhaler use, patient satisfaction, and FEV(1). **RESULTS:** After 6 months, significant reductions were observed in the proportion of patients missing work or school (1.2% vs 11.8%), emergency department visits (4.8% vs 15.7%), hospitalizations (0% vs 9.4%), daily symptoms (47.1% vs 65.9%), and nightly symptoms (14.1% vs 37.6%). Patient satisfaction with asthma control (81.2% vs 31.8%) and average level of FEV(1) (84.0% vs 72.4%) significantly increased from baseline. **CONCLUSIONS:** The model for changing asthma management in this Russian community was effective in improving asthma outcomes and offers a reproducible paradigm approach for improving chronic illness care.

Hesselmar B. et al. *Allergic rhinoconjunctivitis, eczema, and sensitization in two areas with differing climates.* *Pediatr Allergy Immunol.* 2001; 12(4) : 208-15.p **Abstract:** In this 5-year follow-up study we compared the prevalence of allergic rhinoconjunctivitis, eczema, and sensitization, in relation to several background factors, in two Swedish regions (Goteborg and Kiruna). In Goteborg, a city on the southwest coast, the climate is mild and humid. Kiruna is a town north of the Arctic Circle. Questionnaire replies and results of interviews were collected from all 412 7-8-year-old children of a population-based sample (203 in Goteborg and 209 in Kiruna); in addition, 192 children from Goteborg and 205 from Kiruna were skin-prick tested for sensitization to common aero-allergens. After 5 years, at 12-13 years of age, almost all of the initial study cohort were re-investigated. At follow-up the prevalence of allergic rhinoconjunctivitis was 17%, eczema 23%, and sensitization 32%. Allergic rhinoconjunctivitis and eczema were as common in Goteborg as in Kiruna, whereas sensitization was far more common in Kiruna. Children born during the pollen season had allergic rhinoconjunctivitis less often -- and were sensitized to pollen and animal protein less often -- than those born during the rest of the year. Sensitization to birch pollen, cat protein, and horse protein was less common in children living in Goteborg, the region with the highest frequency of cat ownership and horseback riding, and with the longest birch-pollen season. The girls were more commonly horseback riders but the boys were more often sensitized to horses. The results reinforce our previous findings: indoor climate may affect the development of sensitization and allergic diseases, to some extent independently; and if exposure to antigen is unavoidable, high doses might be better than low doses.

Hesselmar B. et al. *Born small for gestational age: relation to future allergy and asthma.* *Acta Paediatr.* 2002; 91(9) : 992-4.p **Abstract:** AIM: To evaluate whether intrauterine growth retardation (IUGR) protects against the development of allergy. **METHODS:** A case-control study of 1515 subjects (15-25 y), of whom 430 were cases (birthweight/length below -2 SD for gestational age). Birth data were from the national birth register. The frequencies of allergic diseases were evaluated by questionnaire. **RESULTS:** For the 950 who replied, the frequencies of allergic diseases were similar in cases and controls. **CONCLUSION:** IUGR does not protect against the development of allergy.

Hestbaek L. et al. *Is comorbidity in adolescence a predictor for adult low back pain? A prospective study of a young population.* *BMC Musculoskelet Disord.* 2006; 7 : 29.p **Abstract:** **BACKGROUND:** It has previously been shown that low back pain (LBP) often presents already in the teenage years and that previous LBP predicts future LBP. It is also well documented that there is a large degree of comorbidity associated with LBP, both in adolescents and adults. The objective of this study is to gain a deeper insight into the etiology of low back pain and to possibly develop a tool for early

identification of high-risk groups. This is done by investigating whether different types of morbidity in adolescence are associated with LBP in adulthood. **METHODS:** Almost 10,000 Danish twins born between 1972 and 1982 were surveyed by means of postal questionnaires in 1994 and again in 2002. The questionnaires dealt with various aspects of general health, including the prevalence of LBP, classified according to number of days affected during the previous year (0, 1-7, 8-30, >30). The predictor variables used in this study were LBP, headache, asthma and atopic disease at baseline; the outcome variable was persistent LBP (>30 days during the past year) at follow-up. Associations between morbidity in 1994 and LBP in 2002 were investigated. **RESULTS:** LBP, headache and asthma in adolescence were positively associated with future LBP. There was no association between atopic disease and future LBP. Individuals with persistent LBP at baseline had an odds ratio of 3.5 (2.8-4.5) for future LBP, while the odds ratio for those with persistent LBP, persistent headache and asthma was 4.5 (2.5-8.1). There was a large degree of clustering of these disorders, but atopic disease was not part of this pattern. **CONCLUSION:** Young people from 12 to 22 years of age with persistent LBP during the previous year have an odds ratio of 3.5 persistent LBP eight years later. Both headache and asthma are also positively associated with future LBP and there is a large clustering of LBP, headache and asthma in adolescence.

Heymann W.R. *Intramuscular triamcinolone.* *J Am Acad Dermatol.* 2006; 54(5) : 866-7.p

Heyworth J. et al. *A comparison of the prevalence of respiratory illness and non-specific health symptoms in two Victorian cities.* *Aust N Z J Public Health.* 2001; 25(4) : 327-33.p **Abstract:** **OBJECTIVE:** To compare the prevalence of respiratory illness and non-specific health symptoms among adults and children aged 4-15 years living in Portland and Warrnambool, Victoria. **METHODS:** A postal survey of 3,903 adults in Portland and Warrnambool systematically selected from the electoral roll was undertaken. Both an adults and children's questionnaire were enclosed in the mailing to each adult. If there were children aged 4-15 years in the household, an adult was asked to complete a questionnaire for the child who would next celebrate a birthday. Questionnaires were returned by 2,111 adults (54%) and for 585 children. **RESULTS:** No significant differences in the prevalence of self-reported asthma or wheeze were observed among adults or children residing in Portland and Warrnambool. The likelihood of itchy eyes, skin rash and stuffy nose was significantly higher in Portland adults and children compared with those in Warrnambool. Dry cough at night was increased among Portland children, but not significantly so. **CONCLUSIONS:** Higher rates of non-specific symptoms were observed in Portland but from a cross-sectional survey such as this, it is not possible to identify the cause of these higher rates. They may be related to environmental factors such as pollens or emissions from aluminium production, fertiliser production or bulk handling activities on the wharf, or they may be attributable to other factors such as response or recall bias.

Higa S. et al. *Association between interleukin-18 gene polymorphism 105A/C and asthma.* *Clin Exp Allergy.* 2003; 33(8) : 1097-102.p **Abstract:** **BACKGROUND:** IL-18 has been shown to exert anti-allergic or allergy-promoting activities, but the existence of genetic polymorphisms in the coding regions of IL-18 gene has not been demonstrated. **OBJECTIVE:** The aim of this study was to investigate whether polymorphism is present in the coding regions of the IL-18 gene and, if so, to further analyse the association between polymorphism and asthma in a case-control study. **METHODS:** We screened the coding regions of the IL-18 gene for polymorphisms by using PCRsingle-stranded conformation polymorphism and direct sequencing of PCR products, followed by analysis of the association between polymorphism and asthma. **RESULTS:** We identified one polymorphism (105A/C) in the coding regions. The frequency of the 105A allele was significantly higher in asthmatic patients than in controls (P<0.01; odds ratio (OR)=1.83 (1.37-2.26)). Significant

linkage disequilibrium was observed between the 105A/C and -137G/C polymorphisms in the 5' flanking region of the IL-18 gene ($D=0.58$, $P<0.0001$). However, in asthmatic patients the 105A allele was not associated with either total serum IgE or IL-18 levels. CONCLUSION: The 105A/C polymorphism of the IL-18 gene may be associated with the pathogenesis of asthma.

Hirota T. et al. *Functional haplotypes of IL-12B are associated with childhood atopic asthma.* J Allergy Clin Immunol. 2005; 116(4) : 789-95.p **Abstract:** BACKGROUND: IL-12 is a heterodimeric proinflammatory cytokine that forms a link between innate and adaptive immunity. Although associations between polymorphisms of IL-12B on chromosome 5q31-33 and asthma have been reported, the genetic influences of the polymorphisms and haplotype of IL-12B are unclear. OBJECTIVE: To examine whether polymorphisms in IL-12B are associated with childhood atopic asthma in a Japanese population. METHODS: We identified a total of 13 polymorphisms and characterized the linkage disequilibrium mapping of the gene. Three variants in the promoter and 3' untranslated region were genotyped, and we conducted case-control and case-only association studies between those variants and asthma-related phenotypes (childhood atopic asthma, $n = 297$; normal controls, $n = 555$). Haplotype association analysis and functional analysis of these variants were also performed. RESULTS: 3' Untranslated region 10841C > A was significantly associated with the risk of childhood atopic asthma ($P = .00062$). The -6415 promoter variant, in linkage disequilibrium with the 10841C > A ($D' = 0.78$ and $r^2 = 0.61$), was also marginally associated with childhood atopic asthma ($P = .051$). We analyzed the 2-locus haplotype by using these 2 polymorphisms and found a positive association with haplotype CTCTAA-C (-6415 CTCTAA and 10841C; $P = .00078$). Furthermore, 10841C > A affects the stability of transcripts, and promoter variant -6415GC enhances the transcriptional level of IL-12B. CONCLUSION: Our results imply that functional haplotype CTCTAA-C, which affects the instability of transcripts and the lower transcriptional level of IL-12B, has a protective effect in childhood atopic asthma. On the basis of these findings, the IL-12B gene might be involved in the development of atopic asthma through functional genetic polymorphisms.

Hodges B. *Asthma camp.* Paediatr Nurs. 2005; 17(6) : 20-2.p

Hoffjan S. et al. *Genetic variation in immunoregulatory pathways and atopic phenotypes in infancy.* J Allergy Clin Immunol. 2004; 113(3) : 511-8.p **Abstract:** BACKGROUND: Asthma is a chronic respiratory disease that often originates in early childhood. Although candidate gene studies have identified many potential asthma susceptibility genes in adult populations, few have studied associations with immune phenotypes in the first year that might be early clinical markers of asthma. OBJECTIVE: The aim of this study was to assess the contribution of genetic variation to cytokine response profiles and atopic phenotypes in the first year of life in the Childhood Origin of Asthma cohort. METHODS: Two hundred seven European American children participating in the Childhood Origin of Asthma study were genotyped for 61 single nucleotide polymorphisms in 35 genes involved in immune regulation. We examined the relationship between these single nucleotide polymorphisms and PHA-induced cytokine (IL-5, IL-10, IL-13, and IFN-gamma) response profiles at birth and at year 1, respiratory syncytial virus-induced wheezing and atopic dermatitis in the first year of life, and total IgE levels, peripheral blood eosinophil counts, and allergic sensitization at age 1 year. The data were analyzed by using censored regression for quantitative measurements and logistic regression for qualitative phenotypes. RESULTS: The 237Gly allele of the high-affinity IgE receptor beta chain (FCER1B) and a silent substitution in the nitric oxide synthase (NOS)2A gene were associated with reduced IL-13 responses in cord blood ($P = .0025$ and $P = .0062$, respectively). A significant gene-gene interaction between FCER1B 237Gly and NOS2A D346D was detected, with

individuals carrying the minor allele for both polymorphisms having the lowest cord blood IL-13 levels. Furthermore, the IL13 110Gln allele showed an association with increased IgE levels at year 1 ($P = .0026$), and the colony-stimulating factor 2 (CSF2) 117Thr allele showed an association with a greater increase in IL-5 responses during the first year ($P = .0092$). The TGF-beta1 (TGFB1) -509T allele was associated with respiratory syncytial virus-related wheezing in the first year ($P = .0005$). None of the polymorphisms included in this study were associated with atopic dermatitis during the first year or a positive RAST result at 1 year of age. CONCLUSION: These data suggest that variations in genes involved in immune regulation are associated with biologic and clinical phenotypes in the first year of life that might increase the risk for the subsequent development of childhood asthma.

Holgate S.T. et al. *Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma.* Clin Exp Allergy. 2004; 34(4) : 632-8.p **Abstract:** BACKGROUND: Patients with severe asthma are often inadequately controlled on existing anti-asthma therapy, constituting an unmet clinical need. OBJECTIVE: This randomized, double-blind, placebo-controlled trial evaluated the ability of omalizumab, a humanized monoclonal anti-IgE antibody, to improve disease control sufficiently to enable inhaled corticosteroid reduction in patients with severe allergic asthma. METHODS: After a run-in period when an optimized fluticasone dose ($> \text{ or } = 1000$ microg/day) was received for 4 weeks, patients were randomized to receive subcutaneous omalizumab [minimum 0.016 mg/kg/IgE (IU/mL) per 4 weeks; $n=126$] or matching placebo ($n=120$) at intervals of 2 or 4 weeks. The study comprised a 16-week add-on phase of treatment followed by a 16-week fluticasone-reduction phase. Short-/long-acting beta(2)-agonists were allowed as needed. RESULTS: Median reductions in fluticasone dose were significantly greater with omalizumab than placebo: 60% vs. 50% ($P=0.003$). Some 73.8% and 50.8% of patients, respectively, achieved a $> \text{ or } = 50\%$ dose reduction ($P=0.001$). Fluticasone dose reduction to $< \text{ or } = 500$ microg/day occurred in 60.3% of omalizumab recipients vs. 45.8% of placebo-treated patients ($P=0.026$). Through both phases, omalizumab reduced rescue medication requirements, improved asthma symptoms and asthma-related quality of life compared to placebo. CONCLUSION: Omalizumab treatment improves asthma control in severely allergic asthmatics, reducing inhaled corticosteroid requirements without worsening of symptom control or increase in rescue medication use.

Holland B.S. *Knock the wind out of asthma with Asthma CareWay.* Hosp Case Manag. 2002; 10(2) : 23-5.p

Holt S. et al. *Asthma morbidity, control and treatment in New Zealand: results of the Patient Outcomes Management Survey (POMS), 2001.* N Z Med J. 2003; 116(1174) : U436.p **Abstract:** AIMS: To determine the magnitude of morbidity from asthma within the New Zealand population, the degree of satisfaction of patients with their asthma control, and the level of asthma control achieved in relation to treatment. METHODS: Participants were randomly selected from 29 randomly chosen general practices throughout New Zealand. Information was collected from demographic and clinical questionnaires and from lung function tests. Criteria based on GINA guidelines were developed to define the level of asthma control for each participant, their opinion of their level of control, and to define which participants were under-treated. RESULTS: A total of 445 patients (327 adults, age 16-68; 118 children, age 7-15) took part in the study. Ninety three per cent of adults had asthma that was sub-optimally controlled, 71% had asthma that was not well controlled, and 19% had asthma that was markedly out of control. For children, these figures were 90%, 42% and 4% respectively. These results were consistent regardless of asthma severity. In adults and children whose asthma was not well controlled, 49% and 71% respectively were under-treated. For those whose asthma was markedly out of

control, 89% and 75% of adults and children respectively were under-treated. CONCLUSIONS: A significant proportion of patients have asthma that is not well controlled or that is markedly out of control, and the majority are under-treated.

Homer C.J. et al. *Impact of a quality improvement program on care and outcomes for children with asthma.* Arch Pediatr Adolesc Med. 2005; 159(5) : 464-9.p **Abstract:** OBJECTIVE: To test a quality improvement intervention, a learning collaborative based on the Institute for Healthcare Improvement's Breakthrough Series methodology, specifically intended to improve care and outcomes for patients with childhood asthma. DESIGN: Randomized trial in primary care practices. SETTING: Practices in greater Boston, Mass, and greater Detroit, Mich. PARTICIPANTS: Forty-three practices, with 13 878 pediatric patients with asthma, randomized to intervention and control groups. Intervention Participation in a learning collaborative project based on the Breakthrough Series methodology of continuous quality improvement. MAIN OUTCOME MEASURES: Change from baseline in the proportion of children with persistent asthma who received appropriate medication therapy for asthma, and in the proportion of children whose parent received a written management plan for their child's asthma, as determined by telephone interviews with parents of 631 children. RESULTS: After adjusting for state, practice size, child age, sex, and within-practice clustering, no overall effect of the intervention was found. CONCLUSIONS: This methodologically rigorous assessment of a widely used quality improvement technique did not demonstrate a significant effect on processes or outcomes of care for children with asthma. Potential deficiencies in program implementation, project duration, sample selection, and data sources preclude making the general inference that this type of improvement program is ineffective. Additional rigorous studies should be undertaken under more optimal settings to assess the efficacy of this method for improving care.

Homer S.D. *Effect of education on school-age children's and parents' asthma management.* J Spec Pediatr Nurs. 2004; 9(3) : 95-102.p **Abstract:** ISSUES AND PURPOSE: Asthma affects 7.4% of school-age children, with poor children or members of ethnic minorities disproportionately affected. DESIGN AND METHODS: A quasiexperimental, year-long pilot study tested the effectiveness of an intervention that included school-based small-group education for children with home-based education for parents. Pretest and two posttest measures were collected. RESULTS: Forty-four families completed the study (41% African American, 36% European American, 23% Mexican American), with 46% coming from poor or working-class families. Asthma management in the treatment group was lower than the comparison group at baseline, but improved significantly at 6 months and stabilized at 12 months, a trend that was most pronounced among the poorer children. PRACTICE IMPLICATIONS: Improvements in asthma management point to the need for ongoing asthma education to address learning needs of the children and families.

Hon K.L. et al. *Brief case series: montelukast, at doses recommended for asthma treatment, reduces disease severity and increases soluble CD14 in children with atopic dermatitis.* J Dermatolog Treat. 2005; 16(1) : 15-8.p **Abstract:** BACKGROUND: The choice of oral therapeutic agents for the treatment of atopic dermatitis (AD) in children is limited. Montelukast, a specific cysteinyl leukotriene (LT) receptor antagonist, may be useful in alleviating AD symptoms. OBJECTIVE: To evaluate the clinical and immunological effects of montelukast in children with AD. METHODS: After a 2-week run-in, children with AD were started on oral montelukast 5 mg once-daily for children < 12 years of age and 10 mg for older children. The clinical severity of AD as indicated by the SCORing Atopic Dermatitis (SCORAD) score, and serum soluble CD14 and urinary leukotriene E4 (LTE4) concentrations were evaluated at baseline and

the end of a 3-month treatment period. RESULTS: Four boys and three girls, with a median (range) age of 12 (3-16) years, participated in the study. The total SCORAD was reduced in five patients (by 30-84%) and remained similar in two patients. Their median (range) SCORAD scores before and after treatment were 34.7 (16.5-54.8) and 17.0 (6.9-36.9) (p = 0.046). The intensity component of SCORAD also decreased from 5 (2-10) to 3 (1-7) (p = 0.042). Serum sCD14 levels increased significantly from 5533 (4575-6452) ng/ml to 6259 (5617-8988) ng/ml (p = 0.028), whereas urinary LTE4 levels remained the same (p = 0.735). CONCLUSIONS: Montelukast, at doses recommended for asthma treatment, resulted in over 30% reduction in the total SCORAD in some children. Treatment with montelukast may also be associated with deviation of the immune system towards the Th1-specific pathway.

Hong C.Y. et al. *Prevalence of respiratory symptoms in children and air quality by village in rural Indonesia.* J Occup Environ Med. 2004; 46(11) : 1174-9.p **Abstract:** AIM: This study compared prevalence of respiratory symptoms in three Indonesian villages and related this to air quality. METHODS: We interviewed caregivers of 382 children, using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, and monitored air quality during the survey period. RESULTS: Respiratory symptom prevalence was highest in Kerinci (40.5%), followed by SP7 (33.3%) and Pelalawan (19.8%). Compared with Pelalawan, adjusted odds ratios were 3.17 (95% confidence interval, 1.43-7.07) for Kerinci, and 2.03 (1.04-3.96) for SP7. Ambient air quality levels were highest in Kerinci for PM10 and hydrocarbon (means: 102.9 microg/m3, 10.5 microg/m3), followed by SP7 (73.7 microg/m3, 6.3 microg/m3) and Pelalawan (26.1 microg/m3, 4.7 microg/m3). CONCLUSIONS: The higher prevalence of respiratory symptoms in Kerinci and SP7 could be the result of higher PM10 and hydrocarbon levels in these locations.

Hopp R. *Wheezing and dog exposure.* J Allergy Clin Immunol. 2002; 110(1) : 184; author reply 184.p

Hopwood A. *'Volunteering is a great way to learn'.* Nurs Times . 2003; 99(35) : 38-9.p

Horak E. et al. *Longitudinal study of childhood wheezy bronchitis and asthma: outcome at age 42.* BMJ. 2003; 326(7386) : 422-3.p

Horner S.D. et al. *Home asthma management for rural families.* J Spec Pediatr Nurs. 2003; 8(2) : 52-61.p **Abstract:** ISSUES AND PURPOSE: To assess home asthma management among rural families with a school-age child who has asthma. DESIGN AND METHODS: Exploratory analysis of baseline data of a tri-ethnic sample of rural families with school-age children who have asthma. RESULTS: Parents and children enact a moderate amount of asthma management behaviors. Preventive behaviors were correlated with the Asthma Behavior Inventory and treatment behaviors were correlated with the child's asthma severity. Factors that could affect asthma management include no insurance, no visits to providers in 12 months, or no asthma medications. PRACTICE IMPLICATIONS: Nurses must use every contact with families to assess their asthma management and availability of resources, and to determine the fit between asthma severity and the asthma management plan.

Hoskins G. et al. *Results of a national asthma campaign survey of primary care in Scotland.* Int J Qual Health Care. 2005; 17(3) : 209-15.p **Abstract:** OBJECTIVE: To identify within primary care in Scotland how far procedures for asthma review and patient education match guideline recommendations. DESIGN AND SETTING: Telephone survey of a one in four stratified random sample of all 1058 general practices in Scotland. PARTICIPANTS: Practice nurses, general practitioners. MAIN OUTCOME MEASURES: Number of practices matching guideline recommendations for asthma review, targeting of

care, use of structured asthma records, provision of management plans, education, and regular audit. RESULTS: Of 276 general practices contacted 91% (251) completed the questionnaire; 93% (228) ran an asthma review service; 74% (166) employed a specially trained asthma nurse; 39% (106) had a policy for providing action plans; 63% (155) had carried out an asthma audit in the previous 3 years; 76% (218) used a structured tool in consultations, 46% with use of computer technology, 34% used only a manual stamp. Sixty-six per cent (173) had searched for patients overusing beta2 agonists; 32% (79) had searched for patients on medication treatment step 3 and above. Single- or two-partner practices were less likely to follow guideline recommendations but neither rurality nor deprivation was related to guideline compliance. CONCLUSIONS: Three-quarters of Scottish general practices have trained asthma nurses and offer patients asthma review, but only a minority have proactive care procedures for targeting patients or a policy for providing patients with action plans. Practice systems are underused for identifying 'at-risk' patients. There is a need for proactive procedures and provision of self-management materials to patients. Access to trained asthma nurses needs to be improved.

Howel D. et al. *Children's respiratory health and daily particulate levels in 10 nonurban communities.* Environ Res. 2001; 87(1) : 1-9.p

Abstract: We conducted a study to assess the association between the acute respiratory health of children and the levels of particulates in communities near and away from active opencast coal mines. The study enrolled children aged 1-11 years from the general population of five socioeconomically matched pairs of nonurban communities in northern England. Diaries of respiratory events were collected for 1405 children, and information was collected on the consultations of 2442 children with family/general practitioners over the 6-week study periods during 1996-1997, with concurrent monitoring of particulate levels. The associations found between daily PM(10) levels and respiratory symptoms were frequently small and positive and sometimes varied between communities. The magnitude of these associations were in line with those from previous studies, even though daily particulate levels were low, and the children were drawn from the general population, rather than from the population with respiratory problems. The associations among asthma reliever use, consultations with general practitioners, and daily particulate levels were of a similar strength but estimated less precisely. The strength of association between all respiratory health measures and particulate levels was similar in communities near and away from opencast coal mining sites.

Hsu C.H. et al. *Efficacy and safety of modified Mai-Men-Dong-Tang for treatment of allergic asthma.* Pediatr Allergy Immunol. 2005; 16(1) : 76-81.p

Abstract: The aim of this study was to evaluate the efficacy and safety of a Chinese herbal formula modified Mai-Men-Dong-Tang (mMMDT) for treatment of persistent, mild-to-moderate asthma. A total of 100 asthmatic patients were enrolled and assigned to three treatment groups in this double-blind, randomized, placebo-controlled clinical trial. Over a period of 4 months, patients in groups A and B received 80 and 40 mg/kg/day of mMMDT, while those in group C received a placebo. Efficacy variables included changes in forced expiratory volume in 1 s (FEV1), symptom score, serum total immunoglobulin E (IgE), and dust mite-specific IgE. Safety assessments included complete blood count, and liver and kidney function. Relative to baseline, significantly greater increases in FEV1 were demonstrated for both A and B groups in comparison with the placebo-treated analog (both $p < 0.05$). Further, similar improvements in symptom score were observed for both mMMDT treatment groups. The serum total IgE for group A showed a decreasing tendency after treatment but no statistical difference was noted. Furthermore, no drug-related adverse effects were reported. Blood test, and liver and kidney function were within normal range during the study, with no marked changes demonstrated over time. In conclusion, the Chinese herbal formula mMMDT provided improvements in lung function and relieved asthma symptoms in our

sample of patients. Given its efficacy and safety, we consider mMMDT a credible treatment regimen for persistent, mild-to-moderate asthma.

Hsu J.T. et al. *Clinical inquiries. Are inhalers with spacers better than nebulizers for children with asthma?* J Fam Pract. 2004; 53(1) : 55-7.p

Huang J.L. et al. *Sequence variants of the gene encoding chemoattractant receptor expressed on Th2 cells (CRTH2) are associated with asthma and differentially influence mRNA stability.* Hum Mol Genet. 2004; 13(21) : 2691-7.p **Abstract:** The gene, CRTH2, encoding a receptor for prostaglandin D(2) (PGD(2)), is located within the peak linkage region for asthma on chromosome (Chr.) 11q reported in African American families. Family-based analysis of asthma and two common SNPs [G1544C and G1651A (rs545659)] in the 3'-untranslated region of CRTH2 showed significant evidence of linkage in the presence of disequilibrium for the 1651G allele ($P = 0.003$) of SNP rs545659. Haplotype analysis yielded additional evidence of linkage disequilibrium for the 1544G-1651G haplotype ($P < 0.001$). Population-based case-control analyses were conducted in two independent populations, and demonstrated significant association of the 1544G-1651G haplotype with asthma in an African American population ($P = 0.004$), and in a population of Chinese children ($P < 0.001$). Moreover, in the Chinese children the frequency of the 1651G allele in near-fatal asthmatics was significantly higher than mild-to-moderate asthmatics ($P = 0.001$) and normal controls ($P < 0.001$). The 1651G allele of SNP rs545659 was also associated with a higher degree of bronchial hyperresponsiveness ($P < 0.027$). Transcriptional pulsing experiments showed that the 1544G-1651G haplotype confers a significantly higher level of reporter mRNA stability, when compared with a non-transmitted haplotype (1544C-1651A), suggesting that the CRTH2 gene on Chr. 11q is a strong candidate gene for asthma.

Hublet A. et al. *Value of a shortened questionnaire in the description of asthma in 10-12-year-old pupils.* Pediatr Allergy Immunol. 2004; 15(3) : 247-52.p

Abstract: Asthma is a common and severe chronic disease in children influencing their quality of life and functioning at school. A 5-item asthma-screening instrument was developed and tested in 1052 children aged 10-12 years. Questionnaires were completed by parents and children separately and data were compared. Children reported less to be diagnosed by a medical doctor as having asthma compared with their parents, although children reported more to have certain asthma symptoms. No difference in prevalence of asthma was found between children and parents' answers. The absolute agreement for the scale was 92% and a good kappa agreement was found. Recoding the "don't know"-answers in "no"-answers resulted in a 4% misclassification. The short 5-item asthma screening tool can be valuable in the categorization of a subgroup of children likely to suffer from asthma in a survey. Recoding 'don't know'-answers to 'no'-answers is justified in large samples.

Huerta C. et al. *Respiratory medications and the risk of cardiac arrhythmias.* Epidemiology. 2005; 16(3) : 360-6.p

Abstract: BACKGROUND: Medications used to treat respiratory diseases include beta-adrenoceptors, antimuscarinics, inhaled and oral corticosteroids, and theophyllines. Most of these drugs have been associated indirectly with cardiac rhythm disorders, but epidemiologic evidence is limited. METHODS: To evaluate the association between respiratory drugs and the occurrence of rhythm disorders among patients with asthma and those with chronic obstructive pulmonary disease, we conducted a case-control study nested in a population-based cohort of individuals 10-79 years of age and registered in the U.K. General Practice Research Database after 1

January 1994. The analysis included 710 confirmed cases and 5000 controls frequency-matched to cases by age (interval of 1 year) and sex. **RESULTS:** No increased risk of arrhythmias overall was found among users of inhaled steroids (relative risk = 1.0; 95% confidence interval = 0.8-1.3). Short-term use of theophylline was weakly associated with arrhythmia (1.8; 1.0-3.3). An increased risk was found among users of oral steroids, and the relative risk was greater at the beginning of therapy (2.6; 2.0-3.5). The risk of atrial fibrillation was increased, especially for short-term use of oral steroids (2.7; 1.9-3.8), and a weak association was seen for theophyllines, especially short-term use (1.8; 0.9-3.7). Supraventricular tachycardia was associated with long-term use of oral steroids (2.1; 0.8-5.7), long-term use of antimuscarinics (1.7; 0.7-4.1), and short-term use of theophylline (4.0; 0.9-18.1). Ventricular arrhythmias were associated with oral steroids (3.2; 0.8-13.3) and beta-adrenoceptors (7.1; 0.8-65.9). **CONCLUSIONS:** Oral steroids and theophylline were the therapeutic groups associated with risk of developing atrial fibrillation, especially with new courses of therapy. Results from this study also are consistent with certain suspected dysrhythmic effects of theophyllines, with supraventricular tachycardia associated with antimuscarinics, and with ventricular arrhythmias associated with beta-adrenoceptors.

Hung C.C. et al. *Effects of systematic nursing instruction of mothers on using medication and on health status of asthmatic children.* J Nurs Res. 2002; 10(1) : 22-32.p **Abstract:** The purpose of this study was to investigate the effects of systematic nursing instruction for mothers of children with asthma on their knowledge of the medication, ability to use inhalation devices, self-efficacy of medication use, and on children's health status. A quasi-experimental study was conducted at the Pediatric Allergy Clinic of a major academically based medical center in Taipei, Taiwan. The sample consisted of 82 mothers and their children recruited by purposive sampling. The intervention group (n = 41) received systematic nursing instruction from the researchers and the control group (n = 41) received regular nursing care from staff nurses. The effects of systematic nursing instruction were evaluated two months later using four questionnaires: the mother's knowledge of medication, inhaling steps, self-efficacy of medication use, and child's health status. The results of this study showed that systematic nursing instruction of mothers of children with asthma significantly improved their knowledge of the medication, ability to use inhalation devices, and self-efficacy, as well as decreasing the number of episodes of respiratory disease of children over a two month period. To sum up, these findings demonstrate that systematic nursing instruction of mothers about asthma medication not only benefited mothers directly, but also improved children's health status indirectly.

Hung C.H. et al. *Evaluation of different nebulized bronchodilators on clinical efficacy and hypokalemia in asthmatic children.* Acta Paediatr Taiwan. 2001; 42(5) : 287-90.p **Abstract:** Acute asthma attack continues to be a major cause for children admitted to the emergency room. Nebulized beta 2-adrenergic agonists are still the first-line drugs for a rapid bronchodilation effect and an easily administered drug during acute asthma attack. The bronchodilator-induced hypokalemia is thought significant in adult group, but is often ignored in children group. In this study, we conducted a randomized study to compare the laboratory and clinical effects between nebulized salbutamol and terbutaline. We found that both salbutamol and terbutaline nebulization induced a significant hypokalemia ($p < 0.05$). Terbutaline nebulization also significantly improved the peak expiratory flow rate (PEFR) and respiratory rate (RR), but not venous partial pressure of oxygen (PvO₂), venous carbon dioxide tension (PvCO₂) and O₂ saturation in venous blood (SvO₂). In contrast, salbutamol improved not only PEFR and RR, but also PvO₂, PvCO₂, and SvO₂ 30 minutes of administration. In conclusion, the nebulized salbutamol, although induced a hypokalemic effect which is similar to terbutaline group, has a better effect on improving O₂ saturation than nebulized terbutaline with the

same dose 30 minutes after administered for children with acute asthma attack.

Hurwitz E.L. et al. *Vaccination and risk of allergic disease.* Am J Public Health. 2005; 95(1) : 6; author reply 6-7.p

Huss K. et al. *House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program.* J Allergy Clin Immunol. 2001; 107(1) : 48-54.p **Abstract:** **BACKGROUND:** Children with asthma have a high prevalence of environmental allergies, especially to indoor allergens. The relationships of exposure to indoor allergens (dust mites, cat, dog, cockroach, and molds) and other host factors to allergy sensitization have not been evaluated simultaneously in a large cohort. **OBJECTIVES:** We studied 1041 children aged 5 to 12 years with mild-to-moderate asthma to determine risk factors associated with having positive allergy skin test responses to indoor allergens. Also, we described, compared, and contrasted 6 allergens in the home environments of these children from 8 North American cities. **METHODS:** Data were used from baseline visits of the Childhood Asthma Management Program. Patients' sensitivities to house dust mites (Dermatophagoides farinae and Dermatophagoides pteronyssinus), cats, dogs, cockroaches, and molds were examined for relationships to demographic variables, home dust allergen exposures, number of other positive allergy skin test responses, total serum IgE levels, and smoking in the home. **RESULTS:** San Diego (78.5%) and Toronto (59.3%) had the topmost percentages of homes with moderate-to-high house dust mite levels. Boston (21.5%), St Louis (16.3%), and Baltimore (13.4%) had the highest percentages of homes with detectable levels of cockroach allergen. For house dust mites, the higher the level of allergen exposure, the more likely patients were to have positive allergy skin test responses, with relative odds of 9.0 (95% confidence interval, 5.4-15.1) for those exposed to high mite levels (>10.0 microg/g dust) relative to those unexposed. Even exposure to low levels of mite allergen (0.020-2.0 microg/g) was found to be a significant risk factor for sensitization. For cockroach allergen, those with detectable home exposure were more likely to have positive skin test responses (relative odds, 2.2; 95% confidence interval, 1.3-3.8) than those with undetectable exposure. In contrast, levels of exposure to cat, dog, and mold allergens were not related to sensitization rates. For cat allergen, this may reflect lower rates of cat ownership among highly sensitized subjects. Furthermore, the number of allergy skin test responses that were positive, excluding the test for the outcome of interest for each model, and total serum IgE levels were strong independent predictors of sensitization. **CONCLUSIONS:** Levels of exposure determined by house dust analysis are important determinants of sensitization for dust mite and cockroach allergen. This relationship was not demonstrable for cat, dog, or mold allergens, possibly because of confounding factors. For all allergens studied, the degree of atopy, determined by the total number of positive skin test responses or by total serum IgE levels, is an important contributing risk factor for sensitization.

Huss K. et al. *Asthma management practices and education needs of head start directors and staff.* J Sch Health. 2002; 72(8) : 329-33.p **Abstract:** Limited information exists regarding asthma management practices and education needs of Head Start directors and staff. This paper describes asthma management practices and education needs of Head Start directors and staff in 15 Baltimore, Md., Head Start programs. From February to December 2000, all Head Start staff and directors were asked to complete a survey. Data from 268 Head Start staff and 12 Head Start directors were analyzed. Results revealed discrepancies between Head Start staff and directors regarding location of asthma medications and presence of asthma action plans in programs. Both Head Start staff and directors stated they had no curriculum to teach Head Start children how to manage asthma. This finding provides evidence that asthma education is needed in Head

Start programs. Findings also indicate a need for improved communication between Head Start directors and staff.

Hyland M.E. et al. *Asthma treatment needs: a comparison of patients' and health care professionals' perceptions.* Clin Ther. 2004; 26(12) : 2141-52.p **Abstract** : BACKGROUND: Patients' perceptions of asthma tend to differ from those of clinicians, who primarily focus on asthma control. Patients' treatment needs and preferences may not be adequately addressed. OBJECTIVE: The aims of this study were as follows: to provide data on unmet treatment needs and to investigate the main finding of a qualitative study using a questionnaire study. METHODS: To assess treatment needs in patients with asthma, focus groups were conducted with patients/parents and clinicians. Based on these results, quantitative surveys of adult patients and parents were performed in the United Kingdom, Germany, and Spain. RESULTS: The UK focus group comprised 11 patients and 8 parents; in Germany, there were 10 patients and 11 parents; in Spain, there were 5 patients and 8 parents. The focus groups showed some differences between clinicians' and patients'/parents' perceptions of treatment. For patients, side effects meant long-term effects (ie, 10-20 years); for clinicians, it meant occasional local problems. The quantitative study comprised 454 participants: 310 adult patients (mean [SD] age, 37.13 [13.12] years) and 142 parents (children's mean [SD] age, 13.98 [1.37] years), plus 2 nonspecified. Some patients reported good asthma control and simultaneously reported frequent exacerbations. Most patients and parents expressed a preference for a simpler regimen using fewer drugs, and most had concerns about their treatment. Although some patients concurred with treatment guidelines, 62.2% tended to rely on reliever medication (ie, bronchodilators). Additionally, 6.9% described their asthma as very well-controlled but reported experiencing asthma symptoms > or =3 days per week. Finally, 1.9% of patients and 2.1% of parents reporting very well-controlled asthma also reported visiting the emergency department or calling a physician for a home visit in the previous 3 months. CONCLUSIONS: Asthma patients and parents of asthmatic children had unmet treatment needs and may interpret medical terminology differently than clinicians.

Hyponen E. et al. *Infant vitamin d supplementation and allergic conditions in adulthood: northern Finland birth cohort 1966.* Ann N Y Acad Sci. 2004; 1037 : 84-95.p **Abstract**: Allergen-induced secretion of Th2-type cytokines and IgE production have recently been reported to be increased in mice treated with 1,25(OH)(2)D, the active form of vitamin D. Our objective was to investigate whether vitamin D supplementation in infancy is associated with the risk of atopy, allergic rhinitis, and asthma. The Northern Finland Birth Cohort consists of all individuals in the two most northern provinces of Finland who were due to be born in 1966. Data on vitamin D supplementation during the first year of life was obtained in 1967. Current asthma and allergic rhinitis were reported at age 31 years (n = 7,648), and atopy determined by skin-prick test in a sub-sample still living in northern Finland or the Helsinki area (n = 5,007). The prevalence of atopy and allergic rhinitis at age 31 years was higher in participants who had received vitamin D supplementation regularly during the first year compared to others (OR 1.46, 95%CI 1.4-2.0, and OR 1.66, 95%CI 1.1-1.6, respectively). A similar association was observed for asthma (OR 1.35, 95%CI 0.99-1.8). These associations persisted after adjustment for a wide range of behavioral and social factors (adjusted: OR 1.33 for all, P = 0.01 for atopy, P = 0.001 for allergic rhinitis, and P = 0.08 for asthma). We observed an association between vitamin D supplementation in infancy and an increased risk of atopy and allergic rhinitis later in life. Further study is required to determine whether these observations reflect long-term effects on immune regulation or differences in unmeasured determinants of vitamin D supplementation.

Hyvarinen M.K. et al. *Teenage asthma after severe early childhood wheezing: an 11-year prospective follow-up.* Pediatr Pulmonol.

2005; 40(4) : 316-23.p **Abstract**: The role of factors related to early wheezing and their associations with subsequent development of asthma are controversial. We reevaluated 81 children who had been prospectively followed up since hospitalization for wheezing at less than 2 years of age. The baseline data on characteristics of the children, family-related factors, and viral causes of wheezing were collected on entry into the study. At the median age of 12.3 years, current symptoms suggestive of asthma and allergy were recorded. As part of the clinical examination, an outdoor exercise challenge test and skin prick tests to common inhalant allergens were performed. Asthma, as indicated by current inhaled anti-inflammatory medication or repeated wheezing and positive result in the challenge test, was present in 32 (40%) children, and 90% of them were sensitized to at least one allergen. Early asthma-predictive factors were atopic dermatitis (odds ratio (OR), 3.5; 95% confidence interval (CI), 1.2-10.1) and the presence of specific IgE to inhalant allergens (OR, 11.3; 95% CI, 1.9-67.6). Respiratory syncytial virus (RSV) identification during wheezing in infancy was relatively rare (20%) among later asthmatics compared with other or no viral identification (52%) or rhinovirus identification (58%). Since the prevalence of childhood asthma in our area is 4.0-5.0%, we conclude that the increased risk of asthma persists until the teenage years after hospitalization for wheezing in infancy. The risk was about 5-fold after respiratory syncytial virus-induced wheezing, and more than 10-fold after rhinovirus-induced wheezing in the present study.

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Iglesias-Cadarso A. et al. *A prospective safety study of allergen immunotherapy in daily clinical practice.* Allergol Immunopathol (Madr). 2004; 32(5) : 278-83.p **Abstract**: BACKGROUND: Despite its clinical effectiveness, allergen immunotherapy (AIT) remains controversial because serious systemic reactions can occur during its administration. Most of the studies on the safety of AIT are retrospective and use different methods, which frequently depart from daily clinical practice. OBJECTIVE: The aim of this study was to determine risk factors for adverse reactions, especially systemic adverse reactions, produced during routine AIT administration. METHODS: We registered 5,768 consecutive doses of standardized extracts administered to 273 patients in conventional schedules, following the recommendations on safety and data collection of the European Academy of Allergy and Clinical Immunology. Of the 273 patients, 236 were asthmatics, 28 had rhinitis and 9 received immunotherapy due to Hymenoptera anaphylaxis. RESULTS: We examined 143 local reactions (2.48 % of the doses) and 145 systemic reactions (78 immediate and 67 delayed). Risk factors for developing an immediate systemic reaction were asthma severity, sensitization to molds, the most concentrated vials and a fall in peak expiratory flow of more than 15 % or an immediate systemic reaction in the previous dose. Late systemic reactions were significantly more frequent with less concentrated vials and in patients with late local reactions in the previous dose. No serious reactions were registered. CONCLUSIONS: We believe that AIT is reliable when used with strict safety protocols and administered by specialized staff. Risk factors for adverse reactions to this type of treatment can be identified and reduced by systematic data collection.

Indrayan A. et al. *Estimates of the years-of-life-lost due to the top nine causes of death in rural areas of major states in India in 1995.* Natl Med J India. 2002; 15(1) : 7-13.p **Abstract**: BACKGROUND: Years-of-life-lost (YLL) contribute nearly two-thirds of the disability-adjusted life-years (DALYs) worldwide and are especially important for India where infant and child mortality is still high. These were estimated for India under the Global Burden of Disease study for the year 1990. No estimates are available for the different states of India. We aimed to prepare state-wise estimates of YLL for

different causes of death in rural areas and to determine the causes responsible for a higher burden in different states. **METHOD:** Percentage deaths of the top 9 causes reported in the Registrar-General's Survey of Causes of Deaths (Rural)--1995 in 13 major states of India and different age groups was applied to the expected number of total deaths. The life lost according to the standard life-table was age-weighted and discounted using the methodology of the Global Burden of Disease 1990 study. The causes of death were based on lay reporting which otherwise seem reliable. **RESULTS:** The all-cause YLL in rural India in 1995 were 207 per 1,000 population. The minimum was 74 in Kerala and maximum 276 in Madhya Pradesh. Pneumonia was the top cause responsible for 15 YLL. The inter-state variation was high as Tamil Nadu had only 1.6 and Uttar Pradesh 30.5 YLL from this cause. Cancers were a uniform burden across the states. Heart attack, and bronchitis and asthma cut across the more and less developed states. Suicides were a heavy burden in Andhra Pradesh and vehicular accidents in Haryana and Rajasthan. Bihar, Gujarat, Madhya Pradesh, Orissa, Rajasthan and Uttar Pradesh had communicable and nutritional conditions as predominant causes while Kerala and Punjab had non-communicable diseases as the predominant cause of YLL due to premature mortality. **CONCLUSION:** These results provide a new perspective about the causes of death that need more attention in rural areas of different states of India. These will also help prioritize areas which require more inputs at the state-level and hence will be useful for health policymakers.

Iqbal S. et al. *Drug delivery and adherence in young children.* *Pediatr Pulmonol.* 2004; 37(4) : 311-7.p **Abstract:** The aim of this pilot study was to compare a the HaloLite Paediatric Nebulizer (HPN) with a pressurized metered dose inhaler and valved holding chamber (pMDI VHC, Aerochamber) in terms of drug delivery, adherence to treatment, compliance with device, true adherence, and acceptability. Fourteen children aged 11-36 months with asthma on regular treatment with inhaled corticosteroids were enrolled into an open, randomized, crossover trial. They received budesonide for 2 weeks with each delivery system. Both devices incorporated a datalogger which recorded information on how the device was used. The HPN was preprogrammed to deliver 25 microg of budesonide to the patient. A single actuation of budesonide 200 microg was used with the pMDI VHC. The median delivered dose of budesonide was 36 microg (range, 31-45 microg; CV, 15%) for the HPN and 53 microg (range, 17-85 microg; CV, 47%) for the pMDI VHC. The median adherence was 68% (range, 11-96%) with the HPN and 71% (range, 11-100%) with the pMDI VHC. The median device compliance was 30% and 51% and the median true adherence was 23% and 36%, respectively. The shape, size, and weight of the HaloLite Paediatric Nebulizer were generally less acceptable than the shape, size, and weight of the pMDI VHC with datalogger. These results indicate that reproducible quantities of drug can be delivered to very young children using AAD technology such as that incorporated into the HPN. Drug delivery with the pMDI VHC was more variable, but parents preferred this device.

Irani A.M. et al. *Effects of budesonide inhalation suspension on hypothalamic-pituitary-adrenal-axis function in infants and young children with persistent asthma.* *Ann Allergy Asthma Immunol.* 2002; 88(3) : 306-12.p **Abstract:** **BACKGROUND:** The initial 12-week, double-blind phases of three studies demonstrated that budesonide inhalation suspension (BIS) is effective and well tolerated in infants and young children (6 months to 8 years of age) with persistent asthma. **OBJECTIVE:** Open-label, 52-week extensions to these studies were conducted to evaluate long-term safety of BIS, including effects of treatment with the lowest effective dose of BIS on hypothalamic-pituitary-adrenal (HPA)-axis function, as compared with conventional asthma therapy (CAT). Complete results of the earlier phases of the studies and of long-term safety are reported elsewhere; only results pertaining to HPA-axis function are summarized here. **METHODS:** Patients eligible for the open-label

phases of the three trials were randomized to treatment with nebulized BIS (n = 447) or CAT (n = 223). CAT included short-acting oral or inhaled beta2-agonists, methylxanthines, or cromolyn sodium; in two of the studies, CAT could have included other inhaled corticosteroids. HPA-axis function, which had been evaluated during the 12-week double-blind studies, was again evaluated at the beginning and end of the 52-week study period using basal plasma cortisol concentrations and response to stimulation with a 250-microg dose of adrenocorticotropic hormone. **RESULTS:** There was no evidence of altered HPA-axis function attributable to BIS treatment. No clinically or statistically significant differences in basal or adrenocorticotropic hormone-stimulated plasma cortisol concentrations were observed between BIS and CAT in either the 12-week, double-blind or 52-week, open-label phases of the three studies. **CONCLUSIONS:** The results indicate that treatment with BIS does not result in clinically significant suppression of HPA-axis function in infants and young children.

Irvine A.D. et al. *Breaking the (un)sound barrier: filaggrin is a major gene for atopic dermatitis.* *J Invest Dermatol.* 2006; 126(6) : 1200-2.p **Abstract:** We have recently shown that loss-of-function mutations in the filaggrin gene, carried by about 10% of people of European ethnicity, cause ichthyosis vulgaris and are strong predisposing factors for atopic dermatitis and asthma secondary to atopic dermatitis. These results demonstrate a prominent role for the epidermal barrier in atopic disease and have important implications for the study of complex traits.

Itazawa T. et al. *Increased lymphoid MxA expression in acute asthma exacerbation in children.* *Allergy.* 2001; 56(9) : 895-8.p **Abstract:** **BACKGROUND:** Although the association between acute asthma exacerbation and viral infection has been well documented, virus identification rates vary. It has recently been reported that the expression of MxA protein in lymphocytes, inducible by type I interferons, can serve as a sensitive marker for viral infection in the host. The objective was to determine the contribution of viral infection to precipitation of asthma attacks in children. **METHODS:** We studied 186 asthmatic children, aged 0-12 years, over a 1-year period to evaluate MxA protein levels in peripheral blood lymphocytes by using a flow cytometric analysis in whole blood. **RESULTS:** Of all the subjects, 80 (47%) exhibited significantly elevated levels of MxA expression in lymphocytes, presumably indicating the states of viral infection. The association of viral infections with acute asthma exacerbation seemed to be marked in younger children: enhanced MxA expression was seen in 73.3% of infants (aged 0-1 year), 49.5% of toddlers (aged 2-5 years), and 26% of schoolchildren (aged 6-12 years). Seasonal changes in the frequency of viral infection associated with deterioration were also observed. **CONCLUSIONS:** Flow cytometric assay of MxA protein expression in whole blood appears to be an easy and useful method to evaluate viral infections in acute asthma exacerbation.

Ito Y. et al. *Trends in asthma mortality in Japan.* *J Asthma.* 2002; 39(7) : 633-9.p **Abstract:** Asthma mortality has been increasing in many developed countries in recent years, so we have described the epidemiological features of asthma in Japan. Data on all certified asthma deaths from 1950 to 1997 were obtained from The National Vital Statistics, published annually by the Ministry of Health and Welfare. Trends in crude and age-adjusted asthma mortality rates, as well as age-specific mortality rates, were analyzed. Age and birth cohort effects on mortality rates were also examined using multiplicative models. Between 1950 and 1980, crude asthma mortality rates steadily decreased in both sexes and began to level off thereafter. Age-adjusted mortality rates have also decreased since 1950, and showed a persistent downward trend in both sexes even in recent years. Asthma mortality rates were higher in males than in females during the entire study period. When analysis was restricted to those aged 5 to 34 years, an upward trend since 1980 was

observed. The multiplicative model showed a rapidly decreasing cohort effect on mortality among those born after 1860. However, the slope increased in the cohorts born after 1950 in both sexes. The age effect increased linearly with advancing age after 50 years in both sexes. Overall asthma mortality rates have been decreasing during the past five decades in Japan, but the mortality rate has increased among the 5-34-year-old age group since 1980. The high fatality rate stemming from the overuse of beta 2-agonists may account for the mortality increase.

Ivaschenko T.E. et al. *Glutathione- S-transferase micro and theta gene polymorphisms as new risk factors of atopic bronchial asthma.* J Mol Med. 2002; 80(1) : 39-43.p **Abstract:** The genetic polymorphism of glutathione- S-transferase M1 (GSTM1) and glutathione- S-transferase T1 (GSTT1) genes and the cytochrome P4501A1 gene responsible for xenobiotic conjugating enzymes of the phase II and phase I detoxification system were studied by PCR-RFLP in the blood spots of 109 patients with atopic bronchial asthma and 90 healthy individuals. GSTM1 gene deletion (GSTM1(0/0)) was detected in 47.8% of individuals in the control group and in 76.1% of asthmatic patients. Individuals without the GSTM1 gene were at approximately 3.5-fold higher risk of developing asthma. The proportion of GSTT1(0/0) genotypes was significantly higher in the group of asthmatics (67.0%) than in controls (23.3%). The proportion of individuals with a deficiency in both GSTM1 and GSTT1 gene activity was more than four times higher in asthmatic patients than in the control group (54.1% and 12.2%, respectively). The frequency of the Ile-Val polymorphism of the CYP1A1 gene was similar in controls and asthmatic patients. This study shows the association of atopic bronchial asthma with GSTM1(0/0), GSTT1(0/0) genotypes.

Izurieta H.S. et al. *Adverse events reported following live, cold-adapted, intranasal influenza vaccine.* JAMA. 2005; 294(21) : 2720-5.p **Abstract:** CONTEXT: In June 2003, the US Food and Drug Administration licensed a trivalent live, attenuated influenza vaccine (LAIV-T) for intranasal administration to healthy persons 5 to 49 years of age. Although precensure testing involved 20 228 vaccinees, clinical trials were not of sufficient size to detect rare adverse events reliably. OBJECTIVE: To identify adverse events reported following LAIV-T administration after licensure. DESIGN, SETTING, AND PARTICIPANTS: All adverse events reported to the US Vaccine Adverse Event Reporting System (VAERS) during the 2003-2004 and the 2004-2005 influenza seasons. MAIN OUTCOME MEASURES: Numbers and proportions of reported adverse events and reporting rates of adverse events per 100,000 vaccinees. RESULTS: Approximately 2,500,000 persons received LAIV-T during the first 2 postlicensure seasons. As of August 16, 2005, VAERS received 460 adverse event reports for vaccinations received from August 2003 through July 2005. No fatalities were reported. There were 7 reports of possible anaphylaxis, 2 reports of Guillain-Barre syndrome, 1 report of Bell palsy, and 8 reports of asthma exacerbation among individuals with a prior asthma history. Events in individuals for whom the vaccine was not indicated accounted for 73 reports (16%). CONCLUSIONS: Reports to VAERS in the first 2 seasons of LAIV-T use did not identify any unexpected serious risks with this vaccine when used according to approved indications. Like many vaccines and other medical products, LAIV-T may rarely cause anaphylaxis. Secondary transmission of the vaccine virus merits further investigation. Reports of asthma exacerbations in vaccinees with prior asthma history highlight the risks of vaccine use inconsistent with approved labeling.

Jaakkola J.J. et al. *Effects of environmental tobacco smoke on the respiratory health of children.* Scand J Work Environ Health. 2002; 28 Suppl 2 : 71-83.p **Abstract:** This review synthesizes current knowledge of the effects of prenatal and postnatal exposure to environmental tobacco smoke on the respiratory health of children. A Medline database search was conducted for 1966 through October 2000. Limited evidence was found that exposure in pregnancy influences fetal growth, increases the risk of preterm delivery, and predicts the development of asthma and reduced lung function later in life. Both occupational and home environments contribute to the exposure of pregnant women and thus indirectly to adverse effects on children. There is strong and consistent evidence that exposure in childhood causes chronic respiratory symptoms (eg, cough, phlegm, and wheezing) and induces asthma. Limited evidence supports the role of childhood exposure in the poor overall control of established disease. Postnatal exposure is likely to have a small adverse impact on lung function growth. Prenatal and postnatal exposures have an important impact on children's respiratory health. These effects are preventable if pregnant women and children are protected from exposure to environmental tobacco smoke.

Jackson P.L. *Peanut allergy: an increasing health risk for children.* Pediatr Nurs. 2002; 28(5) : 496-8.p **Abstract:** Matthew, age 24 months, is brought into the clinic by his frantic mother. She reports Matthew started wheezing and broke out in a blotchy skin rash within 5 minutes of eating a cracker with peanut butter. Matthew has a history of mild, intermittent asthma treated with nebulized albuterol, which the mother administered without improvement in the child's breathing pattern. He also has a history of moderate atopic dermatitis and a prior milk intolerance that he has since outgrown. No other food allergies are noted in his history, and the mother believes this is the first time Matthew has eaten peanut butter. It has been approximately fi hour since he ingested the peanut butter. Matthew's vital signs are temperature 98.6 degrees F, pulse 90, and respirations 60 with audible wheezing and repetitive cough. His blood pressure is 80/60. His face and chest are flushed with urticaria, and some swelling is noted around his mouth.

Jalaludin B.B. et al. *Acute effects of urban ambient air pollution on respiratory symptoms, asthma medication use, and doctor visits for asthma in a cohort of Australian children.* Environ Res. 2004; 95(1) : 32-42.p **Abstract:** We enrolled a cohort of primary school children with a history of wheeze (n=148) in an 11-month longitudinal study to examine the relationship between ambient air pollution and respiratory morbidity. We obtained daily air pollution (ozone, particulate matter less than 10 microm, and nitrogen dioxide), meteorological, and pollen data. One hundred twenty-five children remained in the final analysis. We used logistic regression models to determine associations between air pollution and respiratory symptoms, asthma medication use, and doctor visits for asthma. There were no associations between ambient ozone concentrations and respiratory symptoms, asthma medication use, and doctor visits for asthma. There was, however, an association between PM(10) concentrations and doctor visits for asthma (RR=1.11, 95% CI=1.04-1.19) and between NO(2) concentration and wet cough (RR=1.05, 95% CI=1.003-1.10) in single-pollutant models. The associations remained significant in multipollutant models. There was no consistent evidence that children with wheeze, positive histamine challenge, and doctor diagnosis of asthma reacted differently to air pollution from children with wheeze and doctor diagnosis of asthma and children with wheeze only. There were significant associations between PM(10) levels and doctor visits for asthma and an association between NO(2) levels and the prevalence of wet cough. We were, however, unable to demonstrate that current levels of ambient air pollution in western Sydney have a coherent range of adverse health effects on children with a history of wheezing.

Jang A.S. et al. *The effect of passive smoking on asthma symptoms, atopy, and airway hyperresponsiveness in schoolchildren.* J Korean Med Sci. 2004; 19(2) : 214-7.p **Abstract:** Passive smoking is a major cause of respiratory morbidity, and is associated with increased bronchial responsiveness in children. To evaluate the effect of smoking by a parent on asthma symptoms, atopy, and airway hyperresponsiveness (AHR), we conducted a cross-sectional survey of 503 schoolchildren that involved questionnaires, spirometry, allergy testing, and a bronchial challenge test. If the PC20 methacholine was less than 16 mg/mL, the subject was considered to have AHR. The prevalence of a parent who smoked was 68.7%. The prevalence of AHR was 45.0%. The sensitization rate to common inhalant allergens was 32.6%. Nasal symptoms such as rhinorrhea, sneezing, nasal itching, and nasal obstruction were present in 42.7%. Asthma symptoms such as cough and wheezing were present in 55.4%. The asthma symptoms were significantly more prevalent in children who had a parent who smoked than in those whose parents did not. The nasal symptoms, atopy, and AHR did not differ according to whether a parent smoked. In a multiple logistic regression model, the asthma symptoms and atopy were independently associated with AHR, when adjusted for confounding variables. Passive smoking contributed to asthma symptoms in schoolchildren and was not an independent risk factor of airway hyperresponsiveness in an epidemiological survey.

Janse A.J. et al. *A difference in perception of quality of life in chronically ill children was found between parents and pediatricians.* J Clin Epidemiol. 2005; 58(5) : 495-502.p **Abstract:** BACKGROUND AND OBJECTIVES: Quality of life measurements can help to estimate the well-being of chronically ill patients, and disclose discrepancies in perception between physicians and patients that might otherwise interfere with the effectiveness of treatment. The objective was to investigate the differences in perception of quality of life between parents of chronically ill children and pediatricians. METHODS: A cross-sectional study was conducted in four tertiary pediatric care centers in The Netherlands. The Health Utilities Index mark 3 (HUI3) was used by 37 pediatricians and 279 parents of patients (children aged 1 to 17 years) with cystic fibrosis admitted either in daycare or for a pneumonia, or patients with newly diagnosed acute lymphoblastic leukemia, juvenile idiopathic arthritis, or asthma. RESULTS: Differences in perception of quality of life between parents and pediatricians appeared to be dependent of the disease. In patients with acute lymphoblastic leukemia (OR 7.4; [95% CI 2.88-18.97], juvenile idiopathic arthritis (4.7; [95% CI 2.00-11.22]), and asthma (2.3; [95% CI 1.13-4.69]) a difference in perception was more likely to occur than in patients with cystic fibrosis admitted in daycare. CONCLUSION: At the onset of a chronic disease, the parents of pediatric patients may be misunderstood by health care professionals, especially in subjective attributes. Assessment of quality of life may contribute to better understanding between pediatricians and parents, and thus may even enhance compliance and treatment effects.

Janssen C.L. et al. *Asthmatic children's inhalation techniques in general practice.* Eur J Gen Pract. 2003; 9(4) : 143-5.p

Jedrychowski W. et al. *Prospective epidemiologic study on respiratory diseases in children and immunization against measles.* Int J Occup Med Environ Health. 2004; 17(2) : 255-61.p **Abstract:** BACKGROUND: A hypothesis that vaccination with live attenuated measles virus performed in early childhood may prevent allergic sensitization has been explored in the course of a 3-year follow-up study in Krakow (Poland) among 1005 school children. MATERIALS AND METHODS: The basic respiratory health endpoints were chronic respiratory symptoms, allergy, asthma and susceptibility to acute respiratory infections. Information about immunization status of children was extracted from individual vaccination records kept by school nurses. The study showed the highest rates of chronic respiratory symptoms in non-vaccinated

children who contracted measles while the lowest rates in those vaccinated who did not contract the disease. RESULTS AND CONCLUSIONS: Risk of allergy diagnosed by a physician in vaccinated children after adjustment to potential confounders was about half of that in the reference group (OR = 0.58 95% CI: 0.42-0.80), the same was found for asthma diagnosed by a physician (OR = 0.50 95% CI: 0.24-1.00), and for susceptibility to respiratory infections (OR = 0.51 95% CI: 0.36-0.72). Our data provide indirect evidence that infection with attenuated measles virus is able to alter immunological reactions being responsible for the manifestation of respiratory symptoms and allergy.

Jenkins H.A. et al. *A comparison of the clinical characteristics of children and adults with severe asthma.* Chest. 2003; 124(4) : 1318-24.p **Abstract:** OBJECTIVES: This study sought to better define the clinical characteristics of severe asthma in both children and adults, and to evaluate the effect of asthma duration on multiple parameters of disease severity. DESIGN: Retrospective analysis of prospectively collected data on 275 patients (125 children) with severe asthma who were admitted to a tertiary asthma referral center. METHODS: Demographics, lung function (ie, spirometry and body box plethysmography), glucocorticoid (GC) pharmacokinetic studies, and lymphocyte stimulation assays were performed on all patients. RESULTS: Children were as likely to require therapy with high-dose inhaled GCs and long-term therapy with oral GCs, and to have had a prior intubation, yet they had significantly less airflow limitation (mean [+/- SEM] FEV(1), 74.0 +/- 2.1% predicted vs 57.1 +/- 1.8% predicted, respectively; p < 0.0001), less resistance to airflow (mean airway resistance, 140.3 +/- 8.5% predicted vs 311 +/- 18% predicted, respectively; p < 0.0001), and larger lung volumes (mean total lung capacity, 116.4 +/- 1.6% predicted vs 105.3 +/- 1.8% predicted, respectively; p < 0.0001) compared to adults. Children were more likely to be male and to display greater responsiveness to GCs in vitro. Lung function impairment was associated with asthma duration in children and in adults with onset of asthma in childhood, while there was no relationship between disease severity and asthma duration among those with adult-onset asthma. Despite significant differences in disease duration, patients with adult-onset asthma had equally compromised lung function compared to adults with long-standing asthma. CONCLUSIONS: Children with severe asthma tended to be male, to have less severe airflow obstruction, and to display greater responsiveness to GCs in vitro compared to adults. Symptoms and episodic acute declines in lung function may precede chronic airflow limitation in this group of children. As such, it may be more relevant to follow the deterioration in lung function over time in children. Finally, disease severity in children and adults whose onset of asthma occurred in childhood was related to disease duration, but not in patients with onset of asthma in adulthood.

Jeong K.Y. et al. *Immunoglobulin E binding reactivity of a recombinant allergen homologous to alpha-Tubulin from Tyrophagus putrescentiae.* Clin Diagn Lab Immunol. 2005; 12(12) : 1451-4.p **Abstract:** Storage mites may cause allergic respiratory diseases in urban areas as well as pose an occupational hazard in rural areas. Characterization of storage mite allergens is important for the development of diagnostic and therapeutic agents against mite-associated allergic disorders. Here we report on the cloning and expression of alpha-tubulin from the storage mite (Tyrophagus putrescentiae). The deduced amino acid sequence of the alpha-tubulin from the storage mite showed as much as 97.3% identity to the alpha-tubulin sequences from other organisms. The highly conserved amino acid sequences of alpha-tubulins across different species of mites may indicate that cross-reactivity for this potential allergen exists. The frequency of immunoglobulin E reactivity of this recombinant protein is 29.3% in sera from storage mite-allergic subjects.

- Jian Z. et al.** *No evidence for association between the -112G/A polymorphism of UGRP1 and childhood atopic asthma.* Clin Exp Allergy. 2003; 33(7) : 902-4.p Abstract: BACKGROUND: Susceptibility to asthma is known to involve genetic factors. Genome-wide screens have indicated that the chromosome 5q31-q34 region is linked to and/or associated with asthma. A new gene, named UGRP1 and reported by Niimi et al., encodes uteroglobin-related protein and is expressed in the lung and trachea. Niimi et al. showed the -112G/A polymorphism of the UGRP1 gene to be associated with asthma in a case-control study. OBJECTIVE: The objective of the present study was to replicate this association and confirm the possible role of the UGRP1-112G/A polymorphism in the aetiology of childhood asthma in a Japanese population. METHODS AND RESULTS: We conducted a transmission disequilibrium test (TDT) in 131 families identified through paediatric patients being treated for asthma. A case-control study was also carried out by comparing the probands and 137 unrelated non-atopic non-asthmatic Japanese children and 211 unrelated healthy Japanese adults. The -112G/A polymorphism was genotyped by the PCR-RFLP method. The TDT revealed that the -112A allele was not preferentially transmitted to asthma-affected children (P=0.85). Neither the presence of at least one A allele in an individual's genotype (sum of the G/A and A/A genotypes) nor the -112A allele was more prevalent among the asthma subjects than among the control subjects. CONCLUSION: Our findings indicate that the UGRP1-112G/A polymorphism does not play a substantial role in genetic predisposition to childhood asthma in this Japanese population.
- Jobe A.H.** *An unanticipated benefit of the treatment of preterm infants with CuZn superoxide dismutase.* Pediatrics. 2003; 111(3) : 680.p
- Johansson E. et al.** *Allergenic cross-reactivity between the nematode Anisakis simplex and the dust mites Acarus siro, Lepidoglyphus destructor, Tyrophagus putrescentiae, and Dermatophagoides pteronyssinus.* Allergy. 2001; 56(7) : 660-6.p Abstract: BACKGROUND: The nematode Anisakis simplex is a common parasite on fish and other seafood. It is considered to be a food allergen and to induce IgE-mediated reactions. Allergenic cross-reactivity between A. simplex and other nematodes has been reported, as has cross-reactivity with arthropods: red mosquito larvae and German cockroach. We have here studied the allergenic relationship between A. simplex and four different dust-mite species. METHODS: Serum samples collected from 69 farmers allergic to dust mites were analyzed for IgE to A. simplex by CAP FEIA. Allergenic cross-reactivity between A. simplex and dust mites was studied in two of the sera by CAP FEIA and immunoblotting inhibition. RESULTS: We found that 14/69 farmers had detectable levels of IgE antibodies to A. simplex. The IgE response in CAP FEIA to A. simplex was inhibited to various degrees in the two studied sera by extracts of the dust mites Acarus siro, Lepidoglyphus destructor, Tyrophagus putrescentiae, and Dermatophagoides pteronyssinus. In the reverse inhibition experiment, extract of A. simplex inhibited the response in both sera to A. siro and T. putrescentiae, but not to L. destructor. The IgE binding to D. pteronyssinus was inhibited in one of the two sera. In blotting inhibition experiments, the IgE binding to several allergens in A. simplex was inhibited by each of the four mite extracts, especially by A. siro and T. putrescentiae, which completely inhibited the IgE binding to several allergens. CONCLUSION: The results show allergenic cross-reactivity between several allergens in A. simplex and four dust-mite species. The clinical significance of this cross-reactivity remains to be evaluated.
- Johansson M. et al.** *Trends in the use of inhaled corticosteroids for childhood asthma in New Zealand.* Eur J Clin Pharmacol. 2003; 59(5-6) : 483-7.p Abstract: OBJECTIVE. To compare the dispensed volumes and prescribed doses for inhaled corticosteroids (ICS) for children in New Zealand. DESIGN. Longitudinal analysis of prescribing trends using the Royal New Zealand College of General Practitioners Research Unit database and the Pharm Warehouse database of the New Zealand Health Information System. SETTING. New Zealand from 1993 to 2001. SUBJECTS. Children aged 0-5 years and 6-17 years. MAIN OUTCOME MEASURES. The ratio of potency-adjusted mean daily dose of fluticasone propionate (FP) to beclomethasone (BDP) and dispensed volumes of FP, BDP and budesonide. RESULTS. The ratio of potency-adjusted mean daily dose of FP to BDP prescribed to children aged 0-17 years ranged from 1.22 to 1.91. With the introduction of FP, the total amount of ICS dispensed to children aged 0-5 years in New Zealand nearly doubled, when adjusted for potency. CONCLUSIONS. The introduction of FP into New Zealand corresponds with an increase in the total amount of ICS dispensed and an increase in the adjusted daily dose prescribed.
- Johnson B. et al.** *Using a matrix as an educational approach to asthma.* J Pediatr Health Care. 2003; 17(1) : 3-10.p Abstract: Health care providers agree that asthma care must be individualized to fit the need of the child and family. A written plan in the form of a matrix enables the health care provider to give families a step-by-step individualized plan of care for asthma. This article discusses the use of a long-term treatment plan in matrix form as an educational tool for health care providers and for families. The written long-term plan can be used to guide treatment for any level of asthma severity. Following a review of asthma pathogenesis and diagnosis, categories of medications are presented, along with their role in a long-term treatment plan. The National Heart, Lung, and Blood Institute guidelines are used as a basis for the recommendations in the long-term treatment plan.
- Johnson C.C. et al.** *Antibiotic exposure in early infancy and risk for childhood atopy.* J Allergy Clin Immunol. 2005; 115(6) : 1218-24.p Abstract: BACKGROUND: The increase in pediatric allergy and asthma parallels the increase in use of antibiotics. Antibiotics disturb the flora of the gastrointestinal tract, possibly perturbing the developing immune system. OBJECTIVE: We evaluated whether antibiotic use during early infancy increased the risk for atopy. METHODS: Antibiotic prescriptions documented in medical records were collected from a birth cohort born from 1987 through 1989 (n = 725). At 6 to 7 years of age, 448 were followed by means of examination, including skin prick tests and serum IgE measurements to common allergens. RESULTS: Adjusted odds ratios (aORs) and 95% CIs were calculated comparing children with any versus those with no antibiotic use in the first 6 months and the outcomes of atopy (any positive skin test response), seroatopy (any positive specific IgE test result), either atopy or seroatopy, and both atopy and seroatopy. Atopy increased with antibiotic use approaching statistical significance (aOR, 1.48; 95% CI, 0.94-2.34; P = .09); however, the risk was concentrated among children with less than 2 pets in the home (aOR, 1.73; 95% CI, 1.07-2.80; P = .024) and children breast-fed for 4 or more months (aOR, 3.02; 95% CI, 1.27-7.17; P = .013). The aORs were generally in the same direction for seroatopy and the combined categories. CONCLUSION: Antibiotic use in early life appears to contribute to increased risk for atopy in certain subgroups of children.
- Johnson D.** *Fighting for air.* Newsweek. 2003; 142(12) : 54.p
- Johnson P.** *Choosing an inhaler device for a child.* Practitioner. 2003; 247(1645) : 309-12, 314-6.p
- Johnson P.R. et al.** *Fine particulate matter national ambient air quality standards: public health impact on populations in the northeastern United States.* Environ Health Perspect. 2005; 113(9) : 1140-7.p Abstract: In this article we identify the magnitude of general and susceptible populations within the northeastern United States that

would benefit from compliance with alternative U.S. Environmental Protection Agency (EPA) annual and 24-hr mass-based standards for particulate matter (PM) with an aerodynamic diameter \leq 2.5 microm (PM_{2.5}). Understanding the scale of susceptibility in relation to the stringency or protectiveness of PM standards is important to achieving the public health protection required by the Clean Air Act of 1970. Evaluative tools are therefore necessary to place into regulatory context available health and monitoring data appropriate to the current review of the PM National Ambient Air Quality Standards (NAAQS). Within the New England, New Jersey, and New York study area, 38% of the total population are $<$ 18 or $>$ or \geq 65 years of age, 4-18% of adults have cardiopulmonary or diabetes health conditions, 12-15% of children have respiratory allergies or lifetime asthma, and 72% of all persons (across child, adult, and elderly age groups) live in densely populated urban areas with elevated PM_{2.5} concentrations likely creating heightened exposure scenarios. The analysis combined a number of data sets to show that compliance with a range of alternative annual and 24-hr PM_{2.5} standard groupings would affect a large fraction of the total population in the Northeast. This work finds that current PM_{2.5} standards in the eight-state study area affect only 16% of the general population, who live in counties that do not meet the existing annual/24-hr standard of 15/65 microg/m³. More protective PM_{2.5} standards recommended or enacted by California and Canada would protect 84-100% of the Northeast population. Standards falling within current ranges recommended by the U.S. EPA would protect 29-100% of the Northeast population. These considerations suggest that the size of general and susceptible populations affected by the stringency of alternative PM standards has broad implications for risk management and direct bearing on the U.S. EPA's current NAAQS review and implementation.

Johnston F.H. et al. *Exposure to bushfire smoke and asthma: an ecological study.* Med J Aust. 2002; 176(11) : 535-8.p Abstract: OBJECTIVE: To examine the relationship between the mean daily concentration of respirable particles arising from bushfire smoke and hospital presentations for asthma. DESIGN AND SETTING: An ecological study conducted in Darwin (Northern Territory, Australia) from 1 April - 31 October 2000, a period characterised by minimal rainfall and almost continuous bushfire activity in the proximate bushland. The exposure variable was the mean atmospheric concentration of particles of 10 microns or less in aerodynamic diameter (PM₁₀) per cubic metre per 24-hour period. OUTCOME MEASURE: The daily number of presentations for asthma to the Emergency Department of Royal Darwin Hospital. RESULTS: There was a significant increase in asthma presentations with each 10-microg/m³ increase in PM₁₀ concentration, even after adjusting for weekly rates of influenza and for weekend or weekday (adjusted rate ratio, 1.20; 95% CI, 1.09-1.34; $P < 0.001$). The strongest effect was seen on days when the PM₁₀ was above 40 microg/m³ (adjusted rate ratio, 2.39; 95% CI, 1.46-3.90), compared with days when PM₁₀ levels were less than 10 microg/m³. CONCLUSION: Airborne particulates from bushfires should be considered as injurious to human health as those from other sources. Thus, the control of smoke pollution from bushfires in urban areas presents an additional challenge for managers of fireprone landscapes.

Jokinen P. *The family life-path theory: a tool for nurses working in partnership with families.* J Child Health Care. 2004; 8(2) : 124-33.p Abstract: The purpose of this article is to describe the family life-path theory. The theory may offer nurses an alternative model for use in working in partnership with the family of a child with a long-term illness. It is important that nurses have a deep understanding of a family's everyday life. The better nurses know the family and the context in which it lives, the more individual advice and coping strategies that they are able to find in partnership with a family, and thus to support the family in achieving a good quality of life. The theory describes the life of a family of a child with asthma as a lifepath. The dimensions of the family's life-path are environment,

the child's becoming ill, the family's view of health, their attitude towards illness, everyday routines and social network. The unpredictability of asthma, optimism about the future and normalization of life are factors that guide families towards achievement of a good quality of life for their child.

Jones A.P. et al. *Early life exposures and the prevalence of atopic disorders in a sample of school-age infants.* Monaldi Arch Chest Dis. 2003; 59(1) : 38-43.p Abstract: This study was undertaken to determine the relationship between genetic factors, early life environmental exposures, and the prevalence of atopic disorders in infants. 402 children attending schools in rural Essex were sampled in June 1999. Logistic regression models were fitted to examine the association between asthma, eczema, and rhinitis prevalence and a range of genetic and environmental risk factors. After adjustment, infant asthma was associated with the report of a serious chest infection before 3 years of age, a parent employed in a professional occupation, an asthmatic mother, and an asthmatic sibling. Amongst infants who had attended nursery school there was also an affect of age at first attendance. Associations with a chest infection and a family history of atopic conditions were similarly strong predictors of eczema and rhinitis prevalence. The results suggest that genetic influences and patterns of exposure to infections appear to be the greatest influences on the development of infant atopy.

Jones C. et al. *Adherence to prescribed treatment for asthma: evidence from pharmacy benefits data.* J Asthma. 2003; 40(1) : 93-101.p Abstract: BACKGROUND: Failure to use asthma controller medications as prescribed is associated with more asthma-related adverse events. Medication utilization may vary with ease of drug administration, efficacy, and tolerability as well as other factors. We hypothesized that in usual-care clinical practice settings, there would be greater adherence to oral controller than to inhaled controller asthma medications. METHODS: We compared adherence to newly initiated asthma controller therapy among patients initiating monotherapy with leukotriene receptor antagonists (LTRAs), inhaled corticosteroids (ICS), or inhaled long-acting beta-agonists (ILBA) from March 1998 to July 1999. We measured adherence as the sum of drug supply days between first and last fill dates divided by length of drug therapy. Analyses were stratified by the number of short-acting beta-agonists (SBA) prescriptions per year to control for disease severity. RESULTS: Pharmacy claims data from 48,751 subjects (6 to 55 years) were analyzed (mean age 30.4 years; 56% female). Mean adherence to new start monotherapy on LTRA was 67.7%, to ICS was 33.8%, and to ILBA was 40.0%. Adherence to all three controller agents increased with increasing SBA use. The percent of patients persistent to asthma controller monotherapy at both 6 and 9 months was significantly greater among those on LTRA monotherapy than on either ICS or ILBA. CONCLUSIONS: In clinical practice settings, patients initiating LTRA monotherapy have about twice the adherence as patients initiating ICS or ILBA monotherapy. Because adherence to treatment is a critical component of treatment response, it is important to consider this factor in the prescription of oral vs. inhaled asthma medications.

Jones C.A. et al. *A school-based case identification process for identifying inner city children with asthma: the Breathmobile program.* Chest . 2004; 125(3) : 924-34.p Abstract: BACKGROUND: Striking increases in the prevalence and morbidity of asthma among inner city children have been documented. OBJECTIVE: To establish and evaluate a large-scale, school-based case-detection process designed to efficiently and reliably identify inner city children with asthma. METHODS: A bilingual, seven-question, self-administered, parental asthma screening survey was developed. Clinical validation was achieved in a sample of 675 consecutive parents bringing a child to the school-based Breathmobile Program for initial evaluation, using a comprehensive evaluation by a physician specialist (ie, allergist) as the standard. Survey response patterns were used to construct a novel

seven-model, tiered scoring algorithm and an abbreviated algorithm that predict the probability of a child being clinically classified as "yes asthma" or "no asthma." A systematic survey distribution process administered by a single coordinator was developed, and the impact of a classroom-oriented incentive offering a 25 dollars school supply gift certificate for survey return rates of $\geq 80\%$ was evaluated. RESULTS: A total of 636 parents provided one or more survey responses and information sufficient for clinical classification. The scoring algorithm correctly identified children with asthma ($\geq 80\%$ probability) with a sensitivity of 86.5%, a specificity of 83.6%, and a misclassification rate of 14.3% (91 of 636 children). The sensitivity for identifying persistent asthma was 91.3%. Asthma prevalence estimates derived using survey results from a larger sampling of the general population were similar to rates previously reported for comparable populations. The inclusion of an inexpensive incentive increased the median survey return rates from 35.3 to 65% ($z = -11.9$; $p < .001$). The screening process has been used to conduct 27,526 surveys at inner city schools. CONCLUSIONS: The Breathmobile case-detection process offers a validated, comprehensive, large-scale method with which to identify children with asthma at their school sites.

Jones P.D. et al. *The tolerability, safety, and success of sputum induction and combined hypertonic saline challenge in children.* Am J Respir Crit Care Med. 2001; 164(7) : 1146-9.p **Abstract:** Induced sputum using hypertonic saline (HS) is a useful research tool to study airway inflammation (AI). HS provocation testing can also be used to measure airway hyperresponsiveness (AHR). A combined HS challenge and sputum induction procedure has been developed to permit assessment of AI and AHR in a single test. The aim of this study is to report the success and tolerability of sputum induction alone, and in combination with a HS bronchial provocation challenge. Sputum induction alone was performed with beta2-agonist pretreatment. In the combined challenge, no beta2-agonist pretreatment was used. A high-output ultrasonic nebulizer with valve box and tubing were used to deliver 4.5% saline in doubling time periods from 0.5 s to 4 min. Outcomes assessed were completion of the test protocol, adequacy of sputum samples, decrease in FEV1, and adverse effects during the procedure. Fifty-three children who underwent a sputum induction alone, and 182 children who underwent a combined sputum induction and bronchial provocation using HS. Sputum induction alone was well tolerated, with 98% of children completing the procedure and only 4% experiencing a significant ($> 15\%$) fall in FEV1. An adequate sample of sputum was obtained in 92% of children. The combined challenge was completed by 90% of children. A distressing cough occurred in 13% of children and irritation of the mucosa in 1% of children. In the combined challenge an adequate sample of sputum was obtained in significantly fewer children than with sputum induction alone (70% versus 92%, $p < 0.05$). Sputum cellular changes reflected the shorter nebulization time with sputum induction alone. We conclude that induction of sputum using HS after pretreatment with bronchodilator is well tolerated with a high success rate in children. Combining the HS challenge with sputum induction provides additional information and is a useful means of comparing AHR and AI simultaneously, but at the expense of having a reduced success rate in obtaining an adequate sample of sputum, as well as increased side effects.

Joseph V. *A study compliance to two alternative drug regimens and the effect of health education on drug compliance in school age children with bronchial asthma.* Nurs J India. 2004; 95(7) : 153-4.p

Joshi P. et al. *Interferon-gamma levels in nasopharyngeal secretions of infants with respiratory syncytial virus and other respiratory viral infections.* Clin Exp Immunol. 2003; 131(1) : 143-7.p **Abstract:** Respiratory syncytial virus (RSV) infection, one of the most common causes of hospitalization of children in developed countries, has been implicated as a cause of asthma. We aimed to characterize the cytokine profile in nasopharyngeal aspirates (NPAs) taken from

infants during upper respiratory tract infection to investigate whether RSV induced a unique immune response as compared with other viruses. Additionally, we sought to determine whether this profile was influenced by the infants' atopic status. A prospective birth cohort of babies at high risk of atopy was recruited. Ratios of a T-helper 1 (Th1) cytokine, interferon gamma (IFN-gamma) and a T-helper 2 (Th2)-like cytokine, interleukin-10 (IL-10), in NPAs were determined during episodes of respiratory tract infections in the first year. The viral aetiology of the respiratory tract infections was determined using polymerase chain reaction (PCR), culture and immunofluorescence. Atopic status was ascertained at 1 year of age using skin prick tests. Participants were recruited antenatally and subsequently followed in the community. Sixty babies with one or both parents atopic were enrolled into the study. IFN-gamma : IL-10 ratios in NPAs during upper respiratory tract infections and their correlation with viral aetiology and atopic status were the main outcome measures. The mean IFN-gamma : IL-10 ratio was significantly lower (due to lower IFN-gamma) during RSV infections than during infections with other viruses ($P = 0.035$). The cytokine ratio, however, did not differ between infants with or without wheeze during URTIs ($P = 0.44$), or between infants who were atopic or non-atopic ($P = 0.49$). This study suggests that RSV is associated with lower IFN-gamma production in young babies, regardless of their atopic status, compared to upper respiratory tract infections where either another virus is detected or where no viral identification is made.

Juhn Y.J. et al. *Child care program directors' level of knowledge about asthma and factors associated with knowledge.* Clin Pediatr (Phila). 2002; 41(2) : 111-6.p **Abstract:** Although asthmatic children spend a significant amount of time in child care programs, little is known about child care program directors' knowledge about asthma and what factors influence directors' level of knowledge about asthma. A telephone interview was conducted with directors of a randomly selected sample of all licensed child care centers and group day care homes in Connecticut. Directors of most child care programs were willing to admit asthmatic children to their programs, but their knowledge about asthma needs to be improved. Directors who have served for long periods of time may be a target group for additional education about asthma.

Juntti H. et al. *Serum concentrations of interferon-gamma and intercellular adhesion molecule-1 eight years after an early respiratory syncytial virus infection.* Clin Exp Allergy. 2005; 35(1) : 59-63.p **Abstract:** BACKGROUND: Respiratory syncytial virus (RSV) infection may influence the development of recurrent wheezing and atopy, but the mechanisms are unclear. OBJECTIVE: The purpose was to evaluate serum concentrations of soluble intercellular adhesion molecule-1 (sICAM-1), CD14, IgE, IL-5 and IFN-gamma in children 6-10 years after an RSV infection and their correlation with subsequent asthma and atopy. METHODS: Fifty-one subjects admitted to hospital for RSV infection during the first year of life and controls matched for birth date and sex underwent clinical examinations including lung function, skin prick and blood tests. RESULTS: The RSV subjects had significantly higher serum concentrations of IFN-gamma and sICAM-1 than the controls (for IFN-gamma 224.9 pg/mL (standard deviation (SD) 271.3) vs. 187.1 pg/mL (372.9), difference 37.8 pg/mL, 95% confidence interval (CI) -90.3 to 166.0, $P = 0.05$; for sICAM-1 170.2 ng/mL (SD 63) vs. 147.8 ng/mL (SD 57), difference 22.4 ng/mL, 95% CI -1.4 to 46.1, $P = 0.04$). The RSV subjects with asthma had significantly higher concentrations of IFN-gamma than the controls with asthma, and the RSV subjects with wheezing during the previous 12 months had significantly higher concentrations of both IFN-gamma and sICAM-1 than the controls with wheezing. CONCLUSIONS: Children hospitalized for RSV infection in infancy still differ in IFN-gamma and sICAM-1 production 6-10 years after the infection. The data suggest that the pathomechanism of asthma and wheezing after an

early RSV infection may be different from that of children without an early RSV infection.

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- Juntti H. et al.** *Association of an early respiratory syncytial virus infection and atopic allergy.* Allergy. 2003; 58(9) : 878-84.p **Abstract:** BACKGROUND: Respiratory syncytial virus (RSV) causes postbronchiolitic wheezing but its role in allergic sensitization is controversial. The purpose of the study was to examine the effect of an early RSV infection on allergic sensitization. METHODS: Seventy-six subjects were examined 6-10 years after hospitalization for RSV infection during the first year of life. Fifty-one subjects (68%) attended clinical studies and 25 filled in a questionnaire. The study protocol included lung function, skin-prick and blood tests. The controls were matched for birth date and sex. RESULTS: Eight per cent of the subjects and 37% of the controls had at least one positive skin-prick test (SPT) (difference -35%, 95% CI -50 to -19%, $P < 0.0001$). Allergic rhinitis, atopic dermatitis and asthma occurred as often in both groups, but asthma had been diagnosed significantly earlier in the subjects than in the controls [mean age 3.0 years (SD 2.6) and 5.6 years (SD 3.0), difference 2.6 years, 95% CI 0.57-4.65, $P = 0.014$]. In a logistic regression analysis, RSV infection was associated with negative SPTs. CONCLUSIONS: An early RSV infection results in reduction of SPT positivity but not of occurrence of atopic diseases. This finding might explain why there is less atopic sensitization in countries with a greater probability of acquiring RSV infection at an early age.
- Just J. et al.** *Clinical significance of bronchoalveolar eosinophils in childhood asthma.* J Allergy Clin Immunol. 2002; 110(1) : 42-4.p **Abstract:** To evaluate the relationship between clinical parameters and differential cell counts, bronchoalveolar lavage was performed in 79 asthmatic infants and children with unusual asthma. Multivariate analysis showed significant associations between (1) allergic asthma and the presence of alveolar eosinophils and (2) persistent and longer asthma and an increased number of alveolar neutrophils. Our results provide the first evidence that in asthmatic infants and children eosinophilic inflammation is related to allergic sensitization.
- Just J. et al.** *Short-term health effects of particulate and photochemical air pollution in asthmatic children.* Eur Respir J. 2002; 20(4) : 899-906.p **Abstract:** In a previous panel study in Paris, France, detrimental effects of moderately high levels of winter air pollution on the symptoms and lung function of asthmatic children were demonstrated. A new study was conducted, with the aim of assessing the short-term effects of photo-oxidant and particulate air pollution on childhood asthma during spring and early summer in Paris. Eighty-two medically diagnosed asthmatic children were followed up for 3 months. Outcomes included the incidence and prevalence of asthma attacks, nocturnal cough, supplementary use of beta2-agonists, symptoms of airway irritation, and peak expiratory flow (PEF) value and its variability. The statistical methods controlled for the lack of independence between daily health outcomes, temporal trends and pollen and weather conditions. Black smoke and nitrogen dioxide (NO₂) were associated with increases in the occurrence of nocturnal cough and respiratory infections. Ozone (O₃) was associated with an increase in the occurrence of asthma attacks and respiratory infections and with changes in lung function, as shown by an increase in PEF variability and a decrease in PEF. Statistically significant interactions were demonstrated between O₃ and temperature and between O₃ and pollen count for asthma attacks. O₃ levels had a greater effect on additional bronchodilator use and on irritations of the eyes, nose and throat on days on which no steroids were used. Particulate matter was associated with eye irritation only. This study showed that, although within international air quality standards, the prevailing levels of photo-oxidant and particulate pollution in spring and early summer had measurable short-term effects on children with mild-to-moderate asthma.
- Kabesch M.** *Candidate genes and the genetic epidemiology of asthma.* Paediatr Respir Rev. 2004; 5 Suppl A : S23-5.p
- Kabesch M. et al.** *Glutathione S transferase deficiency and passive smoking increase childhood asthma.* Thorax. 2004; 59(7) : 569-73.p **Abstract:** BACKGROUND: It has been suggested that the genetically determined deficiency of glutathione S transferase (GST) enzymes involved in the detoxification of environmental tobacco smoke (ETS) components may contribute to the development of asthma. METHODS: A large population of German schoolchildren (n = 3054) was genotyped for deficiencies of the GST isoforms M1 and T1. The association between GSTM1 and GSTT1 genotypes and asthma as well as atopy was investigated with respect to current and in utero ETS exposure. RESULTS: In children lacking the GSTM1 allele who were exposed to current ETS the risk for current asthma (OR 5.5, 95% CI 1.6 to 18.6) and asthma symptoms such as wheeze ever (OR 2.8, 95% CI 1.3 to 6.0), current wheezing (OR 4.7, 95% CI 1.8 to 12.6) and shortness of breath (OR 8.9, 95% CI 2.1 to 38.4) was higher than in GSTM1 positive individuals without ETS exposure. Hints of an interaction between ETS exposure and GSTM1 deficiency were identified. In utero smoke exposure in GSTT1 deficient children was associated with significant decrements in lung function compared with GSTT1 positive children not exposed to ETS. CONCLUSIONS: GSTM1 and GSTT1 deficiency may increase the adverse health effects of in utero and current smoke exposure.
- Kabesch M. et al.** *IL-4/IL-13 pathway genetics strongly influence serum IgE levels and childhood asthma.* J Allergy Clin Immunol. 2006; 117(2) : 269-74.p **Abstract:** BACKGROUND: IgE production, a hallmark of asthma and atopic disease, may be under genetic control. Genes of the IL-4 and IL-13 pathway, central for IgE regulation, have so far only been assessed in studies of single gene effects. OBJECTIVE: Here we analyzed combined extended haplotypes involving IL-4, IL-13, their shared receptor chain IL-4Ralpha, and the intracellular signal transducer and activator of transcription, STAT6, to assess the combined effect of single nucleotide polymorphisms in this important immunological signaling pathway. METHODS: We genotyped a large cross-sectional population of 1120 children age 9 to 11 years for 18 polymorphisms in the respective genes of the IL-4/IL-13 pathway. One polymorphism per gene was selected because of its putative functional role, and extended haplotypes were built in a stepwise procedure where gene-by-gene interactions were assessed by using a Cordell model. RESULTS: Combining polymorphisms in all 4 major pathway genes in a stepwise procedure, the risk for high serum IgE levels increased 10.8-fold ($P = .02$) and the risk for the development of asthma increased by a factor of 16.8-fold ($P = .005$) compared with the maximum effect of any single polymorphism. Significant interactions in a model with additive and dominant effects, for both pair and triplet combinations for asthma (lowest $P = .005$), and for pairs of polymorphisms in IgE regulation were observed (lowest $P = .054$). CONCLUSION: These data indicate that only the combined analyses of genetic alterations in the IL-4/IL-13 pathway reveal its actual significance to the development of atopy and childhood asthma.
- Kabesch M. et al.** *A complete screening of the IL4 gene: novel polymorphisms and their association with asthma and IgE in childhood.* J Allergy Clin Immunol. 2003; 112(5) : 893-8.p **Abstract:** BACKGROUND: IL-4, a cytokine with immunomodulatory functions, is involved in the upregulation of IgE production characteristic of asthma and allergy. Thus far, 2 single nucleotide polymorphisms (SNPs) in the promoter (C-589T) and 5' untranslated region (C-33T) of the IL4 gene have been identified.

Polymorphism C-589T was reported to influence total serum IgE levels and bronchial hyperresponsiveness. However, no study has investigated the putative existence of further SNPs in exons, introns, and flanking regions of the IL4 gene. **OBJECTIVE:** A complete screening of the IL4 gene and its flanking regions for new polymorphisms was performed. Large-scale association studies in 1120 German schoolchildren were conducted to determine the effect of all polymorphisms present in the IL4 gene on the phenotypic expression of atopic diseases. **METHODS:** Denaturing HPLC and standard sequencing techniques were performed to detect novel polymorphisms in 33 unrelated subjects unselected for atopic diseases. Linkage disequilibrium was assessed for all polymorphisms in the IL4 gene, and association studies were performed. **RESULTS:** A total of 16 polymorphisms were identified in the IL4 gene, 14 of which were not reported previously. The pattern of linkage disequilibrium observed in IL4 could not be explained by physical distance. A significant association between a cluster of polymorphisms in strong linkage disequilibrium with each other and a physician's diagnosis of asthma and total serum IgE levels was found. **CONCLUSION:** These results indicate a possible involvement of SNPs in the IL4 gene in the development of asthma and the regulation of total serum IgE.

Kable S. et al. *Are the components of the Asthma Management Plan important in managing childhood asthma? A survey of general practitioners.* Aust Fam Physician. 2003; 32(6) : 470-2, 480.p **Abstract:** **AIM:** To gauge the importance and relevance placed by general practitioners on components of the National Asthma Campaign's 'Six step' Asthma Management Plan for childhood asthma. **METHOD:** A cross sectional postal survey of a national randomised sample of 824 GPs. **RESULTS:** Each component was considered to be 'quite' or 'very' important by at least 70% of respondents. All 11 components were rated to be either 'quite' or 'very' important by 44%, and 91% of respondents considered eight or more of the components to be 'quite' or 'very' important. Two characteristics were consistently associated with the rating of importance: gender, (women GPs generally showing higher ratings), and reported frequency of use of the Asthma Management Plan (frequent users rate importance more frequently). **CONCLUSION:** There were high levels of endorsement of the Asthma Management Plan for children with asthma.

Kabra S.K. et al. *Childhood asthma--a challenge to pediatricians.* Indian J Pediatr. 2001; 68 Suppl 4 : S1-2.p

Kahan E. et al. *Exclusion of ill children from child-care centers in Israel.* Patient Educ Couns. 2005; 56(1) : 93-7.p **Abstract:** The aim of the study was to examine criteria for ill children in child-care centers. A questionnaire on practices of exclusion/return of children according to specific signs and symptoms was mailed to the directors of care centers in central Israel. Thirty-six of the 60 questionnaires (60%) were returned by mail and the reminded were completed in personal visits to the CCCs achieving a response rate of 100%. About half (51.7%) used "common sense" and "personal feelings" to exclude children and to allow their return, and 29 (48.3%) used the guidelines of the Ministries of Education and Health or other authorities. The percentage of centers excluding children by signs/symptoms was as follows: high fever (>38 degrees C), 100%; low-grade fever, 76.7%; asthma exacerbation, 80.0%; heavy cough, 75.0%; eye discharge or conjunctivitis, 83.3%; diarrhea and vomiting more than twice per day, 100%; rash, 72.3%; otalgia, 46.7%; and infected skin lesion, 66.7%. Only four centers excluded children with head lice. Most centers required a physician's note on return of a child after high fever (76.7%), eye discharge or conjunctivitis (48.3%), and from 75 to 80%, respectively, for frequent vomiting and bloody or mucinous diarrhea. The results show that exclusion practices among child-care centers (CCCs) vary widely, suggesting the need for the establishment of a uniform exclusion and return policy in Israel, with distribution of clear, up-to-date guidelines on the prevention and

control of communicable diseases to all day-care centers. In a simple way, this study identified attitudes concerning the exclusion/return of sick children in CCCs and was useful for the discussion of the related policy with CCCs responsible and national health and educational authorities.

Kalpakioglu A.F. et al. *Evaluation and impact of chronic cough: comparison of specific vs generic quality-of-life questionnaires.* Ann Allergy Asthma Immunol. 2005; 94(5) : 581-5.p **Abstract:** **BACKGROUND:** Chronic cough is a common condition that has a significant impact on health-related quality of life (HRQoL). **OBJECTIVE:** To investigate whether chronic cough is associated with adverse psychological and physical effects on quality of life (QoL) using different HRQoL questionnaires. **METHODS:** Forty patients were recruited for the study. The diagnostic workup was mainly based on the pathogenic triad in chronic cough: postnasal drip syndrome, asthma, and gastroesophageal reflux disease. The HRQoL was evaluated with the cough-specific quality-of-life questionnaire (CQLQ), Leicester Cough Questionnaire (LCQ), Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), and Hospital Anxiety and Depression Scale. **RESULTS:** Symptom scores were significantly correlated with the CQLQ and LCQ (beta = .415 and beta = -.272, respectively) but not with the SF-36. A statistically significant difference was found in all questionnaires, except the physical component summary domain of the SF-36, after specific therapy. Correlation between the 2 specific HRQoL questionnaires was moderate to high when pretreatment and posttreatment scores were compared (r = -0.42 and r = -0.60). Concurrent validity of the LCQ was higher than the CQLQ when compared with the SF-36 domains. The effect size of each specific QoL questionnaire was 1 or higher after treatment, whereas it was much less in the SF-36. There was no change in depression with treatment despite anxiety. Posttreatment symptom scores were related with anxiety (r > 0.40) **CONCLUSIONS:** Because HRQoL is important to patients, a cough-specific HRQoL instrument, either the CQLQ or LCQ, should be routinely used to optimally evaluate the impact of cough on patients and to evaluate the efficacy of cough-modifying agents.

Kalra M. et al. *Asthma as a risk factor for respiratory complications after adenotonsillectomy in children with obstructive breathing during sleep.* Ann Allergy Asthma Immunol. 2005; 94(5) : 549-52.p **Abstract:** **BACKGROUND:** Children with asthma are at increased risk for obstructive breathing during sleep. Adenotonsillectomy, the treatment of choice for obstructive breathing during sleep, is associated with significant postoperative respiratory morbidity. **OBJECTIVE:** To determine whether asthma is a risk factor for respiratory complications after adenotonsillectomy in children with obstructive breathing during sleep. **METHODS:** This case-control study compared 115 children aged 3 to 18 years with respiratory complications after adenotonsillectomy (study group) with 115 children without respiratory complications after adenotonsillectomy (control group). **RESULTS:** The postoperative respiratory complications ranged from oxygen desaturation to respiratory failure that required mechanical ventilation. The study group had a higher proportion of children with asthma (P < .01). Logistic regression analysis showed that asthma increases the odds of postoperative respiratory complications to 4.4 (95% confidence interval, 2.13-9.0), after controlling for age, weight greater than the 97th percentile for age, sex, race, and medical conditions other than asthma. **CONCLUSIONS:** In children with obstructive breathing during sleep, the presence of asthma is associated with an increased risk of respiratory complications after adenotonsillectomy.

Kamps A.W. et al. *Determinants of correct inhalation technique in children attending a hospital-based asthma clinic.* Acta Paediatr. 2002; 91(2) : 159-63.p **Abstract:** Many children with asthma use their inhaler device incorrectly even after comprehensive inhalation instruction. The aim of this study was to identify factors associated

with correct inhalation technique. Two hundred children with asthma demonstrated their inhalation technique. Patient characteristics and the components of inhalation instructions they had received were compared for children demonstrating a correct or incorrect inhalation technique. In addition, the inhalation technique of 47 newly referred patients was followed-up prospectively after repeated comprehensive instruction sessions. Seventy-eight percent of all patients demonstrated a correct inhalation technique. Patients who had received repeated instruction sessions and patients who had previously been asked to demonstrate the use of their inhaler during an instruction session were more likely than other children to demonstrate a correct inhalation technique ($p < 0.001$ and $p = 0.03$, respectively). Multiple logistic regression analysis showed that repetition of instructions was significantly associated with a correct inhalation technique (odds ratio (OR) 8.2, 95% CI 3.2-21.5; $p < 0.0001$) irrespective of type of inhaler used. Demonstration of the inhaler use by the patient was significantly associated with a correct inhalation technique for patients using a metered dose inhaler plus spacer device (OR 3.5, 95% CI 1.0-12.6; $p = 0.05$), but not for patients using a dry powder inhaler (OR 1.6, 95% CI 0.4-6.4; $p = 0.54$). The number of newly referred patients demonstrating a correct inhalation technique improved from 57.4% to 97.9% after three comprehensive instruction sessions. **CONCLUSION:** Inhalation instruction should be given repeatedly to achieve and maintain correct inhalation technique in asthmatic children.

Kanceljak-Macan B. et al. *The 3 mm skin prick test (SPT) threshold criterion is not reliable for Tyrophagus putrescentiae: the re-evaluation of SPT criterion to dust mites.* Allergy. 2002; 57(12) : 1187-90.p **Abstract:** BACKGROUND: The mean wheal diameter ≥ 3 mm is the usual criterion for positive skin prick test (SPT) reaction to dust mites. The study assessed the accuracy of this SPT criterion with respect to specific IgE values of above 0.35 kUAl (+sIgE). METHODS: Specific IgE (ImmunoCAP, Pharmacia AB Diagnostics, Uppsala, Sweden) and standard SPT to Dermatophagoides pteronyssinus (DP) and farinae (DF), Lepidoglyphus destructor (LD) and Tyrophagus putrescentiae (TP) (ALK, Horsholm, Denmark) were performed in a random sample of 457 subjects, of whom 273 men (mean age 35.3 +/- 11.0 years) and 184 women (mean age 37.9 +/- 9.5 years). Statistical analysis was performed using the chi-square test, regression analysis and discriminant analysis. RESULTS: When the mean wheal diameter of ≥ 3 mm was considered positive (+ SPT), the correlation between + SPT and + sIgE was 0.47 for DP ($P < 0.001$), 0.43 for DF ($P = 0.004$), 0.35 for LD ($P = 0.03$) and 0.37 for TP ($P = 0.014$). Regarding + sIgE, this SPT criterion has a specificity of 92.2% for DP, 82.3% for DF, 80.8% for LD and 70.1% for TP. When the value 4.5 mm was taken as the threshold for the positive SPT reaction to TP, specificity increased significantly from 70.1% to 86.4% ($\chi^2 = 32.04$, $P < 0.001$). **CONCLUSIONS:** The 3 mm SPT threshold criterion is not reliable in evaluating sensitization to TP due to an insufficient specificity of the allergen extract to this mite. It is advisable either to re-evaluate the TP allergen extract or change the threshold criterion for positive SPT reaction to TP.

Kandil A.A. et al. *Eosinophil cationic protein as a diagnostic marker for asthmatic children treated by immunotherapy.* Egypt J Immunol. 2003; 10(1) : 67-76.p **Abstract:** We estimated the eosinophil cationic protein (ECP) levels in serum and sputum of 20 children with bronchial asthma to find whether it correlates with disease activity and examine the effect of immunotherapy. Ten-age- and sex-matched healthy children were also included. Children were subjected to full history, clinical examination and investigation including skin prick test, chest x-ray, complete blood count, and estimation of eosinophil cationic protein. In addition, examination of sputum to determine the eosinophil count and eosinophil cationic protein level was carried out. Patients were classified into 2 groups (10 patients each) according to the line of treatment used (5 mild and 5 moderate in severity). Group I received pharmacotherapy only and

was followed for one year, while group II, received pharmacotherapy plus immunotherapy for one year. A significant increase in eosinophil count and ECP of blood and sputum was found in asthmatic patients as compared to controls. The ECP levels were significantly higher in moderate cases when compared with mild cases. On comparing levels of both eosinophil count and ECP in peripheral blood and sputum, before and one year after treatment, there was a significant reduction after therapy among the two groups of patients. The reduction was significant in group II. On the other hand there was a significant decrease in both symptoms and medication scores after one year of therapy. In conclusion, ECP may be a marker of eosinophilic activity and degranulation that correlates with the severity of bronchial asthma. Immunotherapy may be a good adjuvant therapy for atopic bronchial asthma of childhood.

Kang H. et al. *Maximal airway response to methacholine in cough-variant asthma: comparison with classic asthma and its relationship to peak expiratory flow variability.* Chest. 2005; 128(6) : 3881-7.p **Abstract:** BACKGROUND: In asthmatic subjects, not only airway sensitivity but maximal airway response are increased on the dose-response curve to methacholine, and peak expiratory flow (PEF) variability is closely related to airway hypersensitivity and maximal airway response. OBJECTIVE: The aims of this study were to compare the prevalence and the level of maximal response plateau between patients with cough-variant asthma (CVA) and those with classic asthma (CA), and to examine the relationship between airway hypersensitivity or maximal airway response and PEF variability in patients with CVA. METHODS: A high-dose methacholine inhalation test was performed on 83 patients with CVA and on 83 patients with CA matched for provocative concentration of methacholine causing a 20% fall in FEV1 (PC20). PEF was recorded in the morning and evening for 14 consecutive days in 78 CVA patients, and the amplitude percentage mean was used to express the diurnal PEF variation. RESULTS: Fifty-two CVA subjects (62.7%) but only 33 CA subjects (39.8%) showed a maximal response plateau. This difference was significant after correction by the Bonferroni method (corrected $p = 0.024$). Subjects in the CVA and CA groups showing a plateau had significantly different plateau levels (38.0 +/- 5.9% vs 42.9 +/- 3.9%, corrected $p = 1.0 \times 10^{-4}$). In patients with CVA, no significant relationship was found between PC20 and PEF variability. However, the absence of a maximal response plateau and a higher plateau level were associated with increased PEF variability. **CONCLUSIONS:** Maximal airway response may be an important confounder in the relationship between airway hypersensitivity and the clinical expression of asthma. The identification of a maximal response plateau and the level of this plateau in patients with CVA provide information relevant to PEF variability.

Kannisto S. et al. *Serum dehydroepiandrosterone sulfate concentration as an indicator of adrenocortical suppression in asthmatic children treated with inhaled steroids.* J Clin Endocrinol Metab. 2001; 86(10) : 4908-12.p **Abstract:** ACTH regulates adrenal androgen production, which may thus be reduced during glucocorticosteroid therapy. Dehydroepiandrosterone sulfate is the most abundant androgen secreted by the adrenals. We wished to evaluate whether serum levels of dehydroepiandrosterone sulfate can be used as an indicator of adrenal suppression during inhaled steroid treatment in children. Sixty school-aged children with newly diagnosed asthma were randomly divided into budesonide ($n = 30$) and fluticasone propionate ($n = 30$) groups. Fifteen cromone-treated children served as a control group. The budesonide dose was 800 microg/d during the first 2 months and 400 microg/d thereafter. The respective fluticasone propionate doses were 500 and 200 microg/d. Serum dehydroepiandrosterone sulfate concentrations were measured before and after 2 and 4 months of treatment. In the budesonide group, serum dehydroepiandrosterone sulfate decreased from the baseline by a mean of 21% (95% confidence interval, 13-29%; $P < 0.001$) after 2 months of high dose treatment and by 16% (95% confidence

interval, 8-25%; $P < 0.001$) after 4 months of treatment. In the fluticasone propionate group, the respective figures were 10% (95% confidence interval, 4-16%; $P < 0.01$) and 6% (95% confidence interval, 16% decrease-3% increase; $P = \text{NS}$). A low dose ACTH test indicated adrenocortical suppression at 4 months in 14 (23%) steroid-treated children. In these children, dehydroepiandrosterone sulfate decreased by a mean of 21% (95% confidence interval, 14-28%), whereas in those 46 steroid-treated children with normal ACTH test results, dehydroepiandrosterone sulfate decreased by 8% (95% confidence interval, 0-16%; $P < 0.05$ between these groups). In the control group, dehydroepiandrosterone sulfate levels tended to increase (by a mean of 26%), reflecting the normal physiological change at this age. In conclusion, inhaled steroid treatment suppresses dehydroepiandrosterone sulfate production in a dose-dependent manner. Monitoring of serum dehydroepiandrosterone sulfate concentrations can be used as a practical method to follow adrenocortical function and to detect its suppression during inhaled steroid treatment in children.

Kaplan A.P. *A new mechanism for immunologic initiation of asthma.* Proc Natl Acad Sci U S A. 2005; 102(5) : 1267-8.p

Karadag B. et al. *Does passive smoke exposure trigger acute asthma attack in children?* Allergol Immunopathol (Madr). 2003; 31(6) : 318-23.p **Abstract:** The relationship between asthma and passive smoking has been well established. However, it is still not clear whether an acute asthma attack can be induced by acute smoke exposure. The specific aims of this study were: 1- To assess the degree of smoke exposure through urinary cotinine levels in asthmatic children during and 4 weeks after asthma attacks and, 2- To evaluate the reliability of parental questionnaires in asthmatic children by comparing the data obtained from cotinine measurements and parental reports. Thirty-two consecutive asthmatic children who were admitted to the emergency clinic were included in the study. Parents were asked to complete a questionnaire about their smoking habits and housing conditions. Urinary cotinine and creatinine levels were measured in children during and 4 weeks after the acute asthma attack. The mean age of the patients was 5.7 +/- 3.2 years. The mean attack rate was 3.5 +/- 3.8 per year. Thirty-eight percent of the patients were taking no preventive treatment. In 80 % of patients, urinary cotinine and creatinine ratios (CCR) were significantly above the non-exposed, non-smoker levels. However, CCR levels during acute asthma attacks were not higher than those measured 4 weeks after the acute attack (314.6 +/- 299.1 vs. 203.8 +/- 165.2 ng/mg respectively, $p > 0.05$). Although parental reports of passive smoke exposure was 71 %, CCR levels revealed that 81 % and 97 % of children were exposed to passive smoke during acute attacks and asymptomatic periods, respectively. In conclusion, although the proportion of children with acute asthma attacks who were exposed to passive smoking was high, the degree of passive smoke exposure was not higher during acute attacks. Parental questionnaires were found to be unreliable in reporting passive smoke exposure in asthmatic children during acute attacks.

Karmaus W. et al. *Does maternal immunoglobulin E decrease with increasing order of live offspring? Investigation into maternal immune tolerance.* Clin Exp Allergy. 2004; 34(6) : 853-9.p **Abstract:** **BACKGROUND:** Identifying the protective effect of a higher number of siblings is a significant finding in understanding the aetiology of allergic sensitization, asthma, eczema, and hayfever. Knowledge about causes behind the sibling effect may allow us to prevent atopic manifestations. **OBJECTIVE:** We tested the hypothesis that rising order of live offspring increases maternal immune tolerance (immune non-reactivity) against allergens. To this end, we investigated whether maternal IgE levels are associated with the number of live offspring. **METHODS:** In a cohort of 1456 newborns recruited between January 1989 and February 1990 on the Isle of Wight, UK, we determined maternal and cord serum IgE, and the order of live offspring. The data were analysed by means of

linear and path analysis. **RESULTS:** Maternal and cord serum IgE were available in 820 mother-infant pairs with birth order information. We found that the number of live offspring significantly reduces maternal IgE. The decline was more prominent in mothers with atopy ($n=268$). The geometric means of IgE after the first, second, and third or higher delivery were 74.4, 66.6, and 43.0 kU/L, respectively. Findings of path analysis suggest a significant direct effect of birth order on maternal IgE, but no direct effect of birth order on cord serum IgE. **CONCLUSION:** The findings support that maternal immune tolerance against allergens may increase with increasing order of live offspring and thus pass on a lower risk of developing atopy in children of higher birth order.

Karmaus W. et al. *Atopic manifestations, breast-feeding protection and the adverse effect of DDE.* Paediatr Perinat Epidemiol. 2003; 17(2) : 212-20.p **Abstract:** Despite the numerous studies on the possible protective effect of breast feeding against the onset of atopic manifestations during childhood, this issue remains controversial. As part of an environmental epidemiological study, we investigated whether different blood concentrations of dichlorodiphenyl-dichloroethylene (DDE) modified the protective effect of breast feeding against atopic manifestations in 338 children. DDE concentration, duration of breast feeding and manifestation of atopic disorders were measured in 1994-95 at age 7-8 years. Information gathered on asthma, atopic eczema and hay fever was based on questionnaire data. We measured the total serum concentration of immunoglobulin E (IgE) and specific IgE levels against inhalant allergens. In 1997, we also determined bronchial hyper-reactivity with a hypertonic saline challenge test. To estimate odds ratios from our cross-sectional analysis, we applied logistic regressions, controlling for confounders. Breast feeding had a protective effect on the two asthma variables (e.g. > 12 weeks breast feeding for doctor-diagnosed asthma, OR = 0.32 [95% CI 0.11, 0.87]; for 'ever' asthma, OR = 0.13 [95% CI 0.02, 0.68]), but not on bronchial hyper-reactivity, hay fever, atopic eczema or the two IgE variables. The protective effect became stronger in children with DDE blood levels below the median of 0.29 micro g/L (e.g. doctor-diagnosed asthma, > 12 weeks breast feeding, OR = 0.24 [95% CI 0.06, 0.95]). Also, for specific IgE against inhalant allergens, the association gained statistical significance. For children with a DDE concentration of 0.29 micro g/L and higher, breast feeding did not show a significant protective effect. Our results suggest that contaminants such as DDE may modify the protective effect and may have contributed to inconsistent findings on the protective effect of breast feeding in previous studies. We recommend determining levels of breast milk contaminants in children when assessing the impact of breast feeding on atopic manifestations.

Karmaus W. et al. *Consumption of milk fat and reduced asthma risk in pre-school children.* Thorax. 2004; 59(8) : 725; author reply 725-6.p

Karmaus W. et al. *Infections and atopic disorders in childhood and organochlorine exposure.* Arch Environ Health. 2001; 56(6) : 485-92.p **Abstract:** The authors investigated whether organochlorine exposure is associated with prevalence of otitis media, pneumonia, pertussis, asthma, and increased immunoglobulin E levels in children. Organochlorine concentrations and histories of infection and atopic manifestation were available for 343 children, and immunoglobulin E levels were available for 340 children. The authors applied logistic and linear regressions and controlled for confounders. In general, the prevalence of infections in children was not related to organochlorine exposure. However, for the combined effect of dichlorodiphenyldichloroethene with polychlorinated biphenyls or hexachlorobenzene, a significantly increased relative risk (odds ratios = 3.70 and 2.38, respectively) was found for otitis media. Exposure to dichlorodiphenyldichloroethene resulted in a significantly higher odds ratio for asthma (odds ratio = 3.71; 95% confidence interval = 1.10, 12.56) and in immunoglobulin E

concentrations above 200 kU/l (odds ratio = 2.28; 95% confidence interval = 1.20, 4.31). This is the first study in which dichlorodiphenyldichloroethene has been identified as a substantial risk factor for asthma and for increased immunoglobulin E blood levels.

Karpati A.M. et al. *Pesticide spraying for West Nile virus control and emergency department asthma visits in New York City, 2000.* Environ Health Perspect. 2004; 112(11) : 1183-7.p **Abstract:** Pyrethroid pesticides were applied via ground spraying to residential neighborhoods in New York City during July-September 2000 to control mosquito vectors of West Nile virus (WNV). Case reports link pyrethroid exposure to asthma exacerbations, but population-level effects on asthma from large-scale mosquito control programs have not been assessed. We conducted this analysis to determine whether widespread urban pyrethroid pesticide use was associated with increased rates of emergency department (ED) visits for asthma. We recorded the dates and locations of pyrethroid spraying during the 2000 WNV season in New York City and tabulated all ED visits for asthma to public hospitals from October 1999 through November 2000 by date and ZIP code of patients' residences. The association between pesticide application and asthma-related emergency visits was evaluated across date and ZIP code, adjusting for season, day of week, and daily temperature, precipitation, particulate, and ozone levels. There were 62,827 ED visits for asthma during the 14-month study period, across 162 ZIP codes. The number of asthma visits was similar in the 3-day periods before and after spraying (510 vs. 501, $p = 0.78$). In multivariate analyses, daily rates of asthma visits were not associated with pesticide spraying (rate ratio = 0.92; 95% confidence interval, 0.80-1.07). Secondary analyses among children and for chronic obstructive pulmonary disease yielded similar null results. This analysis shows that spraying pyrethroids for WNV control in New York City was not followed by population-level increases in public hospital ED visit rates for asthma.

Karr C. *Bronchiolitis poses significant public health burden.* *Pediatr Ann.* 2004; 33(7) : 454-9.p **Abstract:** Bronchiolitis is the leading cause of infant morbidity, and hospitalization rates are rising. The effect of this disease is not limited to the acute illness episode. Approximately 40% to 50% of children diagnosed with bronchiolitis suffer from subsequent wheezing and airway reactivity or asthma. Attempts to address the burden of this disease via vaccine development have been largely unsuccessful, and treatment is purely supportive rather than curative. As such, primary prevention is paramount. If outdoor air pollution exacerbates this disease, as has been found for other pediatric respiratory diseases, actions to ensure that regulatory standards protect this vulnerable population will be paramount. Increased anatomic and physiologic susceptibility to the pro-inflammatory effects of air pollutants, coupled with the pro-inflammatory response in bronchiolitis, underlies the concern that infants exposed to higher levels of ambient air pollutants may be at increased risk for developing more severe bronchiolitis requiring hospitalization.

Kashiwabara K. et al. *Airborne water droplets in mist or fog may affect nocturnal attacks in asthmatic children.* *J Asthma.* 2003; 40(4) : 405-11.p **Abstract:** Our study objectives were to evaluate whether or not airborne water droplets in mist or fog affect the occurrence of nocturnal attacks of asthmatic children using a retrospective study. This study included 971 visits by children with bronchial asthma to the emergency department at nighttime (from 18:00 to 09:00) during a 3-year period (April 1, 1998-March 31, 2001). Meteorological data were checked at a local fire station and regional meteorological observatory. We divided nighttime into five 3-hour periods to evaluate the relationship between chronological changes in the frequency of the emergency department visits of asthmatic children and of meteorological conditions. In four of five periods of nighttime, multivariate analysis showed that mist or fog, average

atmospheric temperature, and barometric pressure were related to the number of emergency department visits ($n=1096$, $r=0.165$ - 0.263 , $p<0.0001$). We divided the year into four seasons to eliminate differences between atmospheric temperature and barometric pressure on clear nights and on misty or foggy nights; we also found the mean number of emergency department visits was higher on misty or foggy nights than on clear nights in each seasonal period ($p<0.01$). In addition, average atmospheric temperature on misty or foggy nights with the emergency department visits was higher than that on misty or foggy nights without any visits ($p<0.01$). Asthmatic children frequently visited the emergency department on misty or foggy nights, especially during midnight to dawn periods with high atmospheric temperature. Because a higher atmospheric temperature on misty or foggy nights indicates a larger saturated amount of airborne water droplets, our results suggest that mist and fog, in particular a saturated amount of airborne water droplets, may be a stimulus for bronchoconstriction.

Kashiwabara K. et al. *High frequency of emergency room visits of asthmatic children on misty or foggy nights.* *J Asthma.* 2002; 39(8) : 711-7.p **Abstract:** **STUDY OBJECTIVES:** To examine whether or not the presence of mist or fog affects respiratory conditions in asthmatic children. **DESIGN:** A retrospective study. **PREPARATION AND METHODS:** There were 754 visits by children with asthma to the emergency room at night (between 18:00 p.m. and 9:00 a.m.) during a two-year period. Meteorological data were checked at a local fire station and regional meteorological observatory. We evaluated the relation between meteorological data and the number of emergency room visits of asthmatic children. **RESULTS:** The mean number of asthmatic children who visited the emergency room was higher on misty or foggy nights than on clear nights (1.2 +/- 1.2 people/night vs. 0.8 +/- 0.9 people/night, $p<0.0001$). Mist and fog had an increased odds ratio (OR) of emergency room visits of asthmatic children (1.74, $p<0.001$). In addition, increased OR was found for high atmospheric temperature (4.39, $p<0.0001$). Multivariate analysis showed mist and fog ($p<0.0001$), average atmospheric temperature ($p<0.0001$), and day-to-day change of temperature ($p<0.05$) were related to the number of asthmatic children ($n=731$, $r=0.428$, $p<0.0001$). **CONCLUSIONS:** Our results suggest that the presence of mist and fog causes the exacerbation of asthma in children. It is not clear which is related to the high frequency of emergency room visits of asthmatic children, airborne water droplets or the meteorological condition that causes mist or fog, but the prophylaxis for exacerbation may decrease the frequency of emergency room visits.

Kasper L. et al. *Prevalence of asthma with aspirin hypersensitivity in the adult population of Poland.* *Allergy.* 2003; 58(10) : 1064-6.p **Abstract:** **BACKGROUND:** Acetylsalicylic acid (ASA) and other nonsteroid anti-inflammatory drugs (NSAIDs) are reported to account for 21-25% of all adverse drug reactions. Some asthmatics may react to ASA and other NSAIDs with acute bronchoconstriction, profuse rhinorrhea and skin flushing. This is a distinct clinical syndrome called aspirin-induced asthma (AIA). The prevalence of AIA among asthmatic patients in Poland has not been previously assessed. **METHODS:** A questionnaire survey of 12,970 adults of both sexes, randomly selected from the population of Poland. **RESULTS:** The prevalence of AIA in the general population of Poland was estimated as 0.6%. Thirty patients (4.3%; 95% CI: 2.8-5.8) of 703 asthmatics (5.4% of general population) reported symptoms attesting to hypersensitivity to aspirin. In 27% of them the reactions were precipitated by aspirin, whereas in the remaining subjects by other NSAIDs. **CONCLUSIONS:** The prevalence of AIA in Poland is 4.3%, being somewhat lower than in Finland and Australia, where it was recently reported to account for 8.8 and 10.9% of the adult asthmatics, respectively. These figures indicate that aspirin hypersensitivity might be a significant community problem.

- Kassif Y. et al.** *The course of epiphora after failure of silicone intubation for congenital nasolacrimal duct obstruction.* Graefes Arch Clin Exp Ophthalmol. 2005; 243(8) : 758-62.p **Abstract:** BACKGROUND: One of the indications for dacryocystorhinostomy (DCR) in children with congenital nasolacrimal duct obstruction (CNLDO) is failure of silicone intubation. We evaluated the course of epiphora after failure of silicone intubation for CNLDO when DCR was not performed. METHODS: In a comparative cohort study carried out at a tertiary referral center, ten eyes of seven consecutive children who had failure of silicone intubation manifested as persistent epiphora over 2 months and whose parents refused DCR were followed up for an average of 50.4 months (range 33-70 months). Three lacrimal drainage systems of three other children who had failure of silicone intubation underwent uneventful DCR. RESULTS: In eight (80%) of the ten consecutive eyes with congenital nasolacrimal duct obstruction (six of the seven children, 86%), there was spontaneous complete resolution of the epiphora and normal dye disappearance test (DDT) at the end of the follow-up period. One child with Down's syndrome, allergic rhinitis, asthma and multiple site obstructions had improvement of symptoms but abnormal DDT. The epiphora in all three children who underwent DCR had disappeared by 6 months after surgery when the silicone tube was removed. No complications were noted during the follow-up. CONCLUSIONS: Epiphora can spontaneously resolve after failure of silicone intubation in CNLDO, and DCR should no longer considered be compulsory in such cases unless complications evolve.
- Kato A. et al.** *Association of SPINK5 gene polymorphisms with atopic dermatitis in the Japanese population.* Br J Dermatol. 2003; 148(4) : 665-9.p **Abstract:** BACKGROUND: Netherton's syndrome (NS) is an autosomal recessive disorder characterized by trichorrhexis invaginata ('bamboo hair'), congenital ichthyosiform erythroderma and an atopic diathesis. NS has recently been shown to be due to a defect in the SPINK5 gene, encoding LEKTI, a 15-domain serine protease inhibitor. SPINK5 maps to chromosome 5q31-q32, and has been suggested to be a locus predisposing to atopy in general. Recently, coding polymorphisms in SPINK5 exons 13 and 14 have been reported to be associated with atopy, asthma and atopic dermatitis (AD). OBJECTIVES: To examine whether these polymorphisms are also associated with AD in Japan. METHODS: We characterized eight polymorphisms in SPINK5 exons 13 and 14 in 124 Japanese patients with AD and 110 healthy controls. The polymorphisms we examined were IVS12-26C-->T, IVS12-10A-->G, 1103A-->G (Asn368Ser, in exon 13), 1156G-->A (Asp386Asn, in exon 13), 1188T-->C (His396His, in exon 13), IVS13-50G-->A, 1258G-->A (Glu420Lys, in exon 14) and IVS14+19G-->A. RESULTS: We found significant associations between seven of these polymorphisms and AD in Japanese patients. CONCLUSIONS: This study confirms the previous suggestion of an association between SPINK5 and AD.
- Kattan M. et al.** *Cost-effectiveness of a home-based environmental intervention for inner-city children with asthma.* J Allergy Clin Immunol. 2005; 116(5) : 1058-63.p **Abstract:** BACKGROUND: Exposure to indoor allergens contributes to increased asthma morbidity. The Inner-City Asthma Study, a randomized trial involving home environmental allergen and irritant remediation among children aged 6 through 11 years with moderate-to-severe asthma, successfully reduced asthma symptoms. A cost-effectiveness analysis can help stakeholders to evaluate the potential costs and benefits of adopting such a program. OBJECTIVE: We sought to assess the cost-effectiveness of the environmental intervention of the Inner-City Asthma Study. METHODS: Incremental cost-effectiveness ratios for a 2-year study period were calculated. Health outcome was measured as symptom-free days. Resource use measures included ambulatory visits, hospitalizations, and pharmaceutical use. CIs were obtained by using bootstrapping. RESULTS: The intervention, which cost \$1469 per family, led to statistically significant reductions in symptom days, unscheduled clinic visits, and use of beta-agonist inhalers. Over the year of the intervention and a year of follow-up, the intervention cost was \$27.57 per additional symptom-free day (95% CI, \$7.46-\$67.42). Subgroup analysis showed that targeting the intervention to selected high-risk subgroups did not reduce the incremental cost-effectiveness ratio. CONCLUSIONS: A targeted home-based environmental intervention improved health and reduced service use in inner-city children with moderate-to-severe asthma. The intervention is cost-effective when the aim is to reduce asthma symptom days and the associated costs.
- Kaugars A.S. et al.** *Family influences on pediatric asthma.* J Pediatr Psychol. 2004; 29(7) : 475-91.p **Abstract:** OBJECTIVE: To describe pathways by which families may influence the onset and course of a child's asthma. METHODS: We critically reviewed published articles and book chapters to identify research findings and integrated conceptualizations that demonstrate how families affect pediatric asthma. RESULTS: Family emotional characteristics, asthma management behaviors, and physiological factors account for key influences on pediatric asthma onset and outcomes. CONCLUSIONS: Multiple family characteristics are associated with pediatric asthma onset and outcomes. Behavioral and physiological mechanisms may act independently or may interact to affect asthma manifestations. Families with specific emotional characteristics may be at an elevated risk for poorer asthma outcomes.
- Kaur S. et al.** *Elevated levels of mannan-binding lectin.* Clin Exp Immunol. 2006; 143(3) : 414-9.p **Abstract:** Mannan-binding lectin (MBL), an important component of innate immunity, binds to a range of foreign antigens and initiates the lectin complement pathway. Earlier studies have reported high plasma MBL levels in allergic patients in comparison to healthy controls. In view of varied plasma MBL levels being determined by genetic polymorphisms in its collagen region, we investigated the association of single nucleotide polymorphisms (SNPs) in the collagen region of human MBL with respiratory allergic diseases. The study groups comprised patients of bronchial asthma with allergic rhinitis (n = 49) and allergic bronchopulmonary aspergillosis (APBA) (n = 11) and unrelated age-matched healthy controls of Indian origin (n = 84). A novel intronic SNP, G1011A of MBL, showed a significant association with both the patient groups in comparison to the controls (P < 0.01). Patients homozygous for the 1011A allele showed significantly higher plasma MBL levels and activity than those homozygous for the 1011G allele (P < 0.05). The 1011A allele also showed a significant correlation with high peripheral blood eosinophilia (P < 0.05) and low forced expiratory volume in 1 s (FEV₁) (P < 0.05) of the patients. We conclude that the 1011A allele of MBL may contribute to elevated plasma MBL levels and activity and to increased severity of the disease markers in patients of bronchial asthma with allergic rhinitis and ABPA.
- Kawada T.** *Risk factors and prevalence of asthma or atopic dermatitis in young children by a questionnaire survey.* J Nippon Med Sch. 2004; 71(3) : 167-71.p **Abstract:** Little is known about the relation between atopic disorders and altitude of residence. The author investigated the prevalence of asthma and atopic dermatitis, and their relationship with altitude of residence. A total of 24,631 children aged four years and under in Gunma Prefecture, Japan, were surveyed. The ATS-DLD questionnaire for asthma was distributed together with an item on atopic dermatitis. Some confounding variables were also asked. The author judged subjects as having asthma when positive answers were given to all 6 items in the ATS/DLD questionnaire. The prevalence of asthma in subjects with atopic dermatitis was higher than in those without (5.1% vs. 1.8%). Logistic regression analyses for asthma and atopic dermatitis were conducted, and male sex, increasing age, family history of target disease, and living at higher altitude commonly and significantly contributed to an increase in the risk of each allergic disorder. For

asthma, not being the eldest child, and past or present history of atopic dermatitis were also selected as risk factors. There was an increase in the prevalence of atopic disorders in groups living at a higher altitude was observed in this area.

Kayaba H. et al. *Activation of eosinophils by rice-husk dust exposure: a possible mechanism for the aggravation of asthma during rice harvest.* *Tohoku J Exp Med.* 2004; 204(1) : 27-36.p **Abstract:** Grain dust and other irritants affect the airway of allergic patients in rice-growing area during the harvest. The aim of this study was to elucidate the mechanism of airway hypersensitivity in rice-growing areas during the harvest. Firstly, the effect of rice-husk dust on eosinophil activation was studied. Secondly, the concentration of lipopolysaccharides (LPS), a potent activator of inflammatory cells, in rice-husk dust was measured. Since it is possible for LPS, a component of gram-negative bacterial cell wall, to adhere to the particle of smoke generated from rice-husk dust, LPS contained in the smoke was also measured. Furthermore, chemical irritants contained in the smoke generated from the rice-husk dust were analyzed. Microscopically, the dust contained fine thorns dropped off from the outer sheath of the rice, and irritated the skin, throat and eyes. The grain dust extract increased the expressions of eosinophil activation markers. These up-regulatory effects were largely dependent on LPS. The smoke contained LPS and several chemical irritants such as formaldehyde and acetaldehyde. Rice-husk dust and its smoke, hazardous air pollutants, probably play a major role in the aggravation of airway diseases in agricultural areas.

Kazachkov M.Y. et al. *Release of cytokines by human nasal epithelial cells and peripheral blood mononuclear cells infected with Mycoplasma pneumoniae.* *Exp Biol Med (Maywood).* 2002; 227(5) : 330-5.p **Abstract:** Mycoplasma pneumoniae (Mp) infection is associated with asthma exacerbation in children. We hypothesized that Mp infection may cause airway inflammation by inducing the release of cytokines by respiratory epithelial cells. The levels of chemokines interleukin-8 (IL-8) and released upon activation, normal T cell expressed and secreted (RANTES) released by nasal epithelial cell (NEC) cultures established from asthmatic and nonasthmatic children were measured by ELISA at 4, 24, 48, and 72 hr after cells were inoculated with Mp, and were compared with baseline release of these factors. The presence of MP on apical membranes of NEC after infection was confirmed by transmission electron microscopy, and adherence was shown to be inhibited by erythromycin. Mp infection did not alter NEC release of IL-8 or RANTES at any time point. In contrast, tumor necrosis factor alpha (TNF-alpha) stimulated increased IL-8 at all time points, and respiratory syncytial virus (RSV) infection stimulated RANTES release at 48 and 72 hr by NEC. These results were not significantly different between NEC from asthmatic and nonasthmatic children. As a comparison, peripheral blood mononuclear cells from normal human volunteers were also incubated with Mp and had significantly increased release of IL-2, IL-6, and TNF-alpha. We conclude that Mp, unlike viral pathogens such as RSV, is unlikely to directly stimulate early airway surface cytokine responses via mechanisms involving epithelial cells. We speculate that the chronic presence of mononuclear cells at the airway surface of asthmatics provides a target for Mp-triggered cytokine production.

Kee F. et al. *Fast and frugal models of clinical judgment in novice and expert physicians.* *Med Decis Making.* 2003; 23(4) : 293-300.p **Abstract:** Our objective was to study whether "compensatory" models provide better descriptions of clinical judgment than fast and frugal models, according to expertise and experience. Fifty practitioners appraised 60 vignettes describing a child with an exacerbation of asthma and rated their propensities to admit the child. Linear logistic (LL) models of their judgments were compared with a matching heuristic (MH) model that searched available cues in order of importance for a critical value indicating an admission

decision. There was a small difference between the 2 models in the proportion of patients allocated correctly (admit or not-admit decisions), 91.2% and 87.8%, respectively. The proportion allocated correctly by the LL model was lower for consultants than juniors, whereas the MH model performed equally well for both. In this vignette study, neither model provided any better description of judgments made by consultants or by pediatricians compared to other grades and specialties.

Keeler G.J. et al. *Assessment of personal and community-level exposures to particulate matter among children with asthma in Detroit, Michigan, as part of Community Action Against Asthma (CAAA).* *Environ Health Perspect.* 2002; 110 Suppl 2 : 173-81.p **Abstract:** We report on the research conducted by the Community Action Against Asthma (CAAA) in Detroit, Michigan, to evaluate personal and community-level exposures to particulate matter (PM) among children with asthma living in an urban environment. CAAA is a community-based participatory research collaboration among academia, health agencies, and community-based organizations. CAAA investigates the effects of environmental exposures on the residents of Detroit through a participatory process that engages participants from the affected communities in all aspects of the design and conduct of the research; disseminates the results to all parties involved; and uses the research results to design, in collaboration with all partners, interventions to reduce the identified environmental exposures. The CAAA PM exposure assessment includes four seasonal measurement campaigns each year that are conducted for a 2-week duration each season. In each seasonal measurement period, daily ambient measurements of PM_{2.5} and PM₁₀ (particulate matter with a mass median aerodynamic diameter less than 2.5 microm and 10 microm, respectively) are collected at two elementary schools in the eastside and southwest communities of Detroit. Concurrently, indoor measurements of PM_{2.5} and PM₁₀ are made at the schools as well as inside the homes of a subset of 20 children with asthma. Daily personal exposure measurements of PM₁₀ are also collected for these 20 children with asthma. Results from the first five seasonal assessment periods reveal that mean personal PM₁₀ (68.4 39.2 microg/m³) and indoor home PM₁₀ (52.2 30.6 microg/m³) exposures are significantly greater ($p < 0.05$) than the outdoor PM₁₀ concentrations (25.8 11.8 microg/m³). The same was also found for PM_{2.5} (indoor PM_{2.5} = 34.4 21.7 microg/m³; outdoor PM_{2.5} = 15.6 8.2 microg/m³). In addition, significant differences ($p < 0.05$) in community-level exposure to both PM₁₀ and PM_{2.5} are observed between the two Detroit communities (southwest PM₁₀ = 28.9 14.4 microg/m³), PM_{2.5} = 17.0 9.3 microg/m³; eastside PM₁₀ = 23.8 12.1 microg/m³, PM_{2.5} = 15.5 9.0 microg/m³). The increased levels in the southwest Detroit community are likely due to the proximity to heavy industrial pollutant point sources and interstate motorways. Trace element characterization of filter samples collected over the 2-year period will allow a more complete assessment of the PM components. When combined with other project measures, including concurrent seasonal twice-daily peak expiratory flow and forced expiratory volume at 1 sec and daily asthma symptom and medication dairies for 300 children with asthma living in the two Detroit communities, these data will allow not only investigations into the sources of PM in the Detroit airshed with regard to PM exposure assessment but also the role of air pollutants in exacerbation of childhood asthma.

Kelloway J.S. et al. *Does using a mouthwash instead of water improve the oropharyngeal removal of inhaled fluticasone propionate?* *Allergy Asthma Proc.* 2001; 22(6) : 367-71.p **Abstract:** Rinsing the mouth with water is recommended to remove inhaled corticosteroid (ICS) deposited on the oropharyngeal mucosa. Given the lipophilicity of fluticasone propionate (FP), an ethanol-based mouthwash was hypothesized to be superior to water. This study's purpose was to compare the effectiveness of water versus Listerine (Warner Lambert, Lititz, PA) in removing FP from the oropharyngeal mucosa. Asthma patients were randomly assigned

water or a Listerine-rinsing vehicle. A 440-microgram dose of FP was inhaled. After the second puff, patients rinsed for 30 seconds with 20 mL of the assigned agent and then repeated the process, spitting each "wash" into the same cup. At visit 2, patients used the alternate vehicle and repeated the procedure. Samples were frozen until analyzed using liquid chromatography/mass spectrophotometry (lower limit of detection 0.067 microgram/mL). Thirty-six patients (mean age, 44 years; 66% female) participated. Mean inhaler technique score was 11.3 (scale of 1-12). Eighty-three percent used the closed-mouth technique. The mean concentration of FP removed by Listerine was not statistically different than that removed by water, 1.67 micrograms/mL (range, 0.067-4.195 micrograms/mL) and 1.42 micrograms/mL (range, 0.067-5.107 micrograms/mL), respectively, and the total milliliter returned was assumed to be 40 mL. Regression analysis using sex, age, and inhaler technique showed no statistical relationship with the amount of FP removed. Therefore, Listerine was not more effective than water in removing FP from the oropharyngeal mucosa ($p = 0.53$). Thus, water is an adequate rinsing vehicle for removal of ICS deposited on the oropharyngeal mucosa. Other factors besides the rinsing vehicle are strong factors in determining the amount of drug removed.

Kelly A.M. et al. *Is severity assessment after one hour of treatment better for predicting the need for admission in acute asthma?* *Respir Med* . 2004; 98(8) : 777-81.p Abstract: AIM: To determine if severity assessment after 1 h of treatment is better than assessment at presentation for predicting the requirement for hospital admission for emergency department (ED) patients with acute asthma. METHODS: Prospective, observational study conducted in 36 Australian ED for a 2-week period in 2001 involving patients aged 1-55 years presenting with asthma. Data collected included severity assessment according to the National Asthma Guidelines (Australia) at presentation and 1 h, and disposition. Descriptive analysis was applied. RESULTS: 720 cases were analysed. Patients with 'mild' asthma at either assessment time had a greater than 80% chance of discharge home. Patients assessed as 'severe' at either assessment had a greater than 85% chance of requiring hospital admission, but the 1 h assessment was better at predicting the need for Intensive Care Unit (ICU) admission. For the 'moderate' group, the initial assessment was a poor predictor of the need for admission however those who met the criteria for 'moderate' severity at 1 h had an 84% chance of requiring admission. CONCLUSION: Assessment of asthma severity after 1 h of treatment is better than initial severity assessment for determining the need for hospital admission for patients initially assessed as having 'moderate' asthma and for predicting the need for ICU in patients initially assessed as 'severe'.

Kelly A.M. et al. *Patients with a longer duration of symptoms of acute asthma are more likely to require admission to hospital.* *Emerg Med (Fremantle)*. 2002; 14(2) : 142-5.p Abstract: OBJECTIVE: To determine whether, for patients with moderate or severe asthma presenting to emergency departments, there is a difference in need for hospitalization between those with a duration of symptoms less than 6 h and those with a longer duration of symptoms. METHODS: This prospective, observational study investigated a sample of patients presenting with acute asthma between 21 August and the 3 September 2000, attending study emergency departments and classified as having moderate or severe asthma according to the National Asthma Guidelines. Data collected included duration of symptoms (less than 6 h or greater than 6 h) and disposition following emergency department treatment (home, ward, intensive care unit, high dependency unit, transfer). Data analysis was by Chi square analysis. RESULTS: Of 381 eligible patients, 348 had sufficient data for entry into this study (33 had missing data). Patients with duration of symptoms more than 6 h were more likely to require hospital admission ($P < 0.0001$). The relative risk for hospital admission or transfer as opposed to discharge from the emergency department for the group with a duration of symptoms of more than 6 h was 2.2. CONCLUSION: Patients presenting with moderate or

severe asthma and a duration of symptoms of more than 6 h are more likely to require hospital admission or transfer for further treatment than patients with a shorter duration of symptoms. This has implications for decision making regarding asthma management and disposition in the emergency department.

Kelly H.W. *Severe, acute asthma as therapeutic orphan.* *Ann Pharmacother*. 2002; 36(7-8) : 1287-9.p

Kelly H.W. et al. *Growth and bone density in children with mild-moderate asthma: a cross-sectional study in children entering the Childhood Asthma Management Program (CAMP).* *J Pediatr*. 2003; 142(3) : 286-91.p Abstract: OBJECTIVES: We sought to determine whether mild-moderate persistent asthma sufficient to produce a decrease in baseline lung function is associated with an adverse effect on growth and bone mineral density (BMD) in children. METHODS: This was a cross-sectional study of 1041 children, 5 to 12 years old (32% ethnic/racial minorities and 40% female), enrolled into the Childhood Asthma Management Program (CAMP). Measures of asthma severity included: Spirometry; bronchial hyperresponsiveness; duration of asthma symptoms; and symptom-based assessment of severity. Multiple regression analyses were used to relate the asthma severity on the primary outcome variables: Height by stadiometry and BMD by dual energy radiographic absorptiometry. RESULTS: The mean +/- SD height percentile was 56.0 +/- 28.5 percentile for the population. The only significant relationship between asthma severity and height percentile was with methacholine bronchoprovocation in girls (beta 2.98, $P = .019$, covariate multiple regression). The mean +/- SD BMD was 0.65 +/- 0.10 g/cm² for the population. The past use of corticosteroids did not adversely affect either growth or BMD. CONCLUSIONS: We found that mild-moderate asthma of as long as 4 to 7 years duration in children does not produce an adverse effect on linear growth or BMD.

Kelly K.J. et al. *Emergency Department Allies: a Web-based multihospital pediatric asthma tracking system.* *Pediatrics*. 2006; 117(4 Pt 2) : S63-70.p Abstract: OBJECTIVE: To describe the development of a Web-based multihospital pediatric asthma tracking system and present results from the initial 18-month implementation of patient tracking experience. DESIGN: The Emergency Department (ED) Allies tracking system is a secure, password-protected data repository. Use-case methodology served as the foundation for technical development, testing, and implementation. Seventy-seven data elements addressing sociodemographics, wheezing history, quality of life, triggers, and ED management were included for each subject visit. SETTING: The ED Allies partners comprised 1 academic pediatric ED and 5 community EDs. POPULATION: Subjects with a physician diagnosis of asthma who presented to the ED for acute respiratory complaints composed the asthma group; subjects lacking a physician diagnosis of asthma but presenting with wheezing composed the wheezing group. RESULTS: The tracking-system development and implementation process included identification of data elements, system database and use case development, and delineation of screen features, system users, reporting functions, and help screens. For the asthma group, 2005 subjects with physician-diagnosed asthma were enrolled between July 15, 2002 and January 14, 2004. These subjects accounted for 2978 visits; 10.4% had ≥ 3 visits. Persistent asthma was noted in 68% of the subjects. During the same time period, 1297 wheezing subjects with a total of 1628 ED visits (wheezing group) were entered into the tracking system. After enrollment, 57% of the subjects with ≥ 1 subsequent ED visits received a physician diagnosis of asthma. CONCLUSIONS: Our sophisticated tracking system facilitated data collection and identified key intervention opportunities for a diverse ED wheezing population. A significant asthma burden was identified with significant rates of hospitalization, acute care visits and persistent asthma in 68% of subjects. The surveillance component provided important insights into health care

issues of both asthmatic subjects and wheezing subjects, many of whom subsequently were diagnosed with asthma.

Kennedy M.F. *Exercise and children with asthma.* Can Fam Physician. 2002; 48 : 457-8.p

Kerkhof M. et al. *Risk factors for atopic dermatitis in infants at high risk of allergy: the PIAMA study.* Clin Exp Allergy. 2003; 33(10) : 1336-41.p **Abstract:** **BACKGROUND:** It has been suggested that the period immediately after birth is a sensitive period for the development of atopic disease. **OBJECTIVE:** We investigated whether birth characteristics and environmental factors are associated with the development of atopic dermatitis in the first year of life. **METHODS:** Seventy-six children with and 228 without atopic dermatitis, all children of mothers with respiratory allergy or asthma (PIAMA birth cohort study) were included in the study. Atopic dermatitis was defined as a positive history of an itchy skin condition with at least two of the following characteristics: visible dermatitis, history of outer arms/leg involvement, or general dry skin. Multiple logistic regression analysis was performed to study the independent effects of various risk factors. **RESULTS:** A birth weight ≥ 4000 g compared to 3000-4000 g was a significant risk factor for atopic dermatitis (odds ratio (OR)=2.4; 95% CI: 1.1-5.1) as was day care attendance (OR=2.9; 95% CI: 1.5-5.9). Exclusive breastfeeding in the first 3 months was negatively associated with atopic dermatitis (OR=0.6; 95% CI: 0.3-1.2), especially with visible dermatitis (OR=0.4; 95% CI: 0.2-1.0). Gender, gestational age, the presence of siblings or pets, and parental smoking were not significantly associated with atopic dermatitis. **CONCLUSION:** This study shows that a high birth weight and day care attendance increase the risk of atopic dermatitis in the first year of life, while exclusive breastfeeding is a protective factor when dermatitis is found on inspection.

Kero J. et al. *Could TH1 and TH2 diseases coexist? Evaluation of asthma incidence in children with coeliac disease, type 1 diabetes, or rheumatoid arthritis: a register study.* J Allergy Clin Immunol. 2001; 108(5) : 781-3.p **Abstract:** **BACKGROUND:** Asthma is generally regarded as a disease with strong T(H)2-type cytokine expression, whereas in autoimmune disorders, such as coeliac disease (CD), insulin-dependent diabetes mellitus (IDDM), and rheumatoid arthritis (RA), T(H)1-type expression is seen. According to the cross-regulatory properties of T(H)1 and T(H)2 cells, one would assume that these diseases exist in different patient populations. **OBJECTIVE:** We sought to test the hypothesis that asthma could exist in children with T(H)1-type diseases, such as CD, IDDM, and RA. **METHODS:** Comparison was made of the cumulative incidence of asthma in children with CD, IDDM, or RA by linking Finnish Medical Birth Register data on the whole 1987 birth cohort (n = 60,254 births) with the data of several national health registers to obtain information on the incidences of these diseases during the first 7 years of life. **RESULTS:** The cumulative incidence of asthma in children with CD (24.6%) or RA (10.0%) was significantly higher than in children without CD (3.4%) or RA (3.4%); $P < .001$ and $P = .016$, respectively). Asthma tended to be more common in children with IDDM than in children without IDDM. **CONCLUSION:** These data indicate that the T(H)1 and T(H)2 diseases can coexist, indicating a common environmental denominator behind the disease processes.

Khan M.S. et al. *Background severity of asthma in children discharged from the emergency department.* J Paediatr Child Health. 2003; 39(6) : 432-5.p **Abstract:** **OBJECTIVE:** Attendance at an Emergency Department (ED) with an acute attack of asthma may be indicative of undertreatment of persistent disease. However, many presentations are in children with infrequent episodic asthma. The aim of this study was to characterize the pattern of asthma of children

discharged from ED to determine whether there was potential to improve underlying disease control. **METHODOLOGY:** This was a cohort study. Three hundred and ten parental caretakers of 1 to 15-year-old children, attended and discharged from an ED with asthma, completed an asthma control questionnaire, an asthma knowledge questionnaire and a caregiver's quality of life questionnaire. Background severity of asthma was classified and medication history was assessed. Also included were those with their first attack of asthma. **RESULTS:** One hundred and thirty-two (43%) children had infrequent episodic asthma, 105 (34%) frequent episodic, 40 (13%) persistent asthma and 33 (11%) first attack asthma. Thirty-nine per cent of children were not receiving preventer therapy and this seemed appropriate; 14% of children with frequent episodic and persistent asthma were not receiving appropriate preventer therapy; and a further 34% had frequent symptoms despite receiving preventer therapy. **CONCLUSIONS:** We observed deficiencies in use of preventer medications, use of written asthma management plans and lack of parental knowledge in some children with established asthma who presented to an ED. There was also a large number of children who did not have frequent background symptoms or who presented with their first episode.

Khan M.S. et al. *Randomized controlled trial of asthma education after discharge from an emergency department.* J Paediatr Child Health. 2004; 40(12) : 674-7.p **Abstract:** **OBJECTIVES:** To test the hypothesis that reinforcement of the advice given at the time of discharge from the emergency department by telephone consultation would improve asthma outcomes. **METHODS:** A randomized controlled trial of the parents of 310 children who had been discharged from the emergency department with asthma was undertaken. The parents were randomized to receive either standard care (155 children) or standard care plus education by telephone (155 children) from a trained asthma educator. Symptoms, parental asthma knowledge, parental quality of life and use of asthma action plans and preventer therapy were collected at baseline and 6 months later. The primary measure was days of wheeze in last 3 months; intermediate measures were regular use of preventer medications, possession and use of written asthma action plan, parental asthma knowledge scores and parental quality of life scores. **RESULTS:** A total of 266 parents (136 intervention) completed the follow-up questionnaires after 6 months. Both groups showed similar symptoms and process measures at baseline, apart from more regular use of preventer medication in the control children. At follow up, the intervention group children were significantly more likely than controls to possess (87.5% vs 72.3%; $P = 0.002$) a written asthma action plan. Possession of action plans increased from baseline in the intervention group but tended to decrease in the control group. Use of action plans was greater in the intervention group but decreased from baseline in both groups. Both intervention and control groups showed significant decreases in asthma symptoms. **CONCLUSIONS:** Reinforcement by telephone consultation did not improve the primary outcome of wheeze in the last 3 months. However, it increased the possession and regular use of written asthma action plans in the intervention group.

Khan N. et al. *Etiology, presentation and management outcome of pneumothorax.* J Ayub Med Coll Abbottabad. 2005; 17(1) : 62-4.p **Abstract:** **BACKGROUND:** This study was carried to determine etiology, presentation, complications and management outcomes of pneumothorax in patients presenting at two hospitals in NWFP province of Pakistan. **METHODS:** Pneumothorax patients reporting at the chest unit of Post Graduate Medical Institute, Lady Reading Hospital, Peshawar, and Pulmonology unit of Ayub Teaching Hospital, Abbottabad from 1999 to 2002 were included in the study. Patients of all ages were included. They were admitted and followed up to the full recovery/late complications. **Results:** A total of 146 pneumothorax patients reported during this period. Majority of the patients were diagnosed to have pneumothorax due to pulmonary tuberculosis making about 36.30% of the total cases. Second most

common cause was primary spontaneous pneumothorax (19.86%). Bacterial infections were also sizeable at 16.43%. Other causes included COPD, Asthma, iatrogenic, Interstitial lung disease, tuberous sclerosis and bronchiectasis. Conclusion: It was concluded from this study that pulmonary tuberculosis is the commonest cause of pneumothorax in our setup.

Khan S.R. et al. *Outcome evaluation of early discharge from hospital with asthma.* Respirology. 2003; 8(1) : 77-81.p **Abstract:** OBJECTIVE: The aim of the study was to determine whether it was safe to discharge children with asthma from hospital when stable on 3-hourly rather than 4-hourly doses of salbutamol. METHODOLOGY: A retrospective study of 419 individual admissions of 359 children with asthma was undertaken. We defined a theoretical 'time ready for discharge' (TRD) for asthmatic admissions based on: (i) at least two doses of 3-hourly salbutamol and due for the third dose, (ii) no oxygen supplementation, (iii) no intravenous fluid or therapy, and (iv) time of discharge should be either before 17:30 hours or after 07:30 hours. Each admission was analysed using appropriate parameters to assess for risks and benefits of using this theoretical TRD as a guide for discharging asthmatic children from hospital. RESULTS: A total of 116 (27.7%) children were discharged before our theoretical TRD, including 11 children who received salbutamol no less often than 2-hourly and 37 who had a single dose of 3-hourly salbutamol before discharge. Re-admission to hospital and representation to the Emergency Department without re-admission within 1 week of discharge were less common in the group who were discharged before they had achieved theoretical TRD than in those who were discharged at or after the theoretical TRD, although the numbers were too small to reach statistical significance. Between our theoretical TRD and actual time of discharge two children who received supplemental oxygen and more frequent salbutamol may have required re-admission. CONCLUSIONS: From the medical viewpoint discharge when the child is stable on 3-hourly rather than 4-hourly doses appears safe. This can be expected to shorten length of stay by an average of 5.5 h ($P < 0.001$).

Kidon M.I. et al. *Adverse drug reactions in Singaporean children.* Singapore Med J. 2004; 45(12) : 574-7.p **Abstract:** INTRODUCTION: Allergic reactions to drugs are considered rare in the paediatric population. Host genetic and environmental factors influence the reported incidence and characteristics of adverse drug reactions (ADRs), and cause significant variation according to the population described and case definition used. We aimed to define the prevalence and characteristics of reported drug allergies in hospitalised children in Singapore. METHODS: A retrospective case control study was performed through the hospital's inpatient electronic medical record (EMR) for the period of August 2002 to December 2002. The EMR was used to identify children with a previously reported ADR. The control group was randomly selected from patients hospitalised during the same period. RESULTS: Of the 8437 patients hospitalised during the study period, reports of previous ADRs were found in the records of 222 patients. The mean age of the patients was 7.4 years, range 2 months to 17 years (95 percent confidence interval [CI] 6.3 - 8.4). There were 146 males and 160 Chinese. The most commonly-involved medications were betalactam antibiotics (45 percent) and non steroidal anti-inflammatory drug (18.5 percent). Compared to the control group, children with a reported ADR were more likely to be older, with a mean age of 7.4 years versus 4.6 years (p -value less than 0.001), male (odds ratio [OR] 1.7, 95 percent CI 1.2-2.4), of Chinese descent (OR 1.8, 95 percent CI 1.5-5), have an associated chronic illness (OR 3.5, 95 percent CI 2.5-5), and a diagnosis of asthma (OR 2.7, 95 percent CI 1.7-4.5). CONCLUSION: In our paediatric inpatient population, the risk of reported ADRs increases with age, male gender, Chinese descent and the presence of chronic disease. The major drugs involved are betalactam antibiotics and non-steroidal anti inflammatory drugs.

Kidon M.I. et al. *Bimodal skin reactivity to histamine in atopic children in Singapore: influence of specific sensitizations.* Pediatr Allergy Immunol. 2004; 15(6) : 545-50.p **Abstract:** Histamine skin prick test (SPT) is used as the 'golden standard' for positive control in *in vivo* immediate type hypersensitivity testing. The skin reactivity to histamine can, however, be modulated by a bevy of extraneous factors. We aimed to define whether histamine skin reactivity in atopic children in Singapore is influenced by age, ethnic origin, gender, environmental exposure or specific sensitization patterns. A retrospective analysis of children, with specific aeroallergen sensitization (as measured by at least one allergen-specific SPT with a wheal size > 3 mm compared with the negative control) from the outpatient speciality clinic of the KK Children's Hospital, during 06/2002-06/2003. A total of 315 patients were included, 235 (75%) were males, 252 (80%) were Chinese, age mean was 7.7 yr (range: 2-15). Patients were referred to the SPT with a diagnosis of one or more of: allergic rhinitis 287 (91%), asthma 112 (36%) or atopic dermatitis 60 (19%). The mean histamine response showed a bimodal distribution, independent of age, ethnic origin, gender or phenotypical expression of allergic disease. Histamine skin reactivity was higher in atopic patients with polysensitization (mean 5.0 mm vs. 2.9 mm in monosensitized patients, $p < 0.001$), and in patients with mould sensitization (mean 5.1 mm vs. 3.3 mm in patient not sensitized to moulds, $p < 0.001$). The presence of passive smoking increased the likelihood of a diminished histamine skin response. Histamine skin response data strongly suggested the presence of two heterogeneous subpopulations. Children with polysensitization and mould sensitization were more likely to show a large significant histamine response, whereas children with passive smoke exposure, showed a diminished skin reactivity to histamine.

Kim C.K. et al. *Sputum eosinophilia in cough-variant asthma as a predictor of the subsequent development of classic asthma.* Clin Exp Allergy. 2003; 33(10) : 1409-14.p **Abstract:** BACKGROUND: A significant proportion of patients diagnosed with cough-variant asthma eventually manifest classic asthma signs, such as wheezing and dyspnoea. The aim of this study was to investigate whether the percentage of eosinophils and/or concentration of eosinophilic cationic protein (ECP) in sputum induced from patients with cough-variant asthma can predict the development of classic asthma. METHODS: Sixty-two children with cough-variant asthma were prospectively studied for 4 years. At the initiation of the study, sputum was induced with hypertonic saline, and the sputum samples were analysed for total and differential cell counts, and for ECP. Each subject was checked clinically at least every 3 months, and details of classic asthma signs experienced during the intervening periods were taken. RESULTS: Twenty-four (47.1%) of the 51 subjects available for follow-up developed signs of classic asthma, while 27 did not. The only significant difference in the sputum parameters between these two groups was a higher percentage of sputum eosinophils in subjects who developed classic asthma. A significant association was found between sputum eosinophil percentage and classic asthma development, but not between the concentration of sputum ECP and classic asthma development. CONCLUSION: Sputum eosinophilia in cough-variant asthma may be a correlate of the later development of classic asthma. This suggests that sputum differential cell counts may be useful in the clinical management of patients with cough-variant asthma, as they may enable the prediction of the subsequent classic asthma development.

Kim C.K. et al. *Bronchoalveolar lavage eosinophil cationic protein and interleukin-8 levels in acute asthma and acute bronchiolitis.* Clin Exp Allergy. 2005; 35(5) : 591-7.p **Abstract:** OBJECTIVE: In this study, we measured the levels of eosinophil cationic protein (ECP) and interleukin (IL)-8 in bronchoalveolar lavage (BAL) fluid from patients with acute asthma and acute bronchiolitis, to determine any

similarities or dissimilarities in the profiles of these biochemical markers in the two diseases. **METHODS:** BAL fluids were obtained from children with acute asthma (n=16), infants with acute bronchiolitis caused by respiratory syncytial virus (n=18), and control subjects (n=14). Children with asthma were selected to be free of viral infection. BAL cell counts and differentials were determined, and ECP and IL-8 levels were measured by radioimmunoassay and ELISA, respectively. **RESULTS:** ECP levels in BAL fluids were significantly higher in the asthma group than in the bronchiolitis (P<0.01) or control (P<0.0001) groups. However, IL-8 levels were significantly higher in the bronchiolitis group than in the asthma (P<0.01) or control (P<0.001) groups. IL-8 levels in the asthma group and ECP levels in the bronchiolitis group were similar to those of the control group. **CONCLUSION:** This difference in profiles of ECP and IL-8 in acute asthma and acute bronchiolitis, together with a different inflammatory cell pattern, suggests that the nature of the inflammatory process within the lower respiratory tract may be distinctive in these two diseases.

Kim J.H. et al. *Different IL-5 and IFN-gamma production from peripheral blood T-cell subsets in atopic and nonatopic asthmatic children.* J Asthma. 2004; 41(8) : 869-76.p **Abstract:** Defective Th1 and enhanced Th2-type cytokine responses have been implicated in the development of atopic disease. However, the immunopathology of nonatopic asthma, especially in children, remains unclear, and there have been few studies to compare the cytokine profile in peripheral blood T-cell subsets between atopic and nonatopic asthmatic children. To document whether atopic asthmatic children have a cytokine imbalance and to compare the cytokine profile between atopic and nonatopic asthmatic children, we investigated the interleukin (IL)-5-producing and interferon (IFN)-gamma-producing T-cell subsets from peripheral blood mononuclear cells (PBMC). The percentages of IFN-gamma-producing CD4+ and CD8+ T cells from atopic asthmatic children were decreased, but those in nonatopic asthmatic children were not decreased. In both groups of asthmatic children, the percentages of IFN-gamma-producing CD4+ T cells were inversely correlated with the peripheral blood eosinophils and had a significant correlation with airway responsiveness (PC20). Thus, we found that the mechanism underlying allergic inflammation of nonatopic asthma is not simple a Th1/Th2 cytokine imbalance. Considering the inverse relationship between IFN-gamma-producing CD4+ T cells and eosinophilia or airway hyperresponsiveness, IFN-gamma from CD4+ T cells may play an important role in allergic inflammation and airway hyperresponsiveness in asthmatic children.

Kim J.H. et al. *Effects of air pollutants on childhood asthma.* Yonsei Med J. 2005; 46(2) : 239-44.p **Abstract:** Epidemiologic studies have suggested the association between environmental exposure to volatile organic compounds (VOCs) and polycyclic aromatic hydrocarbons (PAHs) and the increased risk of incurring asthma. Yet there is little data regarding the relationship between personal exposure to air pollution and the incidence of asthma in children. This study was designed to evaluate the effect of exposure to air pollution on children with asthma by using exposure biomarkers. We assessed the exposure level to VOCs by measuring urinary concentrations of hippuric acid and muconic acid, and PAHs by 1-OH pyrene and 2-naphthol in 30 children with asthma and 30 children without asthma (control). The mean level of hippuric acid was 0.158 +/- 0.169 micromol/mol creatinine in the asthma group and 0.148 +/- 0.249 micromol/mol creatinine in the control group, with no statistical significance noted (p=0.30). The mean concentration of muconic acid was higher in the asthma group than in the control group (7.630 +/- 8.915 micromol/mol creatinine vs. 3.390 +/- 4.526 micromol/mol creatinine p=0.01). The mean level of urinary 1-OHP was higher in the asthma group (0.430 +/- 0.343 micromol/mol creatinine) than the control group (0.239 +/- 0.175 micromol/mol creatinine), which was statistically significant (p=0.03). There was no difference in the mean concentration of 2-NAP between the two groups (9.864 +/- 10.037 micromol/mol in the asthma group vs. 9.157 +/- 9.640 micromol/mol

in the control group, p=0.96). In conclusion, this study suggests that VOCs and PAHs have some role in asthma.

Kim J.H. et al. *Prolonged effect of montelukast in asthmatic children with exercise-induced bronchoconstriction.* Pediatr Pulmonol. 2005; 39(2) : 162-6.p **Abstract:** Accumulating evidence shows that cysteinyl leukotrienes are the most important mediators in exercise-induced bronchoconstriction (EIB). In contrast to several studies in adults, there are few long-term studies of leukotriene receptor antagonists (LTRAs) in children with EIB. The aim of this study was to assess the prolonged clinical and bronchoprotective effects of montelukast in asthmatic children with EIB. We randomly assigned 64 asthmatic children with EIB. Forty subjects received montelukast (5 mg/day), and 24 subjects received placebo once daily for 8 weeks. Exercise challenge was performed before and after 8 weeks of treatment. Of the 40 patients in the montelukast group, 28 patients crossed over after 8 weeks. The response was measured as asthma symptom score, maximum percent fall in forced expiratory volume in 1 sec (FEV(1)) from pre-exercise baseline, and time to recovery of FEV(1) to within 10% of pre-exercise baseline (time to recovery). Following 8 weeks of treatment with montelukast, the montelukast group compared with placebo showed significant improvements in all endpoints, including asthma symptom score, maximum percent fall in FEV(1) after exercise, and time to recovery. In the cross-over group, even 8 weeks after stopping montelukast treatment, all endpoints were significantly and persistently improved. These results indicate that montelukast provides clinical protection from airway hyperresponsiveness in asthmatic children with EIB, and suggest that LTRAs may be useful for the long-term management of asthmatic children with EIB.

Kim J.J. et al. *Traffic-related air pollution near busy roads: the East Bay Children's Respiratory Health Study.* Am J Respir Crit Care Med. 2004; 170(5) : 520-6.p **Abstract:** Recent studies, primarily in Europe, have reported associations between respiratory symptoms and residential proximity to traffic; however, few have measured traffic pollutants or provided information about local air quality. We conducted a school-based, cross-sectional study in the San Francisco Bay Area in 2001. Information on current bronchitis symptoms and asthma, home environment, and demographics was obtained by parental questionnaire (n = 1,109). Concentrations of traffic pollutants (particulate matter, black carbon, total nitrogen oxides [NO(X)], and nitrogen dioxide [NO(2)]) were measured at 10 school sites during several seasons. Although pollutant concentrations were relatively low, we observed differences in concentrations between schools nearby versus those more distant (or upwind) from major roads. Using a two-stage multiple-logistic regression model, we found associations between respiratory symptoms and traffic-related pollutants. Among those living at their current residence for at least 1 year, the adjusted odds ratio for asthma in relationship to an interquartile difference in NO(X) was 1.07 (95% confidence interval, 1.00-1.14). Thus, we found spatial variability in traffic pollutants and associated differences in respiratory symptoms in a region with good air quality. Our findings support the hypothesis that traffic-related pollution is associated with respiratory symptoms in children.

Kim Y.K. et al. *Coding single nucleotide polymorphism in the high-affinity immunoglobulin E receptor b chain (FcepsilonRI-beta) gene is associated with immunoglobulin E receptor-mediated histamine release from basophils.* Clin Exp Allergy. 2002; 32(5) : 751-5.p **Abstract:** **BACKGROUND:** Our previous work on linkage analysis showed that histamine release from basophils to anti-IgE stimuli was linked to the gene marker of chromosome 11q13, where the beta chain of the high-affinity receptor for IgE (FcepsilonRI-beta) is located. **OBJECTIVE:** To evaluate the association between FcepsilonRI-mediated histamine release from basophils and four bi-allelic single nucleotide polymorphisms of the FcepsilonRI-beta gene. **METHODS:** Phenotypes of asthma, such as maximal histamine

release from basophils and atopy, were measured from 80 randomly recruited asthmatic children. Polymorphisms of the FcεpsilonRI-beta gene were determined by PCR-based methods. RESULTS: The polymorphism in exon 7, resulting in Glu to Gly substitution, was significantly associated with histamine release from basophils to anti-IgE stimuli, but not with total IgE levels and skin test responses to aeroallergens. CONCLUSION: This study supports a role for the FcεpsilonRI-beta gene in the expression of high affinity IgE receptor-mediated histamine release from basophils.

Kimata H. *Increased incidence of latex allergy in children with allergic diseases in Japan.* Public Health. 2005; 119(12) : 1145-9.p **Abstract:** The incidence of latex allergy is increasing in Japanese adults. However, the changing incidence of latex allergy in children with or without allergic diseases has not been reported in detail. After obtaining written informed consent from parents, Japanese children under 14 years of age were studied. In total, 776 non-atopic children, 802 children with allergic rhinitis (AR), 706 children with bronchial asthma (BA) and 844 children with atopic eczema/dermatitis syndrome (AEDS) were asked about symptoms of latex allergy, and tested by serum latex-specific IgE, skin prick test to latex allergen and latex-glove-wearing test between 2001 and 2003. All the patients were outpatients at Ujitakeda Hospital, while the non-atopic children were children of the staff of Ujitakeda Hospital or Unitika Ltd. This was a retrospective study. The incidence of latex allergy in 2001/2002/2003 was 1.4/3.1/4.7% in non-atopic children, 3.1/5.1/9.1% in AR patients, 3.6/6.5/10.3% in BA patients and 6.1/11.3/15.9% in AEDS patients, respectively. Moreover, although no cases of anaphylactic shock were noted in allergic patients in 2001, two and eight cases were noted in 2002 and 2003, respectively. These results indicate that the incidence of latex allergy is increasing in paediatric patients with allergic diseases. A latex-reduced environment may be desirable in future.

Kimes D. et al. *Temporal dynamics of emergency department and hospital admissions of pediatric asthmatics.* Environ Res. 2004; 94(1) : 7-17.p **Abstract:** Asthma is a chronic disease that can result in exacerbations leading to urgent care in emergency departments (EDs) and hospitals. We examined seasonal and temporal trends in pediatric asthma ED (1997-1999) and hospital (1986-1999) admission data so as to identify periods of increased risk of urgent care by age group, gender, and race. All pediatric ED and hospital admission data for Maryland residents occurring within the state of Maryland were evaluated. Distinct peaks in pediatric ED and hospital asthma admissions occurred each year during the winter-spring and autumn seasons. Although the number and timing of these peaks were consistent across age and racial groups, the magnitude of the peaks differed by age and race. The same number, timing, and relative magnitude of the major peaks in asthma admissions occurred statewide, implying that the variables affecting these seasonal patterns of acute asthma exacerbations occur statewide. Similar gross seasonal trends are observed worldwide. Although several environmental, infectious, and psychosocial factors have been linked with increases in asthma exacerbations among children, thus far they have not explained these seasonal patterns of admissions. The striking temporal patterns of pediatric asthma admissions within Maryland, as described here, provide valuable information in the search for causes.

Kimes D. et al. *Relationships between pediatric asthma and socioeconomic/urban variables in Baltimore, Maryland.* Health Place. 2004; 10(2) : 141-52.p **Abstract:** Spatial relationships between clinical data for pediatric asthmatics (hospital and emergency department utilization rates), and socioeconomic and urban characteristics in Baltimore City were analyzed with the aim of identifying factors that contribute to increased asthma rates. Socioeconomic variables and urban characteristics derived from satellite data explained 95% of the spatial variation in hospital rates.

The proportion of families headed by a single female was the most important variable accounting for 89% of the spatial variation. Evidence suggests that the high rates of hospital admissions and emergency department (ED) visits may partially be due to the difficulty of single parents with limited resources managing their child's asthma condition properly. This knowledge can be used for education towards mitigating ED and hospital events in Baltimore City.

Kini N.M. et al. *Inpatient care for uncomplicated bronchiolitis: comparison with Milliman and Robertson guidelines.* Arch Pediatr Adolesc Med. 2001; 155(12) : 1323-7.p **Abstract:** CONTEXT: Bronchiolitis is the most common lower respiratory tract infection in infancy. A recent Centers for Disease Control and Prevention report confirmed that hospitalization rates for bronchiolitis have increased 2.4-fold from 1980 to 1996. Controversies exist about optimal treatment plans. Milliman and Robertson recommend ambulatory care management; in case of hospitalization, the recommended length of stay is 1 day. OBJECTIVES: To relate actual practice variation for infants admitted with uncomplicated bronchiolitis to Milliman and Robertson's recommendations. DESIGN: Prospective observational study. SETTING: General care wards of 8 pediatric hospitals of the Child Health Accountability Initiative during the winter of 1998-1999. PATIENTS: First-time admissions for uncomplicated bronchiolitis in patients not previously diagnosed as having asthma and who were younger than 1 year. MAIN OUTCOME MEASURES: Respiratory rate, monitored interventions, attainment of discharge criteria goals, and length of stay. RESULTS: Eight hundred forty-six patients were included in the final analysis: 85.7% were younger than 6 months, 48.5% were nonwhite, and 64.1% were Medicaid recipients or self-pay. On admission to the hospital, 18.3% of the infants had respiratory rates higher than higher than 80 breaths per minute, 53.8% received supplemental oxygen therapy, and 52.6% received intravenous fluids. These proportions decreased to 1.9%, 33.8%, and 20.3%, respectively, 1 day after admission, and to 0.7%, 20.1%, and 8.6%, respectively, 2 days after admission. The average length of stay was 2.8 days (SD, 2.3 days). CONCLUSIONS: Milliman and Robertson's recommendations do not correspond to practice patterns observed at the hospitals participating in this study; no hospital met the Milliman and Robertson recommended 1-day goal length of stay. Administration of monitored intervention persisted past the second day of hospitalization.

Kinnula V.L. et al. *Two functional variants of the superoxide dismutase genes in Finnish families with asthma.* Thorax. 2004; 59(2) : 116-9.p **Abstract:** BACKGROUND: Functional polymorphisms in the genes encoding superoxide dismutases (SOD)-that is, superoxide scavenging antioxidant enzymes-may play an important role in the development of inflammatory airway diseases such as asthma. METHODS: The allele frequencies of two missense polymorphisms of SOD genes (Ala16Val in MnSOD (SOD2) and Arg213Gly in ECSOD (SOD3)) were investigated in Finnish patients with asthma and compared with family based controls. Both variants have been shown to be functionally interesting in the lung. The polymorphism at the exon-intron 3 boundary of a third SOD, CuZnSOD (SOD1), was also included in the analysis. RESULTS: None of the SOD genetic variants studied appeared to be major genetic regulators in the development of asthma. We could exclude all models of inheritance that increased the risk of asthma more than 1.2 fold for MnSOD*Val (frequency of allele 0.74 in the population) and more than 6.6 fold for ECSOD*Gly213 (frequency of allele 0.03 in the population) compared with non-carriers. For the intronic polymorphism in CuZnSOD, a relative risk of more than 3.3 (frequency of allele 0.10 in the population) could be excluded. CONCLUSIONS: It is highly unlikely that the functionally important genetic variants Ala16Val and Arg213Gly of SODs play a major role in the genetic susceptibility of asthma.

- Kishida M. et al.** *Mouthpiece versus facemask for delivery of nebulized salbutamol in exacerbated childhood asthma.* J Asthma. 2002; 39(4) : 337-9.p **Abstract:** We compared the bronchodilator response to salbutamol (albuterol) delivered by a compressed air nebulizer through a mouthpiece and via a facemask in 18 asthmatic children, to determine the most appropriate delivery method. Patients using a mouthpiece had significantly better mean percent increases in forced expiratory volume in 1 sec (FEV1) and in forced vital capacity (FVC) than those using a facemask 30 min after inhalation (FEV1, 56.4 +/- 32.6% vs. 28.9 +/- 19.1%, FVC: 34.4 +/- 26.4% vs. 7.5 +/- 14.9%, respectively). Nebulized therapy plays an important role in the management of bronchial asthma in children and should be delivered by a mouthpiece whenever possible in cases of exacerbated asthma.
- Kjellman B. et al.** *Asthma severity, allergy and lung function during young middle life in subjects with asthma in childhood.* Respir Med. 2002; 96(9) : 716-24.p **Abstract:** The further course of asthma severity lung function, bronchial hyperresponsiveness (BHR) to cold air challenge (CACH), clinical allergies and allergic sensitization in young middle adulthood was studied in a cohort of 55 subjects with childhood asthma. All subjects (27 females) have attended all five previous and the current follow-up visit, undertaken at a mean age of 35 years. Twelve subjects (22%) reported no current asthma, 28 (51%) mild/intermittent, and 15 (27%) moderate/severe asthma. Asthma severity changed little in the individual subjects over the last 5-year period. Females continued to have higher asthma severity scores than the males, but the previously noted lower resting and post-bronchodilator % predicted FEV1 in females was not confirmed now. Pathological BHR to CACH tended to be more common among the males. Forty-four subjects were still allergic to animal danders and 35 to pollens. Sensitization rates (skin prick test or RAST) were similar to those recorded 5 years earlier and there was no clear evidence of tolerance developing. Five subjects have never shown evidence of allergy or sensitization. The extent of sensitization to animal danders showed statistically significant relationships to asthma severity and BHR to CACH. Social development and professional careers continued to be good.
- Kleinschmidt-DeMasters B.K.** *Central nervous system aspergillosis: a 20-year retrospective series.* Hum Pathol. 2002; 33(1) : 116-24.p **Abstract:** Over the past 20 years at my institution, 71 patients with invasive necrotizing aspergillosis have been encountered; 42 have shown central nervous system (CNS) involvement by autopsy (40) or surgical biopsy (2). Most non-CNS aspergillosis patients had invasive disease confined to the lung, and only 2 with dissemination to 3 or more organs did not have spread to the CNS. In addition to the expected post-transplantation and hematologic malignancy cases, other risk groups identified included those with chronic asthma and steroid use, acquired immunodeficiency syndrome, thermal burn, hepatic failure, and postoperative infection. Unusual cases manifested with basilar meningitis, myelitis, proptosis caused by sino-orbital disease, or epidural and subdural Aspergillus abscesses. The extent of gross neuropathologic disease ranged from subtle abscesses to massive hemorrhagic necrosis causing herniation and death. In addition to the expected hemorrhagic necrosis, extensive hemorrhage, focal purulent meningitis, and subtle bland infarctions were also seen. Distinctive microscopic findings encountered included 1 case with numerous meningeal granulomas and multinucleated giant cells and 4 cases showing the Splendore-Hoeppli phenomenon. During the same period, single cases of cerebritis caused by morphologically similar fungi (*Pseudoallescheria boydii* [*Scedosporium apiospermum*], *Scedosporium inflatum*, *Chaetomium* sp) were identified and were indistinguishable from CNS aspergillosis clinically and pathologically.
- Klion A.D. et al.** *Familial eosinophilia: a benign disorder?* Blood. 2004; 103(11) : 4050-5.p **Abstract:** Familial eosinophilia (FE) is an autosomal dominant disorder characterized by marked eosinophilia and progression to end organ damage in some, but not all, affected family members. To better define the pathogenesis of FE, 13 affected and 11 unaffected family members (NLs) underwent a detailed clinical evaluation at the National Institutes of Health (NIH). No clinical abnormalities were more frequent in the family members with FE compared with the NLs. There was, however, a decreased prevalence of asthma in family members with FE compared with unaffected family members. Eosinophil morphology as assessed by either light or transmission electron microscopy was normal in family members with and without FE. Although levels of eosinophil-derived neurotoxin (EDN) and major basic protein (MBP) were elevated in patients with FE compared with NL, levels of both granule proteins were lower than in nonfamilial hypereosinophilic syndrome (HES). Similarly, increased surface expression of the activation markers CD69, CD25, and HLA-DR was detected by flow cytometry on eosinophils from patients with FE compared with NL, albeit less than that seen in HES. These data suggest that, despite prolonged marked eosinophilia, FE can be distinguished from HES by a more benign clinical course that may be related to a relative lack of eosinophil activation.
- Knorr R.S. et al.** *Tracking pediatric asthma: the Massachusetts experience using school health records.* Environ Health Perspect. 2004; 112(14) : 1424-7.p **Abstract:** The Massachusetts Department of Public Health, in collaboration with the U.S. Centers for Disease Control and Prevention Environmental Public Health Tracking Program, initiated a 3-year statewide project for the routine surveillance of asthma in children using school health records as the primary data source. School district nurse leaders received electronic data reporting forms requesting the number of children with asthma by grade and gender for schools serving grades kindergarten (K) through 8. Verification efforts from an earlier community-level study comparing a select number of school health records with primary care provider records demonstrated a high level of agreement (i.e., > 95%). First-year surveillance targeted approximately one-half (n = 958 schools) of all Massachusetts's K-8 schools. About 78% of targeted school districts participated, and 70% of the targeted schools submitted complete asthma data. School nurse-reported asthma prevalence was as high as 30.8% for schools, with a mean of 9.2%. School-based asthma surveillance has been demonstrated to be a reliable and cost-effective method of tracking disease through use of an existing and enhanced reporting structure.
- Kobayashi M. et al.** *Late phase responses after nasal challenges with allergen and histamine in asthmatic children with perennial nasal allergy.* Auris Nasus Larynx. 2001; 28(4) : 305-10.p **Abstract:** OBJECTIVE: Late phase response (LPR) is difficult to investigate in patients with perennial nasal allergy because of their continuous presentation with nasal symptoms. Contribution of histamine to the LPR is also controversial. In this study, we investigated whether exogenous histamine can induce LPR in asthmatic patients with perennial nasal allergy to house dust. METHODS: A total of 40 asthmatic children were divided into clinical, subclinical and non-rhinitis groups based on their daily nasal symptoms. Changes in nasal patency and in inflammatory cells in nasal secretion were quantitatively measured for 6 h by acoustic rhinometry and light microscopy respectively before and after nasal challenge with allergen or histamine. RESULTS: The allergen challenge produced a significant biphasic decrease in nasal patency in the subclinical group and a marginal decrease in the clinical group, with increases in eosinophils 6 h after the challenge. By contrast, histamine challenge induced significant responses in the clinical group and only a slight response in the subclinical group. Eosinophils also accumulated in nasal secretion of the clinical group to significant levels 6 h after histamine challenge. Eosinophil accumulation following histamine challenge was earlier than that after exposure to allergen.

CONCLUSION: We conclude that LPR can be demonstrated in asthmatic children with perennial nasal allergy. Exposure to exogenous histamine also induced LPR, mediated mainly by eosinophil-related mediators.

Kocabas C.N. et al. *Burden of rhinitis in children with asthma.* *Pediatr Pulmonol.* 2005; 40(3) : 235-40.p **Abstract:** Although the clinical association of allergic rhinitis and asthma has been recognized for centuries, in recent years the association appears to be stronger than was reported previously. However, data for children are less clear, and some studies indicate that results observed in developing countries may differ from those observed in Western populations. We therefore intended to document the association of rhinitis with pediatric asthma in terms of caregivers' perception, physician practice, and file records. Asthmatic children aged 3-16 years with at least 1-year follow-up in an allergy-asthma outpatient clinic were invited to participate in the study during a 10-month interval. In addition to a face-to-face questionnaire-based interview, file records were evaluated retrospectively to obtain information relating to asthma and rhinitis. Of 396 patients included in the study, 369 with consistent replies were included in the analyses. The mean age of the study group was 10.6 +/- 0.2 (mean +/- SEM) years, and a greater proportion of the respondents were male (63.7%), atopic (78.3%), and mildly asthmatic (50.7%). House dust mite and grass pollens were the most commonly sensitized allergens (50.7% and 46.9%, respectively). Although only 5.4% of our study population regarded themselves as rhinitic and 23.8% had been diagnosed with allergic rhinitis according to the file records, almost 57.7% of patients had required medications for rhinitis within the last year, and 68.8% had findings consistent with allergic rhinitis. Furthermore, 41.2% and 58.8% reported that their rhinitis symptoms caused a significant burden in their daily life and exacerbated their asthma, respectively, and almost 50% felt that their rhinitis had not been given significant consideration by their physician. In conclusion, although we report a large discrepancy between caregivers' perception of rhinitis, documentation in file records, and treatments for rhinitis, the allergic rhinitis prevalence determined in the survey and the medication use for rhinitis appeared to be in agreement. We recommend a greater effort be made to identify, label, and educate children with rhinitis and their families in asthma outpatient clinics.

Koenig J.Q. et al. *Measurement of offline exhaled nitric oxide in a study of community exposure to air pollution.* *Environ Health Perspect.* 2003; 111(13) : 1625-9.p **Abstract:** As part of a large panel study in Seattle, Washington, we measured levels of exhaled nitric oxide (eNO) in children's homes and fixed-site particulate matter with aerodynamic diameters of 2.5 micro m or less (PM(2.5)) outside and inside the homes as well as personal PM(2.5) during winter and spring sessions of 2000-2001. Nineteen subjects 6-13 years of age participated; 9 of the 19 were on inhaled corticosteroid (ICS) therapy. Exhaled breath measurements were collected offline into a Mylar balloon for up to 10 consecutive days. Mean eNO values were 19.1 (SD +/- 11.4) ppb in winter sessions and 12.5 +/- 6.6 ppb in spring sessions. Fixed-site PM(2.5) mean concentrations were 10.1 +/- 5.7 microg/m(3) outside homes and 13.3 +/- 1.4 inside homes; the personal PM(2.5) mean was 13.4 +/- 3.2 microg/m(3). We used a linear mixed-effects model with random intercept and an interaction term for medications to test for within-subject-within-session associations between eNO and various PM(2.5) values. We found a 10 microg/m(3) increase in PM(2.5) from the outdoor, indoor, personal, and central-site measurements that was associated with increases in eNO in all subjects at lag day zero. The effect was 4.3 ppb [95% confidence interval (CI), 1.4-7.29] with the outdoor monitor, 4.2 ppb (95% CI, 1.02-7.4) for the indoor monitor, 4.5 ppb (95% CI, 1.02-7.9) with the personal monitor, and 3.8 ppb (95% CI, 1.2-6.4) for the central monitors. The interaction term for medication category (ICS users vs. nonusers) was significant in all analyses. These findings suggest that eNO can be used as an assessment tool in epidemiologic studies of health effects of air pollution.

Koeppen-Schomerus G. et al. *Genes and environment in asthma: a study of 4 year old twins.* *Arch Dis Child.* 2001; 85(5) : 398-400.p **Abstract:** BACKGROUND: Although the genetic and environmental factors of asthma have been investigated in adolescence and adulthood, no previous studies have focused on the early development of asthma. AIMS: To test, in a large sample of 4 year old twins, the hypotheses derived from the literature on adolescents and adults that genetic influences are substantial and shared environmental influences are modest. METHODS: The sample consisted of 4910 twin pairs who were born in England and Wales in 1994 and 1995. Data on asthma status were obtained from the twins' parents by postal questionnaire. RESULTS: Univariate parameter estimates derived from model fitting were 68% heritability, 13% shared environment, and 19% non-shared environment. CONCLUSIONS: Our findings suggest that asthma is highly heritable in 4 year olds, whereas shared environmental influences are not statistically significant.

Koh Y.Y. et al. *The importance of maximal airway response to methacholine in the prediction of asthma development in patients with allergic rhinitis.* *Clin Exp Allergy.* 2002; 32(6) : 921-7.p **Abstract:** BACKGROUND: Allergic rhinitis is a known predictor and correlate of asthma incidence. However, it is not clear which patients with allergic rhinitis are at greater risk of the development of asthma. OBJECTIVE: The aim of this study was to investigate whether airway hypersensitivity and/or increased maximal response on the dose-response curve to methacholine would predict the development of asthma in subjects with allergic rhinitis. METHODS: One hundred and forty-one children with allergic rhinitis were prospectively studied for 7 years. At the initiation of the study, bronchial provocation test with methacholine using a stepwise increasing concentration technique was performed to measure PC(20) (provocative concentration causing a 20% fall in FEV(1)) and maximal response. Each subject was evaluated at least every 6 months and details of asthmatic symptoms or signs experienced during the intervening period were taken. RESULTS: Twenty of 122 subjects available for the follow-up developed asthma. Nine (19.6%) of 46 hypersensitive (PC(20) < 18 mg/mL) subjects developed asthma, compared with 11 (14.5%) of 76 normosensitive subjects (P = 0.462). Eight (32%) of 25 subjects without maximal response plateau developed asthma, compared with 12 (12.4%) of 97 subjects with maximal response plateau (P = 0.018). Score test for trend revealed a significant association between the level of maximal response (P = 0.007), but not the degree of methacholine PC(20) (P = 0.123), and the future development of asthma. CONCLUSION: An increased maximal airway response to methacholine is shown to be a better predictor for the future development of asthma in patients with allergic rhinitis, than airway hypersensitivity to methacholine.

Koh Y.Y. et al. *Ratio of serum eosinophil cationic protein/blood eosinophil counts in children with asthma: comparison between acute exacerbation and clinical remission.* *Allergy Asthma Proc.* 2003; 24(4) : 269-74.p **Abstract:** Serum eosinophil (Eo) cationic protein (ECP) concentrations during acute exacerbations in asthma patients are significantly elevated compared with those during clinical remission. We measured the ratio of serum ECP concentration to peripheral blood Eo counts (ECP/Eo ratio), to determine whether the ECP release from Eo differs between the two clinical asthma situations. Forty-six children with asthma underwent spirometric assessment and blood sampling at the times of acute exacerbation and clinical remission. Twenty healthy children also were studied as a control group. The peripheral blood Eo count (468 +/- 262 per microL, mean +/- SD), the serum ECP concentration (41.7 +/- 16.9 micrograms/L), and the ECP/Eo ratio (0.104 +/- 0.049) during acute asthma exacerbations were significantly higher than the respective values during clinical remission (383 +/- 191 per microL, 27.4 +/- 11.5 micrograms/L, 0.084 +/- 0.041, all p < 0.05). The

ECP/Eo ratio as well as the serum ECP concentration during acute exacerbations correlated significantly with the degree of airflow obstruction (both, $p < 0.01$). Both the increased peripheral blood Eo counts and the possible enhanced Eo activation may account for the elevated serum ECP concentration observed during acute exacerbations compared with that during clinical remission. Our results suggest a differential release of ECP by the Eo, depending on the disease status and asthma exacerbation severity.

Koimis Mitchell D. et al. *Identifying risk and resource factors in children with asthma from urban settings: the context-health-development model.* *J Asthma.* 2005; 42(6) : 425-36.p **Abstract:** This two-year longitudinal study examined concurrent and across-time associations between characteristics related to context, health, and development (i.e., neighborhood disadvantage, knowledge related to asthma management and asthma management behaviors, and self-competence) and children's asthma-related functioning. Thirty-one 8- to 12-year-old children with asthma and their primary caregivers were interviewed for the baseline of this study, and 29 of these dyads were interviewed for the 1-year follow-up. All participants resided in urban neighborhoods, and most were members of ethnic minority (African American and Hispanic) groups. Cross-sectional support was found for significant inverse relationships between neighborhood disadvantage and children's asthma knowledge. Lower levels of self-competence were consistently cross-sectionally associated with lower levels of asthma knowledge. A combination of higher levels of asthma knowledge, more optimal asthma management strategies, and self-competence was associated with fewer school absences across the study period. These results suggest an interdependence between aspects of children's sociocultural context, health, and developmental characteristics. This multidimensional model provided preliminary support for the risk function of neighborhood disadvantage and the resource functions of asthma knowledge, asthma management, and self-competence for asthma-related functioning among urban children.

Kokki H. *Nonsteroidal anti-inflammatory drugs for postoperative pain: a focus on children.* *Paediatr Drugs.* 2003; 5(2) : 103-23.p **Abstract:** Pain is a common symptom after surgery in children, and the need for effective pain management is obvious. For example, after myringotomy, despite the brief nature of the procedure, at least one-half of children have significant pain. After more extended surgery, such as tonsillectomy, almost all children have considerable pain longer than 7 days. Nonsteroidal anti-inflammatory drugs (NSAIDs) are useful for postoperative pain management because surgery causes both pain and inflammation. Several pediatric studies indicate NSAIDs are effective analgesics in the management of mild and moderate pain. In the treatment of severe pain, NSAIDs should be given with acetaminophen (paracetamol) or opioids, and the use of an appropriate regional analgesic technique should be considered. NSAIDs are more effective in preventing pain than in the relief of established pain. Pain following surgery is best managed by providing medication on a regular basis, preventing the pain from recurring. This proactive approach should be implemented for any procedure where postoperative pain is the likely outcome. In children, the choice of formulation can be more important than the choice of drug. Intravenous administration is preferred for children with an intravenous line in place; thereafter mixtures and small tablets are feasible options. Children dislike suppositories, and intramuscular administration should not be used in nonsedated children. Ibuprofen, diclofenac, ketoprofen and ketorolac are the most extensively evaluated NSAIDs in children. Only a few trials have compared different NSAIDs, but no major differences in the analgesic action are expected when appropriate doses of each drug are used. Whether NSAIDs differ in the incidence and severity of adverse effects is open to discussion. Because NSAIDs prevent platelet aggregation they may increase bleeding. A few studies indicate that ketorolac may increase bleeding more so than other NSAIDs, but the evidence is conflicting. Severe adverse effects of

NSAIDs in children are very rare, but it is important to know about adverse effects in order to recognize and treat them when they do occur. NSAIDs are contraindicated in patients in whom sensitivity reactions are precipitated by aspirin (acetylsalicylic acid) or other NSAIDs. They should be used with caution in children with liver dysfunction, impaired renal function, hypovolemia or hypotension, coagulation disorders, thrombocytopenia, or active bleeding from any cause. In contrast, it seems that most children with mild asthma may use NSAIDs.

Kooistra J.B. *Helping kids breathe easier.* *Med Econ.* 2002; 79(22) : 62.p

Koopman L.P. et al. *Respiratory infections in infants: interaction of parental allergy, child care, and siblings-- The PIAMA study.* *Pediatrics.* 2001; 108(4) : 943-8.p **Abstract:** **OBJECTIVE:** To investigate the association between contacts with other children and the development of respiratory infections in the first year of life in children with or without genetic predisposition for allergy. **METHODS:** Children ($n = 4146$) who participate in a prospective birth cohort study (Prevention and Incidence of Asthma and Mite Allergy study) were investigated. Questionnaires were used to obtain information on doctor-diagnosed upper respiratory tract infection (URTI) and lower respiratory tract infection (LRTI), child care attendance, having siblings, family history of allergic disease, and various potential confounders. **RESULTS:** Child care attendance in the first year of life was associated with doctor-diagnosed URTI (adjusted odds ratio [AOR]: 2.7; 95% confidence interval [CI]: 2.1-3.4 for large child care facility vs no child care) and doctor-diagnosed LRTI (AOR: 5.6; 95% CI: 3.9-7.9). Having siblings was associated with doctor-diagnosed LRTI (AOR: 2.6; 95% CI: 2.0-3.4). In addition, children who have allergic parents and attend child care or have older siblings have a higher risk of developing doctor-diagnosed LRTI than do children who have nonallergic parents. **CONCLUSIONS:** Child care attendance or having siblings increases the risk of developing doctor-diagnosed LRTI in the first year of life to a greater extent in allergy-prone children than in children who are not allergy prone.

Kopp M.V. et al. *Hospital admission with neonatal sepsis and development of atopic disease: Is there a link?* *Pediatr Allergy Immunol.* 2005; 16(8) : 630-6.p **Abstract:** The role of suspected or confirmed neonatal sepsis in modifying the risk of atopic disease during childhood was assessed. Children with early-onset neonatal sepsis were identified from a cohort of neonates, hospitalized between 1990 and 1995. Of 196 individuals, 140 were recruited (71.4%). Pre- and postnatal history was ascertained from neonatal medical records. Based on clinical symptoms and a positive blood culture or at least three of initially defined laboratory or bacteriological criteria, they were stratified in either confirmed neonatal sepsis (CS) or suspected sepsis (SS) group. A control group (C) comprised children who were never hospitalized during infancy ($n = 696$). Primary end-point was the development of atopic dermatitis, bronchial asthma or allergic rhinitis during childhood (mean age 8.4 yr, range 5.7-12.4). CS and SS children had a higher prevalence of atopic dermatitis (CS 15.7%, SS 21.4%) compared with controls (C 5.2%, $p < 0.001$). Similarly, children with SS (7.1%), but not with CS (4.3%) had significantly more often a doctor's diagnosis of bronchial asthma compared to controls (1.9%, $p = 0.02$). No difference in the prevalence of allergic rhinitis was observed (CS 4.3%, SS 10%, C 8.3%). After adjusting for parental history of atopic disease and demographic factors, no significant difference for the risk to develop atopic dermatitis, asthma or allergic rhinitis among the groups was calculated in children with normal birth weight (>2500 g). Our data failed to show a possible link between hospital admission with SS and development of atopic disease.

- Korpas J. et al.** *Analysis of the cough sound frequency in adults and children with bronchial asthma.* Acta Physiol Hung. 2003; 90(1) : 27-34.p Abstract: It is well known that the frequency distribution of cough sound varies in different pathological conditions. Its identification could have diagnostic value. In this study the cough sound frequency in adults (n=20, 51.7 +/- 11 yrs), children (n=21, 11.8 +/- 0.4 yrs) asthmatics and healthy volunteers (n=25, 21 yrs) was explored. All patients were suffering from bronchial asthma. They were on a stable therapeutic regime and in a quiet status. Voluntary cough sound was recorded by a microphone and a tape recorder and digitally processed. Overlapping technique and Fast Fourier Transform were used to estimate the sound spectra. The records were smoothed by the method of Pascal triangle. They demonstrate the mean values of cough sound spectra. The registered pseudo three-dimensional plots of cough sound frequency (1 K spectra as function in time) of adults showed that the intensity of frequencies increased from 100 to 900 Hz in 3-4 waves. These frequencies afterwards decreased and between 1 to 2 kHz a smaller elevation was present. The spectra of children resembled to the spectrum of adults but had a smoother course. The spectra of asthmatics had some specificity and differed from the spectrum of healthy volunteers.
- Koschel M.J.** *Emergency: is it child abuse?* Am J Nurs. 2003; 103(4) : 45-6.p
- Kosrirukvongs P. et al.** *Allergic conjunctivitis.* Asian Pac J Allergy Immunol. 2001; 19(4) : 237-44.p Abstract: The purpose of this research is to study the clinical features and risk factors of various types of allergic conjunctivitis. Four hundred and forty-five patients with a history of itching, foreign body sensation, lacrimation and red eyes were examined, and a skin test was performed and assessed to grade the severity. The mean age of the subjects was 24.5 +/- 16.3 years with female preponderance, except for vernal keratoconjunctivitis. The majority of the patients had perennial allergic conjunctivitis. Ninety-five percent of the patients had associated allergic diseases, especially allergic rhinitis. Sixty-six percent of the patients had a family history of atopy. Most patients had symptoms at night. Symptoms persisted throughout the year and were generally triggered by exposure to house dust. The allergy skin tests to common aero-allergens were positive in 95% of patients tested. Common allergens causing sensitization were house-dust mites, house dust, cockroaches, and grass pollen. Environmental control and avoidance of these allergens should be stressed in the management of these conditions.
- Kostianev S.S. et al.** *Tidal breathing analysis in school-age children. Comparison with the parameters of forced expiration.* Folia Med (Plovdiv). 2004; 46(3) : 32-40.p Abstract: Tidal breathing analysis is a method which has the potential to be used for distinguishing and follow-up of airflow obstruction (AFO) in infants, children and critically ill patients. The aim of the present study was to analyse the tidal breathing parameters (TBP) in healthy and in asthmatic school-age children and to compare them with the parameters of forced expiration. SUBJECTS: Two hundred and twenty five healthy children and 100 asthmatics (7 to 14 years- old) took part in the present study. RESULTS: The results show that TBPs exhibit great inter- and intraindividual variability, even if the mean value of 10 consecutive breathing cycles is used. Parameters that reflect the tidal expiratory flow pattern--V(PTEF)/V(E) and T(PTEF)/T(E) demonstrate high variability and no correlation with age, sex and anthropometric parameters in healthy children. These indices are useful for detection of acute changes in bronchomotor tonus in asthmatics - V(PTEF)/V(E) = 36.1 +/- 6.6% vs. 32.6 +/- 6.2% (methacholine) vs. 37.4 +/- 7.5% (salbutamol) and T(PTEF)/T(E) = 34.2 +/- 6.2% vs. 28.6 +/- 7.8% vs. 35.3 +/- 7.5%, resp. (P < 0.05 everywhere; n = 34) as well as for discriminating a group of subjects with AFO vs. controls (V(PTEF)/V(E) = 30.9 +/- 6.5% vs. 35.3 +/- 8.0%; P = 0.005, and T(PTEF)/T(E) = 29.0 +/- 6.7% vs. 32.8 +/- 7.6%; P = 0.016). The evaluation of the area under the ROC curves (AUC) in the asthmatic group showed weak discriminative capacity of T(PTEF)/T(E) and V(PTEF)/V(E) in comparison to FEV1 (AUC of T(PTEF)/T(E) = 0.62; 95% CI 0.51-0.74). CONCLUSIONS: Tidal breathing parameters could add insight to the functional profile but are not capable of substituting forced expiration regarding detection of overt airflow obstruction in school-age children.
- Kotaniemi-Syrjanen A. et al.** *Respiratory syncytial virus infection in children hospitalized for wheezing: virus-specific studies from infancy to preschool years.* Acta Paediatr. 2005; 94(2) : 159-65.p Abstract: AIM: To evaluate whether the presence of immunoglobulin G (IgG) antibodies against respiratory syncytial virus (RSV) in early childhood is associated with later asthma, and to evaluate a new diagnostic test for RSV, reverse-transcription polymerase chain reaction (RT-PCR), comparing it to the antigen and antibody assays initially used in RSV diagnostics in the present cohort. METHODS: At the start of the study in 1992-1993, RSV was studied by antigen detection (using time-resolved fluoroimmunoassay) and complement-fixing antibody assay. Advances in methodology allowed us to supplement RSV studies by RT-PCR in frozen nasopharyngeal aspirates obtained on admission, and by specific IgG antibodies (using enzyme immunoassay) in frozen serum samples obtained during the follow-up. RESULTS: On admission, 29 of the 100 children hospitalized for wheezing at <2 y of age were RSV positive. When compared with conventional methods, the sensitivity of RT-PCR was 83% (100% w.r.t. antigen detection) and its specificity was 92% in diagnosing RSV infection. RSV-specific IgG antibody concentrations rose with age, but were not predictive of asthma at any age. In the present cohort, wheezing without RSV was particularly associated with increased risk for later childhood asthma. CONCLUSION: Hospitalization for wheezing in infancy is associated with increased risk for later childhood asthma, particularly in children without RSV infection on admission, although children with RSV have also slightly increased risk for later asthma. However, mere serological evidence of RSV infection is not associated with the development of asthma. In addition to RSV, more attention should be paid to less virulent agents in order to find those wheezing infants who are at particular risk of later childhood asthma.
- Kotaniemi-Syrjanen A. et al.** *Sodium cromoglycate therapy in wheezing infants: preliminary evidence of beneficial outcome at early school age.* Pediatr Int. 2005; 47(6) : 627-34.p Abstract: BACKGROUND: In order to affect the natural course of childhood wheezing and asthma, anti-inflammatory therapy is often prescribed for young wheezing children, but there is lack of long-term follow-up data. METHODS: Eighty-two of the original 100 children, hospitalized for wheezing under the age of 2 years in 1992-1993, were re-examined at school age in 1999. The children had participated in an open, randomized, parallel-group trial including a 4-month intervention with inhaled sodium cromoglycate (SCG) or budesonide (BUD). The baseline data, including data on atopy, eosinophilia and viral etiology, were prospectively collected on admission. RESULTS: At early school age (median 7.2 years), asthma was present in 33 (40%) children. There was less asthma in the original SCG (21%) than in the control group (54%) (OR 0.23; 95% CI 0.07-0.77). The figure was 46% in the BUD group. When the analyses were performed separately for atopic and non-atopic infants, the difference was significant only among atopics. The lowered risk for asthma in the SCG group remained significant in the multivariate logistic regression analysis when adjusted for age, sex and atopy, and further when adjusted for earlier episodes of wheezing and respiratory syncytial virus identification. However, after adjustment for blood eosinophilia, the significance was lost, albeit the risk for asthma remained low (OR 0.21; 95% CI 0.04-1.12). A sensitivity analysis, which was done by including the six drop-outs of the SCG group as unfavorable and the 12 drop-outs of other groups as favorable outcomes in the model, did not change the direction of the result (OR 0.70; 95% CI 0.26-1.89). CONCLUSIONS: An early

SCG intervention in infants hospitalized for wheezing was associated with a lowered risk for early school-age asthma, especially in infants with evidence of atopy.

Kouriba B. et al. *Analysis of the 5q31-q33 locus shows an association between IL13-1055C/T IL13-591A/G polymorphisms and Schistosoma haematobium infections.* J Immunol. 2005; 174(10) : 6274-81.p **Abstract:** Millions of humans are exposed to schistosome infections, which cause severe kidney and liver disease and 280,000 deaths annually. Th2-mediated immunity is critical to human defenses against this pathogen and susceptibility to infection is controlled by a major genetic locus that includes IL4, IL5, and IL13 genes. These observations led us to evaluate whether certain polymorphisms in IL4, IL5, or IL13 determine schistosome infection. The study was performed in two Dogon villages where Schistosoma haematobium is endemic. Schistosome infections were evaluated by counting eggs and measuring worm Ags in urine. Genetic polymorphisms were determined by restriction enzyme analysis or by primer extension and denaturing high-performance liquid chromatography analysis. Associations were tested using family-based association tests and logistical regression analysis. The alleles IL13-1055C (p = 0.05) and IL13-591A (p = 0.01) are shown, by family-based association test, to be preferentially transmitted to children with the 10% highest infections. A logistic regression analysis that included IL13-1055 G/G, G/T and T/T genotypes, age, gender, and village of residency, applied to the whole study population, showed that subjects bearing the IL13-1055T/T genotype were on average much less infected than individuals with other genotypes. Previous studies on asthma indicated that the IL13-1055T allele increased gene transcription, which is in agreement with the fact that this cytokine enhances resistance to infection by schistosome in humans.

Kozyrskyj A.L. et al. *Antibiotic treatment of wheezing in children with asthma: what is the practice?* Pediatrics. 2006; 117(6) : e1104-10.p **Abstract:** **OBJECTIVE:** Antibiotics are not recommended for the treatment of wheezing in children with asthma, but little is known about their use. This study was undertaken to evaluate trends and determinants of antibiotic use in children with wheezing during the fiscal years 1995 through 2001. **METHODS:** Using the population-based health care and prescription databases in Manitoba, Canada, this descriptive study examined time trends in antibiotic prescription use for wheezing episodes in a population of children with asthma. The likelihood of receiving an antibiotic prescription according to child and physician characteristics also was determined. Annual population-based rates of antibiotic prescriptions for wheezing episodes were modeled by age and antibiotic class, using general estimating equations. The odds ratio for receiving an antibiotic prescription according to child demographics and physician factors was determined from hierarchical linear modeling. **RESULTS:** The antibiotic prescription rate for wheezing decreased by 28% from 708 prescriptions per 1000 children with asthma in 1995 to 511 prescriptions in 2001. Fifteen-fold increases in use were observed for broader spectrum macrolides in preschool children. Twenty-three percent of physician visits for wheezing resulted in an immediate antibiotic prescription, but this percentage increased to 64% for antibiotics that were received within 7 days of the episode. General practitioners prescribed antibiotics more often than did pediatricians. Physicians who were not trained in Canada or the United States were 40% more likely to prescribe antibiotics than their counterparts. **CONCLUSIONS:** Antibiotic use for wheezing in children declined in the 1990s, but the increased use of broader spectrum macrolides has implications for antibiotic resistance. A link between antibiotic prescribing and physician specialty and location of training identifies opportunities for intervention.

Kozyrskyj A.L. et al. *Childhood wheezing syndromes and healthcare data.* Pediatr Pulmonol. 2003; 36(2) : 131-6.p **Abstract:** There is

convincing evidence that several distinct wheezing syndromes exist in childhood. The purpose of this research was to assess the potential of using healthcare utilization profiles to identify wheezing syndromes in children which are distinct from asthma. Using population-based healthcare administrative data, a cohort of children, aged 5-15 years, with bronchitis diagnoses from time of birth to 1995, but no physician diagnoses of asthma, was followed over the period January 1996-March 1998. In this follow-up period, 13% had subsequent healthcare utilization for asthma, 23% had continued healthcare utilization for bronchitis, and 64% had no further healthcare utilization. The likelihood of bronchitis vs. asthma outcomes was determined for a variety of asthma risk factors. In a cohort of 11,043 children with initial healthcare contact for bronchitis but not asthma, two potentially distinct entities of bronchitis emerged from our data: 1) transient bronchitis, similar to transient wheezing of early childhood, which was associated with winter-only healthcare utilization and absence of allergy, and 2) recurrent bronchitis which differed from asthma on the basis of winter-only healthcare utilization, prematurity at birth, absence of allergy, and low socioeconomic status. Healthcare administrative records can be used to describe the natural history of wheezing in children and to identify markers which may discriminate asthma from other syndromes.

Kozyrskyj A.L. et al. *Income-based drug benefit policy: impact on receipt of inhaled corticosteroid prescriptions by Manitoba children with asthma.* CMAJ. 2001; 165(7) : 897-902.p **Abstract:** **BACKGROUND:** Drug benefit policies are an important determinant of a population's use of prescription drugs. This study was undertaken to determine whether a change in a provincial drug benefit policy, from a fixed deductible and copayment system to an income-based deductible system, resulted in changes in receipt of prescriptions for inhaled corticosteroids by Manitoba children with asthma. **METHODS:** Using Manitoba's health care administrative databases, we identified a population-based cohort of 10,703 school-aged children who met our case definition for asthma treatment before and after the province's drug benefit policy was changed in April 1996. The effects of the program change on the probability of receiving a prescription for an inhaled corticosteroid and on the mean number of inhaled corticosteroid doses dispensed were compared between a group of children insured under other drug programs (the comparison group) and 2 groups of children insured under the deductible program: those living in low-income neighbourhoods and those living in higher-income neighbourhoods. All analyses were adjusted for a measure of asthma severity. **RESULTS:** For higher-income children with severe asthma who were covered by the deductible program, the probability of receiving an inhaled corticosteroid prescription and the mean annual number of inhaled corticosteroid doses declined after the change to the drug policy. A trend toward a decrease in receipt of prescriptions was also observed for low-income children, but receipt of prescriptions was unaltered in the comparison group. Before the policy change, among children with severe asthma, the mean annual number of inhaled corticosteroid doses was lowest for low-income children, and this pattern persisted after the change. Among children with mild to moderate asthma, those covered by the deductible program (both low income and higher income) were less likely to receive prescriptions for inhaled corticosteroids than those in the comparison group, and this difference was statistically significant for the higher-income children. **INTERPRETATION:** The change to an income-based drug benefit policy was associated with a decrease in the use of inhaled corticosteroids by higher-income children with severe asthma and did not improve use of these drugs by low-income children.

Kozyrskyj A.L. et al. *Inhaled corticosteroids in childhood asthma: Income differences in use.* Pediatr Pulmonol. 2003; 36(3) : 241-7.p **Abstract:** Asthma hospitalization rates in children increase with decreasing level of household income. This research was undertaken to determine whether use of inhaled corticosteroid drugs, which can

prevent asthma hospitalizations, followed a similar socioeconomic gradient in children with asthma. We performed a cross-sectional study of association, using population-based prescription and healthcare data sources. Our subjects were 16,862 Manitoba children, aged 5-15 years, with prescriptions for asthma drugs during January 1995-March 1996. Our measures were adjusted for asthma severity, physician specialty, and proportion of children with an inhaled corticosteroid prescription by neighborhood income. Forty-five percent of children treated for asthma had at least one inhaled corticosteroid prescription during January 1995-March 1996. The proportion of children with inhaled corticosteroid prescriptions decreased with successive decreases in neighborhood income. The socioeconomic gradient in the likelihood of an inhaled corticosteroid prescription was most evident among children with mild-moderate asthma who were not in the care of an asthma specialist. In conclusion, a socioeconomic gradient in the use of inhaled corticosteroids prescriptions can be found among children with universal access to healthcare and drug insurance.

Kozyrskij A.L. et al. *Socioeconomic status, drug insurance benefits, and new prescriptions for inhaled corticosteroids in schoolchildren with asthma.* Arch Pediatr Adolesc Med. 2001; 155(11) : 1219-24.p
Abstract: BACKGROUND: Low-income children with asthma are less likely to receive inhaled corticosteroid prescriptions that can prevent asthma morbidity. OBJECTIVE: To determine whether the receipt of inhaled corticosteroids in children with asthma is related to household socioeconomic status and type of drug insurance. DESIGN: Using population-based prescription and health care data from Manitoba, a cohort study of the determinants of receiving new prescriptions for inhaled corticosteroids was conducted in children treated with asthma drugs. PARTICIPANTS: School-aged children (n = 12 481) receiving asthma prescriptions from January 1995 to March 1996 but no inhaled corticosteroid prescriptions in the initial 6-month period. MAIN OUTCOME MEASURES: Household socioeconomic and drug insurance predictors of the probability of receiving a new inhaled corticosteroid prescription from July 1995 to March 1998, following adjustment for disease and health care utilization factors. RESULTS: In comparison with higher-income children insured through a provincial cost-sharing drug plan, the adjusted likelihood ratio for a new inhaled corticosteroid prescription was 0.88 (95% confidence interval, 0.80-0.97) in low-income children insured through the same drug plan and 0.82 (95% confidence interval, 0.76-0.88) in children receiving prescriptions at no charge through provincial income assistance or First Nations benefits programs (Winnipeg, Manitoba). CONCLUSION: Independent of asthma severity, type of drug insurance, or health care utilization patterns, low-income children with asthma are significantly less likely to receive inhaled corticosteroid prescriptions.

Krauss H. et al. *A child with bronchial asthma--his functioning in a peer group.* Rocznik Akad Med Białymost. 2005; 50 Suppl 1 : 210-2.p
Abstract: PURPOSE: Aim of the study is to show problems parents have to account for in the process of treatment and their knowledge how to solve them. MATERIAL AND METHODS: Fifty girls and boys aged 5-12 years were participated in this study. The research employed an own questionnaire prepared for this particular purpose. It consisted of three parts: the first part dealt with social-demographic data, the second one with the age of a child at the onset of asthma and accompanying it problems, and finally, the third part was concerned with the knowledge of parents about asthma and its treatment at the time of exacerbation. RESULTS: Out of all children under study, 60% were boys and 40% were girls, 85% of them come from a district town and 15% from rural areas. Almost 42% of parents answered that the most frequent reaction of the peers and particularly children attending the same class to this information was understanding. Only 11% of peers were able to help the children with bronchial asthma in difficult moments. CONCLUSIONS: The study has shown that hay fever and atopic dermatitis accompanying

bronchial asthma markedly make their functioning among peers difficult. Bronchial asthma makes most children suffering from it resign from favorite games and plays connected with physical effort. The attitude of peers to these children can be described as indifferent.

Krieger J.W. et al. *The Seattle-King County Healthy Homes Project: a randomized, controlled trial of a community health worker intervention to decrease exposure to indoor asthma triggers.* Am J Public Health. 2005; 95(4) : 652-9.p
Abstract: OBJECTIVES: We assessed the effectiveness of a community health worker intervention focused on reducing exposure to indoor asthma triggers. METHODS: We conducted a randomized controlled trial with 1-year follow-up among 274 low-income households containing a child aged 4-12 years who had asthma. Community health workers provided in-home environmental assessments, education, support for behavior change, and resources. Participants were assigned to either a high-intensity group receiving 7 visits and a full set of resources or a low-intensity group receiving a single visit and limited resources. RESULTS: The high-intensity group improved significantly more than the low-intensity group in its pediatric asthma caregiver quality-of-life score (P=.005) and asthma-related urgent health services use (P=.026). Asthma symptom days declined more in the high-intensity group, although the across-group difference did not reach statistical significance (P=.138). Participant actions to reduce triggers generally increased in the high-intensity group. The projected 4-year net savings per participant among the high-intensity group relative to the low-intensity group were 189-721 dollars. CONCLUSIONS: Community health workers reduced asthma symptom days and urgent health services use while improving caregiver quality-of-life score. Improvement was greater with a higher-intensity intervention.

Kristinsson G. et al. *PR-segment changes in childhood pericarditis.* J Pediatr. 2002; 140(3) : 378.p

Kristjansson S. et al. *Respiratory syncytial virus and other respiratory viruses during the first 3 months of life promote a local TH2-like response.* J Allergy Clin Immunol. 2005; 116(4) : 805-11.p
Abstract: BACKGROUND: Respiratory syncytial virus (RSV) infections during infancy are considered to be a risk factor for developing asthma and possibly allergic sensitization. OBJECTIVE: The aim of this study was to investigate the cytokines, chemokines, and eosinophil cationic protein in the nasopharyngeal secretions of infants < or = 7 months of age with RSV infections or other respiratory viral infections and healthy infants as controls. Groups were also analyzed according to age, < or = 3 months and >3 months, and the levels were compared within and between groups. RESULTS: Thirty-nine infants with RSV, 9 with influenza or parainfluenza virus infections and 50 controls with no history of infections, were enrolled in the study. The RSV-infected infants had significantly higher levels of IL-4; macrophage inflammatory protein 1beta, a chemoattractant for T cells; and eosinophil cationic protein in nasopharyngeal secretions compared with the control group. The levels of the TH2 cytokine IL-4 were significantly higher in RSV-infected infants < or = months of age compared with RSV-infected infants >3 months of age. In infants < or = 3 months of age, infections with influenza or parainfluenza virus caused TH2-like responses similar to those produced by RSV. CONCLUSION: Infections with RSV as well as with influenza and parainfluenza virus during early infancy preferentially promote a TH2-like response in the nose with local production of IL-4, IL-5, and macrophage inflammatory protein 1beta and infiltration and activation of eosinophils.

Krolak E. et al. *Heavy metal pollution and children morbidity rate in the Rejowiec Fabryczny area.* Ann Univ Mariae Curie Skłodowska [Med]. 2004; 59(2) : 397-402.p
Abstract: The concentrations of heavy metals (Pb, Cd, Cr, Cu, Mn and Zn) were analyzed in the soils

of the Rejowiec Fabryczny area. The levels of these metals were also measured in the raw materials used in cement production, in cement itself, and in dust removed by electrofilters mounted over the clinker kilns. Morbidity rates were also analyzed of children up to 6 years of age examined and treated in the local ambulatory medical center in Rejowiec Fabryczny in 1982 and 2002. The soils of the Rejowiec Fabryczny area showed elevated levels of Pb, Cd, Zn and Cu, comparing to the reference values. Installation of electrofilters in the cement plant resulted in a considerable reduction of Pb and Cd discharge. It was observed that the frequency of respiratory disorders in children from the Rejowiec Fabryczny area was higher comparing to other regions. Over the last 20 years, the frequency of allergies and asthma increased.

Krone C.A. *Diisocyanates and nonoccupational disease: a review.* Arch Environ Health. 2004; 59(6) : 306-16.p **Abstract:** More than 32 million people in the United States suffer from chronic lung diseases; 12 million experienced at least one asthma attack in 2002. The causes of this "epidemic" are complex and uncertain; however, there is a strong possibility that environmental exposures play a role. The most common and well-studied cause of occupational asthma is diisocyanates, but their use in consumer products as a potential cause of respiratory disease in the general population has been overlooked. These substances are found in or are used to produce an array of polyurethane-containing products, including adhesives, sealants, paints, flexible foams, and rigid foams, among others. The world market for polyurethane products has tripled since 1985 to more than 9.3 billion kg in the year 2000. In this article, the author reviews biologically plausible explanations, as well as the epidemiologic, experimental, and clinical evidence for the role of diisocyanates and polyurethanes in the genesis of nonoccupational allergy and respiratory disease.

Krone C.A. et al. *Polyurethanes and childhood asthma.* Med Sci Monit. 2003; 9(12) : HY39-43.p **Abstract:** BACKGROUND: Asthma is the most common chronic disease of children. Its prevalence in affluent nations has steadily and dramatically increased in recent decades. Genetic and environmental factors play a role in development of atopy and asthma. Imbalance in the immune system favoring respiratory diseases has been linked to exposure to environmental stressors (e.g. biological and chemical) very early in life. Isocyanates, used in the production of polyurethane, can elicit asthma and produce immune responses (e.g. antibodies, cytokines, etc.) typical of atopy. MATERIAL/METHODS: Numerous medical materials that directly contact human neonates are constructed of polyurethanes. A detailed survey and listing of such materials was undertaken in the neonatal unit of a large urban hospital. Representative samples of polyurethane-containing materials were tested for isocyanate residues using a semi-quantitative colorimetric method. RESULTS: Isocyanate residues were detected in wound dressings, adhesive films, oximetry sensors, etc. that directly contact neonatal skin. CONCLUSIONS: Dermal exposure to polyurethane and, thus, to isocyanates could occur early in life through contact with medical materials. In an animal model, dermal exposure to isocyanates leads to dermal sensitization and asthma. We postulate that dermal contact with polyurethane-containing medical materials may be involved in dysregulation of the neonatal immune system and could predispose infants to the development of childhood asthma.

Kuhlthau K.A. et al. *Comparing a diagnosis list with a survey method to identify children with chronic conditions in an urban health center.* Ambul Pediatr. 2002; 2(1) : 58-62.p **Abstract:** OBJECTIVE: To compare a diagnosis list to the Questionnaire for Identifying Children with Chronic Conditions (QuICCC) to assess their relative usefulness as measures for identifying children with chronic conditions. METHODS: Comparison of health encounter data and survey data for a cohort of 304 children aged 0-18 years at an urban health center affiliated with a teaching hospital. We used 2 strategies to identify

children with a chronic condition: 1) identification by the existence of an encounter with an International Classification of Diseases, Ninth Revision code indicating a chronic condition and 2) identification by the QuICCC. We compared the characteristics of children identified by the diagnosis list with those of children identified by the QuICCC. RESULTS: This population had high rates of chronic conditions, with 44% identified by the diagnosis list and 36% identified by the QuICCC. These 2 methods jointly identified 66% of children, yet only half (53%) of the children who had a diagnosis of a chronic condition in the encounter data were identified by the QuICCC. Asthma, anorexia, developmental delay, and adjustment reaction were among the common chronic conditions for children identified by the diagnosis list approach only. CONCLUSIONS: We found only moderate concordance among the children identified as having chronic conditions by a diagnosis list and by the QuICCC in this high-risk urban population. These different results indicate that encounter data and survey approaches do not serve as simple substitutes for identifying children with chronic conditions for clinical or monitoring purposes.

Kull I. et al. *Breast-feeding reduces the risk of asthma during the first 4 years of life.* J Allergy Clin Immunol. 2004; 114(4) : 755-60.p **Abstract:** BACKGROUND: The evidence for a preventive effect of breast-feeding on asthma and other allergic diseases in childhood is inconclusive. OBJECTIVE: The aim of this study was to investigate the effect of breast-feeding on asthma and sensitization to airborne allergens among children up to 4 years of age. METHODS: A birth cohort of 4089 children was followed. Exposure data were collected at 2 months and 1 year of age. The total dose of breast milk was estimated by combining periods of exclusive and partial breast-feeding. Outcomes data were collected at 1, 2, and 4 years of age. The response rate at 4 years was 90%, and 73% participated in a clinical investigation, including blood sampling for analysis of specific IgE and lung function testing. Children with onset of wheeze during lactation (n=217) were excluded in some of the analyses to avoid disease-related modification of exposure. RESULTS: Exclusive breast-feeding for 4 months or more reduced the risk of asthma at the age of 4 years (odds ratio [OR], 0.72; 95% CI, 0.53-0.97), irrespective of sensitization to common airborne allergens (P=.72). Excluding children with wheeze during lactation tended to strengthen the risk estimate (OR, 0.64; 95% CI, 0.46-0.88). A duration of 3 months or more of partial breast-feeding seemed to offer additional protection; exclusive breast-feeding for 3 to 4 months combined with partial breast-feeding for 3 months or more resulted in an OR of 0.44 (95% CI, 0.21-0.87). The effects tended to be stronger in children without heredity for allergy (P interaction=.36). CONCLUSION: Breast-feeding reduces the risk of asthma during the first 4 years of life.

Kull I. et al. *Breast-feeding reduces the risk for childhood eczema.* J Allergy Clin Immunol. 2005; 116(3) : 657-61.p **Abstract:** BACKGROUND: The evidence for a preventive effect of breast-feeding on the development of eczema in childhood remains controversial. OBJECTIVE: To investigate the effect of breast-feeding in various phenotypes of eczema to 4 years. METHODS: A birth cohort of 4089 children made up the study base. Data on breast-feeding, allergic symptoms, and potential confounders were obtained from questionnaires when the children were 2 months and 1, 2, and 4 years old. At 4 years, blood specific IgE was analyzed. Children with symptoms of eczema and asthma during the period of breast-feeding were excluded in most analyses on risk assessment of eczema and asthma, respectively, to avoid disease-related modification of exposure. RESULTS: Exclusive breast-feeding for >or=4 months reduced the risk for eczema at the age of 4 years (odds ratio [OR], 0.78; 95% CI, 0.63--0.96) irrespective of combination with asthma, sensitization to common allergens, or parental allergic disease. This decreased risk was most evident for children with onset of eczema during the first 2 years persisting to 4 years (OR, 0.59; 95% CI, 0.45-0.77). Among children with early-onset eczema, irrespective of

persistence, followed by late onset of asthma or early-onset asthma irrespective of persistence, followed by late-onset eczema to 4 years, a protective effect of breast-feeding was also seen (OR, 0.48; 95% CI, 0.30–0.76). CONCLUSION: Breast-feeding 4 months or more reduces the risk for eczema and onset of the allergy march to age 4.

Kull I. et al. *Breast feeding and allergic diseases in infants—a prospective birth cohort study.* Arch Dis Child. 2002; 87(6) : 478-81.p Abstract: AIMS: To investigate the effect of breast feeding on allergic disease in infants up to 2 years of age. METHODS: A birth cohort of 4089 infants was followed prospectively in Stockholm, Sweden. Information about various exposures was obtained by parental questionnaires when the infants were 2 months old, and about allergic symptoms and feeding at 1 and 2 years of age. Duration of exclusive and partial breast feeding was assessed separately. Symptom related definitions of various allergic diseases were used. Odds ratios (OR) and 95% confidence intervals (CI) were estimated in a multiple logistic regression model. Adjustments were made for potential confounders. RESULTS: Children exclusively breast fed during four months or more exhibited less asthma (7.7% v 12%, OR(adj) = 0.7, 95% CI 0.5 to 0.8), less atopic dermatitis (24% v 27%, OR(adj) = 0.8, 95% CI 0.7 to 1.0), and less suspected allergic rhinitis (6.5% v 9%, OR(adj) = 0.7, 95% CI 0.5 to 1.0) by 2 years of age. There was a significant risk reduction for asthma related to partial breast feeding during six months or more (OR(adj) = 0.7, 95% CI 0.5 to 0.9). Three or more of five possible allergic disorders—asthma, suspected allergic rhinitis, atopic dermatitis, food allergy related symptoms, and suspected allergic respiratory symptoms after exposure to pets or pollen—were found in 6.5% of the children. Exclusive breast feeding prevented children from having multiple allergic disease (OR(adj) = 0.7, 95% CI 0.5 to 0.9) during the first two years of life. CONCLUSION: Exclusive breast feeding seems to have a preventive effect on the early development of allergic disease—that is, asthma, atopic dermatitis, and suspected allergic rhinitis, up to 2 years of age. This protective effect was also evident for multiple allergic disease.

Kumar S.S. et al. *Amrita Bindu—an antioxidant inducer therapy in asthma children.* J Ethnopharmacol. 2004; 90(1) : 105-14.p Abstract: Studies all over the world on the therapeutic use of antioxidants as supplements has revealed their capacity to control inflammatory processes. Amrita Bindu an Ayurvedic health food supplement has already shown to be an antioxidant inducer and to combat free radical-mediated tissue damage studied in rats. Amrita Bindu is a salt-spice herbal mixture designed for positive health. It was tested as a supplement to therapy for a period of 12 months in 36 children suffering from asthma. Asthma is a chronic inflammatory disease with excessive free radical generation in lungs and blood cells. The patients were followed up by monitoring their clinical conditions, therapeutic doses of anti-asthmatic drugs, free radical generation, lipid peroxidation (LPO) and antioxidants in blood. At the end of 3 months of Amrita Bindu supplementation, the patients had stopped all anti-asthmatic medications and were free from attacks of asthma.

Kumaratne M. et al. *Addition of ipratropium to nebulized albuterol in children with acute asthma presenting to a pediatric office.* Clin Pediatr (Phila). 2003; 42(2) : 127-32.p Abstract: A prospective, randomized, double-blind study was conducted to determine whether there was any benefit to the addition of ipratropium to a single nebulized albuterol treatment in infants and children with mild to moderate acute asthma presenting to a pediatric office. There were no significant differences between the albuterol group and the combined albuterol-ipratropium group in the relief of the respiratory distress, disposition of the patients from the office, or in the incidence of relapse. The addition of ipratropium to nebulized albuterol is of no added benefit in the treatment of infants and children with mild-to-moderate acute asthma presenting to a pediatric office.

Kuo I.C. et al. *An extensive study of human IgE cross-reactivity of Blo t 5 and Der p 5.* J Allergy Clin Immunol. 2003; 111(3) : 603-9.p Abstract: BACKGROUND: Dual sensitization by *Blomia tropicalis* and *Dermatophagoides pteronyssinus* mites is common in tropical and subtropical countries. The human IgE cross-reactivity between clinical important group 5 allergens, Blo t 5 and Der p 5, remains controversial. OBJECTIVE: This study was undertaken to assess the levels of the IgE cross-reactivity between Blo t 5 and Der p 5 by using sera from a large cohort of asthmatic children in subtropical and tropical countries. METHODS: Purified recombinant Blo t 5 and Der p 5 were produced in *Pichia pastoris* and tested against sera from 195 asthmatic children. The IgE cross-reactivity was examined by direct, inhibitory and competitive human IgE enzyme-linked immunosorbent assay as well as skin prick tests. RESULTS: The Blo t 5 IgE responses were 91.8% (134 of 146) and 73.5% (36 of 49) for Taiwanese and Malaysian sera, respectively. The Blo t 5 specific IgE titers were significantly higher than those of Der p 5 ($P < .02$). The correlation of IgE reactivity between Blo t 5 and Der p 5 was low, and only limited cross-reactivity was observed. This was further confirmed by the dose-response inhibition studies. Skin prick tests performed on asthmatic children in Thailand also showed differential IgE response to Blo t 5 and Der p 5. CONCLUSION: By using a large panel of asthmatic sera and a combination of in vitro and in vivo assays, the major allergen of *B. tropicalis* in tropical and subtropical regions, Blo t 5, exhibits low levels of IgE cross-reactivity with homologous Der p 5. These findings suggest that highly specific clinical reagents are necessary for precise diagnosis and immunotherapeutic treatment of sensitization to group 5 mite allergens.

Kupczyk M. et al. *Long-term deterioration of lung function in asthmatic outpatients.* Respiration. 2004; 71(3) : 233-40.p Abstract: BACKGROUND: Although the long-term deterioration of lung function in asthmatic patients has been described, the exact mechanism remains to be determined. OBJECTIVES: The aim of this study was to find correlations between age, sex, atopic status, duration of asthma, asthma severity and the decline in pulmonary function. METHOD: The medical histories of 1,006 randomly chosen asthmatic outpatients were studied and retrospective data on asthma duration, spirometry results, treatment and symptomatology were gathered. A screening spirometry was performed. RESULTS: 598 women and 408 men (age: 44.59, range 12-95 years) participated in the study. Intermittent asthma was diagnosed in 35.4%, chronic mild asthma in 33.4%, moderate asthma in 23.8% and severe asthma in 7.45% of the patients. Statistically significant correlations between patient age, asthma duration and lung function measurements were found. Linear regression revealed the following differences in lung functions per year of asthma duration: FEV1: -0.882% of predicted; FVC: -0.509% of predicted; FEV1/FVC: -0.324% of predicted. The unadjusted annual decline was 80.1 ml/year ($p = 0.00003$) in FEV1 and 20.5 ml/year ($p = 0.036$) in FVC. A multiple regression model revealed that asthma severity appears to be the strongest factor influencing pulmonary function ($\beta = -0.55$, $p < 0.001$ for FEV1). Also, significant associations between pulmonary function measurements, patient age, atopic status and male sex were noted. CONCLUSIONS: The results of this large cohort study show that asthmatic patients develop a progressive decline in pulmonary function correlated with age, sex, duration of asthma and asthma severity. Early diagnosis and intervention is necessary to ameliorate any potential negative impact of asthma on lung function.

Kurtaran H. et al. *A reappraisal of nasal saline solution use in chronic sinusitis.* Chest. 2003; 124(5) : 2036-7; author reply 2037-8.p

Kurukulaaratchy R.J. et al. *The prevalence of asthma and wheezing illnesses amongst 10-year-old schoolchildren.* Respir Med. 2002;

96(3) : 163-9.p **Abstract:** Asthma and wheezing illnesses carry a significant burden of disease during childhood. Prevalence studies have the capacity to provide invaluable insights into the nature of these common conditions. As part of the Isle of Wight Whole Population Birth Cohort Study (n=1456) we have examined wheezing and asthma development amongst 10-year-old children. At this age 1373 children completed ISAAC written questionnaires whilst 1043 children performed further testing including skin-prick testing, serum inhalant IgE antibody screening, spirometry and bronchial challenge. At 10-years, prevalence of current wheeze was 18.9%, current asthma (symptomatic bronchial hyper-responsiveness--BHR) 14.4% and currently diagnosed asthma (current wheeze and asthma ever--CDA) 13.0%. Both wheezing and asthma at 10 years were associated with average symptom onset at 3 years of age indicating an early life origin for such conditions. Current wheeze (P=0.011) and CDA (P=0.008) showed significant male predominance. Considerable disease morbidity was identified for these states that tended to be greatest amongst children defined asthmatic rather than simply current wheezers. Wheezing and asthma were significantly associated with both atopy (P<0.001) and allergic co-morbidity. Children with these states, particularly current asthma, also demonstrated impaired lung function (FEV1, P<0.001 and FEV1/FVC, P=0.010) and increased BHR (inverse slope, P<0.001). In conclusion, Asthma and wheezing showed substantial prevalence at 10 years of age. Strong associations to male gender, atopy, impaired lung function and BHR were seen for both wheeze and asthma. In regard to prevalence and morbidity characteristics, a questionnaire-based definition of currently diagnosed asthma gave similar results to the use of symptomatic BHR in defining current asthma.

Kurz T. et al. *Multilocus haplotype analyses reveal association between 5 novel IL-15 polymorphisms and asthma.* J Allergy Clin Immunol. 2004; 113(5) : 896-901.p **Abstract:** **BACKGROUND:** IL-15 is a T(H)1-related cytokine that is involved in the inflammatory response in various infectious and autoimmune diseases. IL-15 has recently been shown to be upregulated in T-cell-mediated inflammatory disorders. The observations suggest a potential role for this cytokine in a variety of pathologic conditions, including T(H)1-mediated and T(H)2-mediated inflammatory diseases. **OBJECTIVE:** In this study, we searched for single nucleotide polymorphisms in the whole IL-15 gene and investigated their association with inflammatory and/or atopic phenotypes. **METHODS:** The screening for single nucleotide polymorphisms was performed by single-strand conformation polymorphism analysis. Genotyping of the identified polymorphisms was performed by restriction fragment length polymorphism. Genotypic association analysis used the Armitage trend test. Haplotype frequency estimation and subsequent testing for differences between cases and controls were performed by using the programs FASTEHPLUS and FAMHAP. **RESULTS:** We identified 5 novel noncoding nucleotide sequence variants, all of which were typed in our asthmatic, our atopic, and our control population. According to the Armitage trend test, none of the 5 polymorphisms is associated with the phenotype bronchial asthma or atopy. However, multilocus haplotype analysis based on simulations to find out whether the haplotype frequencies differed between cases and controls by using the program FAMHAP yielded a P value of 6.1×10^{-5} in the asthmatic versus the control population, which is highly significant. Furthermore, we obtained a nominally significant result of P=.0232 for the atopic versus the control population by using FAMHAP. **CONCLUSION:** These results strongly underscore previous findings that suggest a potential role of this cytokine in allergic diseases.

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La Grutta S. et al. *Clinical and biological heterogeneity in children with moderate asthma.* Am J Respir Crit Care Med. 2003; 167(11) : 1490-5.p **Abstract:** To evaluate the relationship between inflammatory markers and severity of asthma in children, the amount of interleukin-8 (IL-8) and granulocyte/macrophage colony-stimulating factor (GM-CSF) released by peripheral blood mononuclear cells, exhaled nitric oxide (FE NO) levels, p65 nuclear factor-kappaB subunit, and phosphorylated IκBα expression by peripheral blood mononuclear cells were assessed in six control subjects, 12 steroid-naïves subjects with intermittent asthma, and 17 children with moderate asthma. To investigate their predictive value, biomarker levels were correlated with the number of exacerbations during a 18-month follow-up period. We found that GM-CSF release was higher in moderate and intermittent asthmatics than in control subjects, whereas IL-8 release was higher in moderate than in intermittent asthmatics and control subjects. FE NO levels were similar among study groups. In moderate asthmatics, IL-8, GM-CSF, and FE NO significantly correlated with the exacerbation numbers. Moreover, p65 and phosphorylated IκBα levels were greater in moderate than in intermittent asthmatics and control subjects. According to GM-CSF, IL-8, and FE NO levels, two distinct subgroups of moderate asthmatics (low and high producers) were identified. High producers experienced more exacerbations than low producers. This study shows ongoing inflammation associated with biological and clinical heterogeneity in moderate asthmatics despite regular treatment and proposes that large prospective studies confirm the importance of biomarkers to assess inflammation and asthma control in children with asthma.

Labrecque M. et al. *Effect of age on the conformity rate to short-acting beta-agonist use criteria in asthma.* J Asthma. 2003; 40(7) : 829-35.p **Abstract:** **STUDY OBJECTIVES:** Assess compliance to asthma guidelines and influence of age concerning inhaled short-acting beta2-agonist (SABA) utilization in 5 to 45-year-old asthmatic subjects in the province of Quebec. **DESIGN:** Population-based retrospective drug utilization review using a computerized database of claims submitted to a private prescription drug insurance plan. **PATIENTS:** Subjects who received at least one outpatient prescription of SABA (age range, 5 to 45 years) for the treatment of asthma between January 1996 and December 1997. **MEASUREMENTS:** Percentages of patients whose use was appropriate according to the criteria regarding the average daily dose of SABA. Use was considered appropriate if the consumption rate corresponded to a maximum of two puffs per day (Salbutamol equivalent) in subjects who did or did not use inhaled corticosteroids (ICS) at an estimated maximum dose of 800 mcg/day of Beclomethasone (BDP) equivalent for the 5 to 11-year-olds and 1000 mcg/day for the 12 to 45-year-olds. **RESULTS:** In 1996, use was found to be appropriate for 74.4% of the 394 patients who received an SABA without ICS as compared with 70.7% for 593 patients in 1997. If we consider those who received an ICS at low to moderate doses, appropriate use was found for 51% of the 375 patients in 1996 and 57.6% for 254 patients in 1997. If we exclude patients who did not renew their SABA, appropriate use drops to 46.3% for 1996 and 34.3% for 1997 for the group who receive SABA without ICS (29.4% and 37.6%, respectively, for those with ICS). There is a relationship between age and appropriateness; the percentage of appropriateness was higher for the younger ones (5 to 14-year-old group; 83% in 1996 and 86% in 1997 for the patients who received a SABA without IS and 58.5% in 1996 and 73% in 1997 for the patients who received a SABA using ICS (p < 0.05). **CONCLUSION:** Our results indicate that adherence to asthma guidelines concerning SABA is poor. SABA are still overused, particularly among ICS users, which might be explained by undertreatment or poor compliance. Appropriate SABA use was significantly more common among younger groups (p < 0.05). This can be explained by better treatment in that age group, better compliance or less severe asthma.

- Laerum B.N. et al.** *Is birth weight related to lung function and asthma symptoms in Nordic-Baltic adults?* *Respir Med.* 2004; 98(7) : 611-8.p **Abstract:** Studies of birth characteristics and respiratory outcomes show contradictory findings. We wanted to investigate the association of birth weight with adult lung function as well as asthma symptoms while addressing the influence of demographic and environmental factors. Data was collected from the birth records of 1683 men and women born in 1947-1973 who were included in 6 Nordic-Baltic population samples investigated within the European Community Respiratory Health Survey (ECRHS). In the adults, an increase in birth weight from below 2500 g to above 4000 g was associated with an increase from 96% to 104% predicted one-second forced expiratory volume ($P < 0.01$) and from 1.00% to 107% predicted forced vital capacity ($P < 0.01$). However, birth weight was not associated with symptoms of asthma. After adjustment for birth length, gender, age, study centre, adult BMI, allergic rhinitis, parental and adult tobacco smoke exposure in multivariate regression analyses, birth weight was not associated with adult lung function or asthma symptoms. Further sub-sample analyses revealed no influence of gestational age, gender, age or geographical area. In this historic prospective cohort study an association was neither found between birth weight and adult lung function nor between birth weight and asthma symptoms.
- Lafata J.E. et al.** *Risk factors for emergency department use among children with asthma using primary care in a managed care environment.* *Ambul Pediatr.* 2002; 2(4) : 268-75.p **Abstract:** **OBJECTIVE:** To identify risk factors for emergency department (ED) use among children with asthma using primary care in a managed care environment. **DESIGN:** Using automated data sources, children with asthma were identified and followed for 2-year periods. We fit logistic regression models using generalized estimating equation approaches to identify ED risk factors. **PATIENTS:** Children with asthma aged 5-14 with a visit to a pediatrician practicing with a large group practice and enrolled in an HMO for 2 consecutive years between 1992 and 1996 ($N = 411$ children). **MAIN OUTCOME MEASURES:** Asthma-related ED use. **RESULTS:** Twenty-three percent of children incurred an asthma-related ED visit. Asthma-related ED use was greater among children with prior asthma-related ED use (OR [odds ratio] = 8.26, 95% CI [confidence interval] = 4.79-14.25), decreased with increasing age (OR = 0.87, 95% CI = 0.79-0.96) and frequency of visits to a primary care physician for asthma (OR = 0.82, 95% CI = 0.70-0.96), and tended to be less among children who saw an allergist (OR = 0.59, 95% CI = 0.33-1.04). No significant relationship was found between asthma-related ED use and race, household income, or other patient characteristics. **CONCLUSIONS:** Targeting children with prior asthma-related ED use and encouraging routine primary care visits as well as the use of an allergist may afford opportunities to reduce ED use among children with asthma currently receiving primary care.
- Lai C.K. et al.** *Asthma control in the Asia-Pacific region: the Asthma Insights and Reality in Asia-Pacific Study.* *J Allergy Clin Immunol.* 2003; 111(2) : 263-8.p **Abstract:** **BACKGROUND:** Few data on asthma management are available for the Asia-Pacific region. **OBJECTIVE:** This study examined asthma symptoms, health care use, and management in the Asia-Pacific region. **METHODS:** We performed a cross-sectional survey, followed by administration of a questionnaire in a face-to-face setting in the respondents' homes in their language of choice. Urban centers in 8 areas were surveyed: China, Hong Kong, Korea, Malaysia, The Philippines, Singapore, Taiwan, and Vietnam. **RESULTS:** A population sample of 3207 respondents with physician-diagnosed asthma was identified by screening 108,360 households. Daytime asthma symptoms were reported by 51.4% of respondents, and 44.3% reported sleep disturbance caused by asthma in the preceding 4 weeks. At least 2 in every 5 respondents (43.6%) had been hospitalized, attended a hospital emergency department, or made unscheduled emergency visits to other health care facilities for treatment of asthma during the
- previous 12 months. Overall, 15.3% of respondents reported that they had required admission to the hospital for asthma treatment. Asthma severity correlated with the frequencies of hospitalizations and emergency visits for asthma in the past year. Even in those patients with severe persistent asthma, 34.3% regarded their disease as being well or completely controlled. Current use of an inhaled corticosteroid was reported by only 13.6% of respondents, and 56.3% used quick-relief bronchodilators. Absence from school and work in the past year was reported by 36.5% of children and 26.5% of adults. **CONCLUSION:** As reported for other regions, current levels of asthma control in the Asia-Pacific region fall markedly short of goals specified in international guidelines for asthma management.
- Lai C.L. et al.** *Specific IgE to 5 different major house dust mites among asthmatic children.* *Acta Paediatr Taiwan.* 2002; 43(5) : 265-70.p **Abstract:** Asthma is one of the most commonly occurring manifestation of allergy in Taiwan. Sensitivity to house dust mites is closely related to childhood asthma. This study was designed to investigate sensitized rates and average concentrations of specific IgE antibodies to 5 major house dust mites (HDMs) among asthmatic children. A total of 93 asthmatic children aged from 3 to 15 years were enrolled to measure their specific IgE concentrations in response to 5 different species of mites: *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df), *Dermatophagoides microceras* (Dm), *Euroglyphus maynei* (Em), and *Blomia tropicalis* (Bt). The severity of hypersensitivity was classified based on the concentration of specific IgE as mild (0.35-3.5 kuA/L), moderate (3.5-50 kuA/L), and severe (> 50 kuA/L). Sixty-three asthmatic children were found to have specific IgE to at least one mite. The percentage of these 63 children who had specific IgE to Dp, Df, Dm, Em and Bt were 87%, 85%, 84%, 77%, and 65%, respectively. Patients with specific IgE to Dp, Df, Dm, and Bt, had a high percentage of moderate and severe hypersensitivity (83.6%, 83.4%, 81.4%, 70.6%, respectively). However, patients sensitized to Em have relatively lower concentration of specific IgE Ab, with 75% of them in the mild range. Some patients had positive IgE antibody to Em (3.2%), and Bt (3.2%) even though they had none to Dp and Df. We conclude that Dm and Bt are also important mite allergens in atopic children. Conventional testing that assays only for sensitivity to Dp and Df would fail to demonstrate 6.4% of mite sensitized asthmatic children.
- Lajoie P. et al.** *Cartography of emergency department visits for asthma - targeting high-morbidity populations.* *Can Respir J.* 2004; 11(6) : 427-33.p **Abstract:** **BACKGROUND:** Asthma education should be offered with priority to populations with the highest asthma-related morbidity. In the present study, the aim was to identify populations with high-morbidity for asthma from the Quebec Health Insurance Board Registry, a large administrative database, to help the Quebec Asthma and Chronic Obstructive Pulmonary Disease Network target its interventions. **METHODS:** All emergency department (ED) visits for asthma were analyzed over a one-year period, considering individual and medical variables. Age- and sex-adjusted rates, as well as standardized rate ratios related to the overall Quebec rate, among persons zero to four years of age and five to 44 years of age were determined for 15 regions and 163 areas served by Centres Locaux de Services Communautaires (CLSC). The areas with rates 50% to 300% higher ($P < 0.01$) than the provincial rate were defined as high-morbidity areas. Maps of all CLSC areas were generated for the above parameters. **RESULTS:** There were 102,551 ED visits recorded for asthma, of which more than 40% were revisits. Twenty-one CLSCs and 32 CLSCs were high-morbidity areas for the zero to four years age group and five to 44 years age group, respectively. For the most part, the high-morbidity areas were located in the south-central region of Quebec. Only 47% of asthmatic patients seen in ED had also seen a physician in ambulatory care. **CONCLUSION:** The data suggest that a significant portion of the population seeking care at the ED is undiagnosed and undertreated. A map of high-morbidity

areas that could help target interventions to improve asthma care and outcomes is proposed.

Lambiase A. et al. *Montelukast, a leukotriene receptor antagonist, in vernal keratoconjunctivitis associated with asthma.* Arch Ophthalmol. 2003; 121(5) : 615-20.p **Abstract:** OBJECTIVE: To evaluate the effects on signs and symptoms of a coexisting vernal keratoconjunctivitis in patients treated with oral montelukast sodium for asthma. METHODS: Twelve patients with vernal keratoconjunctivitis and asthma were enrolled in this pilot study. Topical eyedrops or any systemic treatment was discontinued for at least 7 days before montelukast treatment. Patients were asked to grade their ocular discomfort daily. The following signs and symptoms were also recorded and graded through medical examination at baseline, after 15 days of treatment, and 15 days after treatment discontinuation: physician-evaluated tarsal and bulbar papillae, hyperemia, secretion, and chemosis; and patient-evaluated itching, burning, tearing, photophobia, foreign body sensation, secretion, and redness. Peak expiratory flow rate at 8 AM was also recorded. Samples were collected at the same time points for enzyme-linked immunosorbent assay measurement of leukotriene B4 in tears and leukotriene E4 in urine. RESULTS: Eight of the 10 patients evaluated reported a reduction in symptoms at the end of treatment. Montelukast treatment significantly decreased physician-rated hyperemia, secretion, and chemosis as well as patient-rated burning, tearing, photophobia, secretion, and redness. Effects persisted 15 days after discontinuation of treatment. Clinical changes were associated with a significant increase in leukotriene B4 in tears and a significant decrease in leukotriene E4 in urine after 15 days of treatment. CONCLUSION: The significant and persistent reduction of ocular signs and symptoms in asthmatic patients with vernal keratoconjunctivitis treated for 15 days with montelukast strongly suggests the need for double-masked placebo-controlled trials to confirm the potential of this new treatment in vernal keratoconjunctivitis.

Lanes S.F. et al. *Respiratory medications and risk of asthma death.* Thorax. 2002; 57(8) : 683-6.p **Abstract:** BACKGROUND: The effect of respiratory medications on risk of asthma death in the UK was studied using the General Practice Research Database. METHODS: A total of 96 258 individuals with a diagnosis of asthma were identified, 43 of whom had died as a result of their asthma. For each case 20 controls were selected. Relative risk (RR) estimates and 95% confidence intervals (CI) were computed for each respiratory drug category controlling for effects of age, sex, body mass index, smoking, frequency of visits to the GP, hospital admissions for asthma, and visits to a specialist. RESULTS: The strongest associations were found for at least 13 prescriptions of short acting beta agonists during the previous year (RR=51.6, 95% CI 7.9 to 345) and 7-12 prescriptions of short acting beta agonists (RR=16.2, 95% CI 2.6 to 101). Short acting beta agonists and inhaled steroids tended to be prescribed most frequently to the same patients. In patients who received more than one prescription per month of short acting beta agonists during the previous year, regular use of inhaled steroids was associated with a 60% reduced risk of asthma death (RR=0.4, 95% CI 0.2 to 1.0). CONCLUSIONS: Regular use of inhaled steroids is associated with a decreased risk of asthma death, and excessive use of short acting beta agonists is associated with a markedly increased risk of asthma death.

Lang D.M. et al. *Physical activity in urban school-aged children with asthma.* Pediatrics. 2004; 113(4) : e341-6.p **Abstract:** OBJECTIVES: To compare the physical activity levels of children with and without asthma and evaluate predictors of activity level in children with asthma. METHODS: Parents of 137 children with asthma and 106 controls 6 to 12 years old who attended an urban primary care pediatric clinic were interviewed by telephone. A structured survey evaluated 1 day's total activity and the number of

days active in a typical week; asthma characteristics and treatment; physician advice; opportunities for physical activity; and caregiver beliefs about physical activity. The activity levels of children with and without asthma were compared. Predictors of activity level of children with asthma were evaluated. RESULTS: Children with asthma were less active than their peers. The mean amount of daily activity differed by group: 116 (asthma) vs 146 (nonasthma) minutes; 21% (asthma) vs 9% (nonasthma) were active <30 minutes/day; and 23% (asthma) vs 11% (nonasthma) were active <3 days/week. Among children with asthma, disease severity and parental beliefs regarding exercise and asthma predicted activity level. Children with moderate or severe persistent asthma were more likely to be active <30 minutes/day (odds ratio: 3.0; confidence interval: 1.2-7.5), and children whose parents believed exercise could improve asthma were more likely to be highly active > or = 120 minutes/day (odds ratio: 2.5; confidence interval: 1.2-5.4). CONCLUSIONS: Disease severity and parental health beliefs contribute to the lower activity level of children with asthma. Pediatricians should evaluate exercise level as an indicator of disease control and address exercise and its benefits with patients and caregivers to help achieve the goal of normal physical activity in children with asthma.

Lange C. et al. *Using the noninformative families in family-based association tests: a powerful new testing strategy.* Am J Hum Genet. 2003; 73(4) : 801-11.p **Abstract:** For genetic association studies with multiple phenotypes, we propose a new strategy for multiple testing with family-based association tests (FBATs). The strategy increases the power by both using all available family data and reducing the number of hypotheses tested while being robust against population admixture and stratification. By use of conditional power calculations, the approach screens all possible null hypotheses without biasing the nominal significance level, and it identifies the subset of phenotypes that has optimal power when tested for association by either univariate or multivariate FBATs. An application of our strategy to an asthma study shows the practical relevance of the proposed methodology. In simulation studies, we compare our testing strategy with standard methodology for family studies. Furthermore, the proposed principle of using all data without biasing the nominal significance in an analysis prior to the computation of the test statistic has broad and powerful applications in many areas of family-based association studies.

Lange C. et al. *Power and design considerations for a general class of family-based association tests: quantitative traits.* Am J Hum Genet. 2002; 71(6) : 1330-41.p **Abstract:** In the present article, we address family-based association tests (FBATs) for quantitative traits. We propose an approach to analytical power and sample-size calculations for general FBATs; this approach can be applied to virtually any scenario (missing parental information, multiple offspring per family, etc.). The power calculations are used to discuss optimal choices of the phenotypes for the FBAT statistic and its power's dependence on ascertainment conditions, on study design, and on the correct specification of the distributional assumptions for the phenotypes. We also compare the general FBAT approach with PDT and QTDT. The practical relevance of our theoretical considerations is illustrated by their application to an asthma study.

Lange C. et al. *A multivariate family-based association test using generalized estimating equations: FBAT-GEE.* Biostatistics. 2003; 4(2) : 195-206.p **Abstract:** In this paper we propose a multivariate extension of family-based association tests based on generalized estimating equations. The test can be applied to multiple phenotypes and to phenotypic data obtained in longitudinal studies without making any distributional assumptions for the phenotypic observations. Methods for handling missing phenotypic information are discussed. Further, we compare the power of the multivariate test with permutation tests and with using separate tests for each outcome

which are adjusted for multiple testing. Application of the proposed test to an asthma study illustrates the power of the approach.

Lanier B.Q. et al. *Omalizumab is effective in the long-term control of severe allergic asthma.* *Ann Allergy Asthma Immunol.* 2003; 91(2) : 154-9.p **Abstract:** **BACKGROUND:** Previous reports show that addition of omalizumab to standard therapy reduces asthma exacerbations and simultaneously decreases use of inhaled corticosteroids (ICSs) and rescue medication in patients with allergic asthma. **OBJECTIVE:** To determine the effect of omalizumab on long-term disease control in patients with severe allergic asthma. **METHODS:** The present study concerns the 24-week, double-blind extension phase to a previous 28-week core study in which patients received subcutaneous omalizumab or matching placebo (at least 0.016 mg/kg/IgE [IU/mL] every 4 weeks) for 16 weeks in addition to their existing ICS therapy (beclomethasone dipropionate [BDP]; steroid-stable phase), followed by a 12-week phase in which controlled attempts were made to gradually reduce ICS therapy (steroid-reduction phase). During the extension phase patients were maintained on randomized treatment (omalizumab or placebo) and the lowest sustainable dose of BDP. The use of other asthma medications was permitted during the extension phase. Investigators were also allowed to switch patients from BDP to other ICS medications if considered necessary. **RESULTS:** A total of 460 patients (omalizumab, n = 245; placebo, n = 215) entered the extension phase. Overall, omalizumab-treated patients experienced significantly fewer exacerbations vs placebo during the extension phase (0.60 and 0.83 exacerbations per patient, respectively; P = 0.023), despite a sustained significant reduction in their use of ICS (mean BDP equivalent dose: omalizumab, 227 microg/d; placebo, 335 microg/d; P < 0.001). Treatment with omalizumab was well tolerated and the incidence of adverse events was similar in both treatment groups. **CONCLUSIONS:** These results indicate that omalizumab is effective in the long-term control of severe allergic asthma.

Lasserson T.J. et al. *Fluticasone versus HFA-beclomethasone dipropionate for chronic asthma in adults and children.* *Cochrane Database Syst Rev.* 2005; (4) : CD005309.p **Abstract:** **BACKGROUND:** The relative efficacy of fluticasone (FP) and beclomethasone (BDP) propelled with CFCs has been well established. The potency of HFA-BDP is thought to have been improved with new propellant and some studies suggest that it may equipotent at half the dose of CFC propelled-BDP. There is a need to revisit this question in the light of a potentially more potent new non-CFC propellant. **OBJECTIVES:** To determine the relative efficacy of FP and HFA-propelled BDP in chronic asthma. **SEARCH STRATEGY:** The Cochrane Airways Group Specialised Register was searched using pre-specified terms. Searches were current as of March 2005. **SELECTION CRITERIA:** Randomised controlled trials were eligible for inclusion in the review. We compared either CFC or HFA-propelled FP with HFA-propelled BDP. We made a distinction between HFA-BDP and HFA-BDP extra fine, which dispenses smaller particles of drug, leading to different, usually more peripheral distribution in the airways. Any inhaler device was considered, and there was no restriction on studies with or without spacers. We included studies which assessed HFA-BDP given via either pMDI, breath-actuated MDI, or DPI. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently assessed studies for inclusion in the review. Data were extracted and entered in to RevMan 4.2 using standard meta-analytical techniques with predefined criteria for exploring statistical heterogeneity. **MAIN RESULTS:** Seven studies (1230 participants) met the inclusion criteria of the review. One study was conducted in children. Study reporting quality was fair, but all studies were of short duration (three to twelve weeks). Only studies assessing HFA-BDP extra fine in comparison with FP were identified. Lung function was not significantly different between extra fine BDP and FP when compared at the same dose in parallel studies, change in FEV1: 0.04

litres (95% CI -0.03 to 0.11 litres; three studies, 659 adults); change in am PEF: -0.69 litres (95% CI -11.21 to 9.83 litres; two studies, 364 adults). Individual studies reported non-significant findings in symptom scores and quality of life questionnaires. There was no significant difference between FP and HFA-BDP in the risk of study withdrawal, dysphonia or when data were reported as any adverse event. **AUTHORS' CONCLUSIONS:** There was no significant difference between FP and extra fine HFA-BDP on FEV(1) or peak flow at a dose ratio of 1:1. However, the number of studies and width of the confidence intervals in the analyses do not exclude a clinically meaningful difference between these two drugs. Difficulty in the successful manipulation of the devices studied may be a barrier to the widespread use of MDIs. One paediatric study was included in the review, so extrapolation of the findings of this review to children is limited. Further longer term studies in adults and children with moderate and severe asthma are required.

Lasserson T.J. et al. *Fluticasone versus HFA-beclomethasone dipropionate for chronic asthma in adults and children.* *Cochrane Database Syst Rev.* 2006; (2) : CD005309.p **Abstract:** **BACKGROUND:** The relative efficacy of fluticasone (FP) and beclomethasone (BDP) propelled with CFCs has been well established. The potency of HFA-BDP is thought to have been improved with new propellant and some studies suggest that it may equipotent at half the dose of CFC propelled-BDP. There is a need to revisit this question in the light of a potentially more potent new non-CFC propellant. **OBJECTIVES:** To determine the relative efficacy of FP and HFA-propelled BDP in chronic asthma. **SEARCH STRATEGY:** The Cochrane Airways Group Specialised Register was searched using pre-specified terms. Searches were current as of January 2006. **SELECTION CRITERIA:** Randomised controlled trials were eligible for inclusion in the review. We compared either CFC or HFA-propelled FP with HFA-propelled BDP. We made a distinction between HFA-BDP and HFA-BDP extra fine, which dispenses smaller particles of drug, leading to different, usually more peripheral distribution in the airways. Any inhaler device was considered, and there was no restriction on studies with or without spacers. We included studies which assessed HFA-BDP given via either pMDI, breath-actuated MDI, or DPI. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently assessed studies for inclusion in the review. Data were extracted and entered in to RevMan 4.2 using standard meta-analytical techniques with predefined criteria for exploring statistical heterogeneity. **MAIN RESULTS:** Eight studies (1260 participants) met the inclusion criteria of the review. One study was conducted in children. Study reporting quality was fair, but all studies were of short duration (three to twelve weeks). Only studies assessing HFA-BDP extra fine in comparison with FP were identified. Lung function was not significantly different between extra fine BDP and FP when compared at the same dose in parallel studies, change in FEV1: 0.04 litres (95% CI -0.03 to 0.11 litres; three studies, 659 adults); change in am PEF: -0.69 litres (95% CI -11.21 to 9.83 litres; two studies, 364 adults). Individual studies reported non-significant findings in symptom scores and quality of life questionnaires. There was no significant difference between FP and HFA-BDP in the risk of study withdrawal, dysphonia or when data were reported as any adverse event. **AUTHORS' CONCLUSIONS:** There was no significant difference between FP and extra fine HFA-BDP on FEV(1) or peak flow at a dose ratio of 1:1. However, the number of studies and width of the confidence intervals in the analyses do not exclude a clinically meaningful difference between these two drugs. Difficulty in the successful manipulation of the devices studied may be a barrier to the widespread use of MDIs. One paediatric study was included in the review, so extrapolation of the findings of this review to children is limited. Further longer term studies in adults and children with moderate and severe asthma are required.

Lau B.H. et al. *Pycnogenol as an adjunct in the management of childhood asthma.* *J Asthma.* 2004; 41(8) : 825-32.p **Abstract:** A

randomized, placebo-controlled, double-blind study involving 60 subjects, aged 6-18 years old, was conducted over a period of 3 months to determine the effect of Pycnogenol (a proprietary mixture of water-soluble bioflavonoids extracted from French maritime pine) on mild-to-moderate asthma. After baseline evaluation, subjects were randomized into two groups to receive either Pycnogenol or placebo. Subjects were instructed to record their peak expiratory flow with an Assess Peak Flow Meter each evening. At the same time, symptoms, daily use of rescue inhalers (albuterol), and any changes in oral medications were also recorded. Urine samples were obtained from the subjects at the end of the run-in period, and at 1-, 2-, and 3-month visits. Urinary leukotriene C4/D4/E4 was measured by an enzyme immunoassay. Compared with subjects taking placebo, the group who took Pycnogenol had significantly more improvement in pulmonary functions and asthma symptoms. The Pycnogenol group was able to reduce or discontinue their use of rescue inhalers more often than the placebo group. There was also a significant reduction of urinary leukotrienes in the Pycnogenol group. The results of this study demonstrate the efficacy of Pycnogenol as an adjunct in the management of mild-to-moderate childhood asthma.

Laubereau B. et al. *Vaccination against Haemophilus influenzae type b and atopy in east German schoolchildren.* Eur J Med Res. 2002; 7(9) : 387-92.p **Abstract:** INTRODUCTION: Although routine childhood immunisations are known to prevent severe diseases there is an ongoing discussion on possible side effects in later life. In this paper we investigated the association of Haemophilus influenzae type b (Hib)-vaccination and atopic diseases and allergic sensitisation in children in Eastern Germany. METHODS: From 1998-1999 a cross-sectional survey of school children aged 5 to 14 years on long-term health effects of air pollution was conducted in three regions of Eastern Germany. Atopic outcome was defined by parental reporting of wheezing and doctor's diagnosed asthma (including asthma-like bronchitis), hay fever and eczema. Specific serum IgE against 5 aeroallergens were analysed by RAST-technique. Vaccination status was assessed by vaccination records from the respective local health authorities. Analysis is restricted to 1943 children with complete information on age, gender, place of residence, parental education and 1676 children with available blood data. RESULTS: Lifetime prevalence were 4.9% for asthma, 21.1% for wheezing, 6.6% for hay fever, 11.4% for eczema. 32% of the children had at least one specific IgE RAST>0. Hib-vaccination coverage was 42 % overall, 93 % in 5-7 yr olds, 59 % in 8-10 yr olds and 11 % in 11-14 yr olds. Odds Ratios adjusted for age, gender, place of residence, and parental education were 1.86 (1.05-3.32) for asthma, 1.55 (0.95-2.54) for hay fever, 1.03 (0.70-1.50) for eczema and 1.25 (0.94-1.67) for at least 1 specific IgE RAST>0. CONCLUSION: We found little evidence for an association between Hib-vaccination and some atopic outcomes and causality cannot be ascertained. Our findings do not give sufficient support to question the value of Hib vaccination given the substantial contribution of mass immunisations to public health. Specific research on possible long-term effects of vaccines is needed to enable final conclusions on this topic.

Lazo-Velasquez J.C. et al. *Evaluation of severity of bronchial asthma through an exercise bronchial challenge.* Pediatr Pulmonol. 2005; 40(5) : 457-63.p **Abstract:** Optimum treatment of bronchial asthma requires accurate diagnosis and severity classification. We studied the use of an exercise bronchial challenge in the asthmatic patient as a diagnostic tool. An exercise bronchial challenge test was carried out in 431 asthmatic children and 114 children without a history of asthma in a moderate-altitude environment (2,230 m above sea level/7,314 feet above sea level). Values of peak expiratory flow (baseline and maximum fall) were analyzed through time in each asthma severity group (intermittent, mild persistent, moderate persistent, severe persistent, and nonasthmatic controls). There was a significant difference among responses of asthma severity groups for almost all variables. No difference was found between nonasthmatic and intermittent groups who had similar behavior, except in

bronchodilator response. An exercise bronchial challenge helps classify a patient according to asthma severity; it is easy to reproduce and does not require expensive equipment. It allows diagnosing and classifying asthma severity easily and supplementing the clinical evaluation. Based on our results, we propose a fall of PEF \geq 11% as new cutoff point for making a diagnosis of persistent bronchial asthma. A fall of 11-25% indicates mild persistent asthma; from 25-50%, moderate persistent asthma; and a bigger fall, severe persistent asthma.

Le Gouldec N. et al. *[The physician-pharmacist team in the education of patients concerning inhalant therapy].* Allerg Immunol (Paris). 2001; 33(10) : 383-7.p **Abstract:** The value of educational measures in consideration of the asthmatic patient appeared at first twenty years ago to the eyes of clinical physicians, generalists or specialists. Round about the year 76 the first associations for asthmatic patients were born, under pressure from pneumologists, with the aim of clarifying their illness to asthmatics, to counsel them and especially to enable them to associate their symptoms with their treatment, to assure them of a ready availability of materials more or less onerous to test, aerosolizers, nebulizers, ionizers of the environment, peak flow meters, inhalation chambers, acaricides.... Twenty years after these pioneers of this education of the patient to these responsibilities, the associations devoted to asthma as well as schools of asthma have recently been instigated in order to complete the venture on the ground, often with only feeble means. It is hardly necessary to make an illusion: asthmatic patients, children or adults within these associations are always the same: it is those who are prepared to stir themselves to take part in meetings. There remains the great majority of asthmatics who necessarily need a particular treatment that is adapted to their personal case: it is the duo of physician-pharmacist which is and which constitutes always the best point of impact to devote the time necessary at the best appropriate moment. Such is the aim of this presentation which should not be considered as a return to the past, but an advance towards the individualized formulation of patients by benefitting from the former experiences of corporative formations.

Le Souef P. *Prediction of asthma in children at 6 and 12 years of age: Perth infant asthma follow-up study.* Pediatr Allergy Immunol. 2002; 13 Suppl 15 : 44-6.p **Abstract:** Longitudinal studies, starting in infancy, provide an opportunity to assess risk factors prior to long-term exposure to environmental factors. The status of the infant soon after birth is determined by genetic background and factors related to in utero influences. As a result of recent advances in molecular biology, the genetic component can now be evaluated.

Le Souef P.N. *Mechanisms of steroid resistance in asthma.* Pediatr Pulmonol Suppl. 2004; 26 : 34-5.p

Lee C.S. et al. *Protein sequence analysis of a novel 103-kDa Dermatophagoides pteronyssinus mite allergen and prevalence of serum immunoglobulin E reactivity to rDer p 11 in allergic adult patients.* Clin Exp Allergy. 2004; 34(3) : 354-62.p **Abstract:** BACKGROUND: House dust mites are regarded as important indoor allergens. While the most studied mite allergens are low molecular weight (mw), a high mw Dermatophagoides farinae mite paramyosin (Der f 11) has recently been cloned. We have also cloned a novel high mw Dermatophagoides pteronyssinus (Dp) mite allergen, Der p 11. OBJECTIVE: The aim of this study was to isolate and express a cDNA gene coding for a Der p 11 allergen, to compare the sequence of Der p 11 with other antigens and to evaluate the presence of IgE reactivity to the recombinant protein (rDer p 11) in the sera of allergic adult patients. METHODS: The full-length Der p 11 gene was isolated by cDNA library screening, 5'-3' rapid amplification of cDNA ends and PCR. The cDNA gene was expressed as a glutathione-S-transferase fusion protein in Escherichia coli. The

allergenicity of rDer p 11 was tested by human IgE immunodot or immunoblot assay in a large panel of 100 allergic patients with bronchial asthma, allergic rhinitis or eczema. RESULTS: Der p 11 is a 2965 bp cDNA gene with a 2625 bp open reading frame coding for a 875 amino acid protein. The deduced amino acid sequence of the Der p 11 showed significant homology with various invertebrate paramyosins. The prevalence of serum IgE reactivity to rDer p 11 on immunodot assay ranged from 41.7% to 66.7% in different allergic patient groups, whereas it was rare in non-atopic patients with urticaria (18.8%) and in normal individuals (8%). A high frequency (five out of eight) of MAST(Dp)- allergic serum samples had specific IgE-binding activity to rDer p 11 or its fragments on immunoblot assay, even though their IgE-binding activity to Dp extract was either weak or negative. CONCLUSION: The 103-kDa Der p 11 appears to be major Dp mite allergen with a high frequency of IgE reactivity in sera of patients allergic to mites.

Lee E. et al. *Evaluation of a physician-focused educational intervention on medicaid children with asthma.* Ann Pharmacother. 2004; 38(6) : 961-6.p **Abstract:** BACKGROUND: The 1990 Omnibus Budget Reconciliation Act mandated drug utilization review in response to inappropriate drug use. In the Pennsylvania Medicaid program, pediatric asthma is associated with high healthcare utilization and cost. OBJECTIVE: To determine the effects of a physician-focused educational intervention on asthma drug use and healthcare utilization. METHODS: Pre- and postintervention comparison design was used in children 5-18 years of age who were enrolled in the Pennsylvania Medicaid fee-for-service program from July 1, 1998, to March 31, 1999 (preintervention), and July 1, 1999, to March 31, 2000 (postintervention). The intervention packet included patients' drug profiles, medical history, monograph with national asthma management guidelines, and patient education materials to physicians. Main outcome measures are changes in asthma drug utilization among high-users of short-acting beta(2)-agonists (SAB). RESULTS: The intervention focused on 2 asthma drug use criteria: (1) high-use of quick-relief medication and (2) use of salmeterol without the availability of a quick-relief medication. The intervention reduced quick-relief medication use by 26% among patients with higher use without significant changes in long-term control drugs. In addition, 82% of the recipients evaluated had a positive change in salmeterol utilization as either having an SAB inhaler added after the intervention or salmeterol discontinued after the intervention. There was no significant change in asthma-related emergency department visits or hospitalizations. CONCLUSIONS: Although the physician responders agreed on the usefulness of the educational materials, the results suggest that the intervention had limited success in improving the pharmacologic management and no effect on the health outcomes. We believe that mailed educational materials to physicians can be effective to change prescribing behavior; however, a more multifaceted intervention may be necessary to improve health outcomes.

Lee J.H. et al. *Gender differences in IgE-mediated allergic asthma in the epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) study.* J Asthma. 2006; 43(3) : 179-84.p **Abstract:** BACKGROUND: The TENOR study consists of a large cohort of subjects with severe or difficult-to-treat asthma. The objective of this analysis was to evaluate demographic and clinical characteristics of subjects 12 years of age or older with immunoglobulin E (IgE)-mediated allergic asthma (skin test positive with an IgE level = 30 to =700 IU/mL), and specifically, to assess gender differences in this cohort. METHODS: A total of 4,756 subjects were enrolled by 283 US study sites between January and October 2001. Of those subjects 12 years or older at baseline with an IgE measure and who were skin tested (n = 2,843), 1,783 (63%) were skin test positive and had an IgE level between = 30 to = 700 IU/mL. RESULTS: Compared to males, females reported significantly greater healthcare utilization (steroid bursts in previous 3 months: 50% vs 42%, p < 0.001; unscheduled office visits in previous 3

months: 50% vs 36%, p < 0.0001; missed 1+ days of work/school in previous 2 weeks: 14% vs 10%, p < 0.01). Females also reported significantly more asthma control problems and lower asthma-related quality of life (4.6 +/- 1.3 vs 5.2 +/- 1.2; p < 0.0001); the difference was clinically meaningful. Asthma triggers and allergic comorbidities, such as allergic rhinitis and atopic dermatitis, were more common in female subjects. Despite their overall worse health outcomes, female subjects demonstrated better lung function, had similar treatment patterns, and showed no differences in physician-assessed asthma severity when compared with males. CONCLUSIONS: The reasons for these gender differences in subjects with IgE-mediated allergic asthma are complex, but results from this analysis suggest that detailed evaluations of asthma patients, including symptom-related questions and asthma-related healthcare utilization, are needed to accurately assess asthma severity and control.

Lee J.H. et al. *Increased levels of serum-specific immunoglobulin e to staphylococcal enterotoxin a and B in patients with allergic rhinitis and bronchial asthma.* Int Arch Allergy Immunol. 2005; 138(4) : 305-11.p **Abstract:** BACKGROUND: The association between staphylococcal enterotoxins and atopic dermatitis (AD) is well characterized. We aim to evaluate the association between sensitization to staphylococcal enterotoxin A (SEA) and/or B (SEB) and the development of allergic airway disease. METHODS: Two hundred and seventy-four patients were grouped into allergic rhinitis (AR) and/or bronchial asthma (BA) only, AD only and AR/BA+AD. The AR/BA only group was further divided into AR only, AR and airway hyperresponsiveness (AR+AHR) and BA. The allergen-specific and total immunoglobulin E (IgE) antibodies were determined by the CAP system. The associations of sensitization to SEA/SEB with allergic airway disease were analyzed by logistic regression analysis. RESULTS: The overall rate of sensitization to SEA/SEB was 25.7%, whereas the rate of the AD only group (45.5%) was significantly higher than that of the AR/BA only group (24.5%, chi2=8.1). After sensitization to SEA/SEB, the geometric mean total IgE levels were significantly elevated in patients with AR+AHR and BA, but not in those with AR only. BA patients had higher geometric mean values of SEA- and SEB-specific IgE than AR only and AR+AHR patients. Logistic regression revealed that AR/BA only was more associated with sensitization to SEA/SEB (odds ratio 6.57) than AD only and AR/BA+AD (odds ratio 2.44 and 1.72). CONCLUSIONS: Atopic status after sensitization to SEA/SEB was more closely associated with BA than with other airway allergy, implying that SEA/SEB may play a role in exacerbating airway allergy and increasing the risk of allergic airway disease. Our study suggests that staphylococcal enterotoxins play a prominent role in the pathogenesis of allergic airway disease as well as AD.

Lee J.H. et al. *ADAM33 polymorphism: association with bronchial hyper-responsiveness in Korean asthmatics.* Clin Exp Allergy. 2004; 34(6) : 860-5.p **Abstract:** BACKGROUND: A disintegrin and metalloprotease 33 (ADAM33) is expressed in the lung by fibroblasts and bronchial smooth muscle cells. Given its structure and cellular provenance, ADAM33 may be associated with airway remodelling and bronchial hyper-responsiveness. Single nucleotide polymorphisms (SNPs) and haplotypes of the ADAM33 gene have previously been associated with asthma susceptibility in the Caucasian population. OBJECTIVE AND METHODS: To assess whether genetic variants of ADAM33 are related to asthma in a Korean population, we conducted an association study of the ADAM33 gene with asthma susceptibility, bronchial hyper-reactivity and serum IgE in Korean asthmatics (n=326) and normal controls (n=151). Five of the 14 polymorphisms originally reported to be associated with asthma development (S1 G>A, T1 T>C, V-1 C>A, V1 T>A, V4 C>G) were genotyped using single base extension and electrophoresis. Haplotypes and their frequencies were inferred using the algorithm implemented by the software Arlequin. Allele

frequencies of each SNP and haplotypes were compared between the patients and the normal controls using logistic regression analysis. RESULTS: There was no significant difference in the distribution of SNPs and the six haplotypes between asthmatics and normal controls. All single SNPs and six haplotypes in ADAM33 were also analysed for the association with level of PC(20) using general linear models. The distribution of the T1 T>C SNP and one haplotype (ht4: GCGG) showed significant association with log-transformed PC(20) methacholine level in the asthma patients (P=0.03 and 0.0007, respectively, using a co-dominant model). CONCLUSION: Polymorphism of ADAM33 may contribute to development of BHR in asthma.

- Lee S.G. et al.** *Gene-gene interaction between interleukin-4 and interleukin-4 receptor alpha in Korean children with asthma.* Clin Exp Allergy. 2004; 34(8): 1202-8.p **Abstract:** BACKGROUND: Interleukin-4 receptor alpha (IL-4Ralpha), which binds IL-4 and IL-13, is involved in signal transduction of those cytokines that lead to IgE production, and is also a key functional component of the Th2 lymphocyte phenotype. OBJECTIVE: To determine whether IL-4 and IL-4Ralpha polymorphisms are associated with susceptibility to asthma and whether there are gene-gene interactions between IL-4 and IL-4Ralpha polymorphisms. METHODS: We genotyped three groups of Korean children, consisting of 196 atopic asthmatics, 60 non-atopic asthmatics, and 100 healthy children, for an IL-4 promoter polymorphism (C-590T) and three IL-4Ralpha polymorphisms (Ile50Val, Pro478Ser, and Arg551Gln) using PCR-RFLP (restriction fragment length polymorphism) assays. RESULTS: The allele frequencies of the IL-4 (C/T) polymorphism and the Ile50Val and Pro478Ser polymorphisms of IL-4Ralpha did not differ statistically among the three groups of children. For the Arg551Gln polymorphism, the combined genotype frequency of the Arg/Gln heterozygote and the Arg/Arg homozygote was significantly higher in atopic asthmatics (27.6%) than in healthy children (16.0%) (odds ratio (OR) = 1.97, 95% CI (confidence interval) = 1.07-3.71). The eosinophil fraction (%) and bronchial responsiveness were higher in children with the Arg/Gln and Arg/Arg genotype than in those with the Gln/Gln genotype (P = 0.036 and 0.024, respectively). In asthmatic children, combinations of the IL-4 CT/TT genotype and the IL-4Ralpha Arg/Gln and Arg/Arg genotypes were associated with significantly increased risk for development of asthma (OR = 3.70, 95% CI = 1.07-12.78, P = 0.038). CONCLUSIONS: In Korean children, the IL-4Ralpha Arg551 allele may play a role in susceptibility to atopic asthma and correlate with markers of asthma pathogenesis, including increased eosinophil fraction and enhanced bronchial hyper-responsiveness. In addition, a significant gene-gene interaction between the IL-4-590C and the IL-4Ralpha Arg551 allele significantly increases an individual's susceptibility to asthma.
- Lee T. et al.** *Asthma prevalence among inner-city Asian American schoolchildren.* Public Health Rep. 2003; 118(3): 215-20.p **Abstract:** OBJECTIVE: Though asthma has been studied in many inner-city populations in the United States, there have been no studies specifically on Asian American immigrants. The authors conducted a cross-sectional survey of the prevalence of asthma among schoolchildren at the Josiah Quincy Elementary School, located in Boston Chinatown. Roughly 62% of the students in the school are Asian American. METHODS: The authors utilized the Brief Asthma Pediatric Screen (BAPS), a five-question instrument that was validated through the Chicago public schools. The survey was administered to kindergarten through fifth grade students. RESULTS: Of the 606 respondents (69.9% of the students), 16% had previously diagnosed asthma and 3% had possible undiagnosed asthma. Asthma was more prevalent in boys than in girls (relative risk [RR] 1.75; 95% confidence interval [CI] 1.20, 2.56). In addition, the respondents who lived in Chinatown were less likely to have been diagnosed with asthma (RR 0.59; 95% CI 0.39, 0.90), as were those with Asian surnames (RR 0.65; 95% CI 0.44, 0.97). CONCLUSION: Although this study was preliminary, our results

suggest that asthma rates are substantial among inner-city Asian immigrant children, but possibly lower than for other inner-city children.

- Lee Y.L. et al.** *The association between glutathione S-transferase P1, M1 polymorphisms and asthma in Taiwanese schoolchildren.* Chest. 2005; 128(3): 1156-62.p **Abstract:** STUDY OBJECTIVES: Genetic polymorphisms in the glutathione S-transferase P1 gene (GSTP1) and the glutathione S-transferase M1 gene (GSTM1) have been implicated as risk factors for asthma. However, their roles in asthma pathogenesis and the interaction between these two genes have not been extensively investigated. This study, therefore, examined the relationship among GSTP1 and GSTM1 genotypes and childhood asthma, and evaluated their gene-gene interactions. SETTING: The population from three southern Taiwan communities of a 2001 national survey. SUBJECTS AND METHODS: Two hundred sixty-six fourth-grade to ninth-grade schoolchildren were recruited for oral mucosa samplings based on questionnaire information. Polymerase chain reaction-based assays were performed to determine GSTP1 and GSTM1 genotypes among asthmatic subjects and nonasthmatic control subjects. Multiple logistic regression was used to adjust for potential confounding factors. RESULTS: All of the participants were homozygous at the GSTP1 Ala-114 locus. After controlling for age, sex, and atopic eczema, compared with participants carrying any Val-105 allele, children who were homozygous for GSTP1 Ile-105 had a significantly increased risk of physician-diagnosed asthma (adjusted odds ratio [adjOR], 1.94; 95% confidence interval [CI], 1.08 to 3.59). A positive risk for childhood asthma was also noted on the GSTM1 null genotype but did not reach statistical significance (adjOR, 1.37; 95% CI, 0.80 to 2.38). Among children with GSTM1 present genotypes, GSTP1-105 polymorphisms were associated with the increased risk of asthma. However, the reduced and statistically insignificant asthma risk was observed among those with GSTM1 null genotype. CONCLUSIONS: We concluded that GSTP1-105 was a predictor for childhood asthma, whereas GSTM1 polymorphism might modify the risk. Our study also suggested a competitive effect for homozygous GSTP1 Ile-105 and GSTM1 null genotypes on childhood asthma.
- Lee Y.L. et al.** *Glutathione S-transferase P1 gene polymorphism and air pollution as interactive risk factors for childhood asthma.* Clin Exp Allergy. 2004; 34(11): 1707-13.p **Abstract:** BACKGROUND: Polymorphisms at the glutathione S-transferase (GST) P1 locus were associated with asthma-related phenotypes and bronchial hyper-responsiveness. OBJECTIVE: This study investigated whether GSTP1 genotypes and outdoor air pollution were interactive risk factors on childhood asthma. METHODS: Four hundred and thirty-six subjects were recruited for oral mucosa samplings from 2853 fourth- to ninth-grade schoolchildren from three districts with different air pollution levels in southern Taiwan. PCR-based assays were performed by oral mucosa DNA to determine GSTP1 genotypes. We also conducted a nested case-control study comprising 61 asthmatic children and 95 controls confirmed by International Study of Asthma and Allergies in Childhood questionnaire results and methacholine challenge test. Multiple logistic regression was used to adjust for potential confounding factors. RESULTS: All participants were homozygous at the Ala-114 locus. Although only a marginally significant association existed between the frequency of homozygosity at the Ile-105 locus and asthma when air pollution was not considered, we found a significant gene-environmental interaction between GSTP1-105 alleles and air pollution after adjusting for confounders (P=0.035). Specifically, we found that compared with participants carrying any Val-105 allele in low air pollution, those who are Ile-105 homozygotes in high air pollution district had a significantly increased risk of asthma (adjusted odds ratio (AOR)=5.52, 95% confidence interval (CI)=1.64-21.25). Compared with participants carrying any Val-105 allele, in high air pollution district, children with Ile-105 homozygotes had a significantly increased risk of asthma

(AOR=3.79, 95% CI=1.01-17.08), but those who carried two Ile-105 alleles in low or moderate air pollution districts did not show similar tendencies. The risk of asthma also revealed a clear dose-response relationship with outdoor air pollution in children with Ile-105 homozygotes. CONCLUSION: Our result suggests a gene-environmental interaction between GSTP1-105 genotypes and outdoor air pollution on childhood asthma.

Leeder J.S. *Developmental and pediatric pharmacogenomics.* Pharmacogenomics. 2003; 4(3) : 331-41.p Abstract: Children, as well as adults, should benefit from the discoveries of the genomic era. Many diseases with complex etiologies originate during childhood (e.g., asthma, autism, attention deficit/hyperactivity disorder, epilepsy and juvenile rheumatoid arthritis) and persist into adulthood. Attempts to better understand the genetic basis of age-specific disease processes requires an appreciation that the period of human development encompasses the prenatal period through adolescence, and is a rapidly changing, dynamic process. As a result, pharmacologic modulation of developing gene networks may have unintended and unanticipated consequences that do not become apparent or relevant until later in life. Thus, there is considerable potential for large-scale pharmacogenomic technologies to impact the development and utilization of new therapeutic strategies in children.

Leflein J.G. et al. *Safety of budesonide inhalation suspension (Pulmicort Respules) after up to 52 weeks of treatment in infants and young children with persistent asthma.* Allergy Asthma Proc. 2001; 22(6) : 359-66.p Abstract: Three open-label extension trials evaluated the safety of budesonide inhalation suspension (BIS; Pulmicort Respules) in 670 children (8 months-9 years of age) with mild-to-severe persistent asthma. Patients were randomized to receive either BIS or conventional asthma therapy (CAT) for 52 weeks. The percentage of patients who discontinued because of clinical adverse events was low and similar among the CAT (0.4%) and BIS (0.7%) groups. After adjusting for length of time in the studies, there were no clinically relevant differences between the BIS and CAT groups in the type, incidence, or intensity of adverse events; vital signs or physical examination outcomes; or changes in clinical laboratory evaluations or oral fungal cultures.

Leflein J.G. et al. *Nebulized budesonide inhalation suspension compared with cromolyn sodium nebulizer solution for asthma in young children: results of a randomized outcomes trial.* Pediatrics. 2002; 109(5) : 866-72.p Abstract: OBJECTIVE: The availability of antiinflammatory asthma medications for infants and young children has been limited. The objective of this study was to compare effects of nebulized budesonide inhalation suspension and cromolyn sodium nebulizer solution on asthma-related health outcomes in young children with asthma. METHODS: We conducted a randomized, parallel-group, 52-week, open-label study in 36 US clinical sites. Patients included 335 children who were 2 to 6 years of age and had persistent asthma that had been treated with at least 1 long-term control medication; 287 children (86%) completed the study. Patients received budesonide inhalation suspension, 0.5 mg daily (n = 168), or cromolyn sodium nebulizer solution, 20 mg 4 times daily (n = 167), for 8 weeks, followed by dose titration at the investigator's discretion. The main outcome measure was the rate of asthma exacerbations over 52 weeks. Secondary measures included times to first asthma exacerbation and first use of additional asthma therapy, asthma symptom scores, rescue medication use, and health care resource use. RESULTS: The budesonide group had a mean (median) asthma exacerbation rate of 1.23 (0.99) per year compared with 2.41 (1.85) for the cromolyn group, significantly longer times to first exacerbation and first use of additional long-term asthma medication, greater improvements in asthma symptom scores, reduced use of rescue medication, and fewer urgent care visits. Both treatments were well tolerated. CONCLUSIONS: Budesonide

inhalation suspension was more effective than nebulized cromolyn sodium in young children with persistent asthma. Both treatments were well tolerated with similar adverse event profiles.

Lenney W. et al. *Family genetic studies.* Arch Dis Child. 2002; 87(4) : 272-3.p

Leonardi G.S. et al. *Respiratory symptoms, bronchitis and asthma in children of Central and Eastern Europe.* Eur Respir J. 2002; 20(4) : 890-8.p Abstract: The multicentre Central European Study of Air Pollution and Respiratory Health (CESAR) aimed to measure the respiratory health of schoolchildren using a standardised questionnaire in six countries of Central and Eastern Europe (CEE), allowing comparisons within this region and with other European countries. A cross-sectional study was conducted in 25 urban areas of Bulgaria, Czech Republic, Hungary, Poland, Romania, and Slovakia in 1996. Parents of 21,743 schoolchildren of age 7-11 yrs completed a questionnaire based on items from the World Health Organization and International Study of Asthma and Allergies in Childhood questions on cough and wheeze symptoms, as well as on diagnoses by doctors. Life-time prevalence of bronchitis was 55.9%, asthma 3.9%, and asthmatic, spastic or obstructive bronchitis 12.3%. In CEE countries the prevalence of bronchitis is higher and prevalence of asthma appears lower than in Western Europe. However, if asthma is defined as a diagnosis of either asthma or asthmatic, spastic or obstructive bronchitis, then its prevalence is comparable to Western Europe, or higher. In this region, within-country variation for most respiratory parameters is less than between-country variation. Between-country comparisons in doctors' diagnoses appear dependent on the choice of definition of asthma. Europe-wide comparisons in prevalence of respiratory symptoms and diagnosis are reported in this study. Some of the East-West difference in asthma prevalence may be attributable to differences in diagnostic practice.

Lesho E.P. et al. *Do clinical practice guidelines improve processes or outcomes in primary care?* Mil Med. 2005; 170(3) : 243-6.p Abstract: BACKGROUND: Clinical practice guidelines (CPGs) are common, but it is not clear whether they improve care. METHODS: Quality indicators for processes and outcomes of care were obtained from a computerized system-wide database by patient administration and utilization management personnel unaware of this study and without connection to or interests in guideline implementation. These indicators were compared before and after guideline implementation. RESULTS: After the asthma CPG, nebulizer treatments, emergency department visits, and admissions decreased significantly (p < 0.001 for all three) and education increased significantly (p < 0.001). Periodic measurements of lung function and controller medication prescriptions were unchanged. After the diabetes mellitus CPG, microalbumin screens and education increased significantly (p < 0.001). Angiotensin-converting enzyme inhibitor prescriptions and yearly foot examinations decreased significantly, along with the percentage of patients with blood pressure of < or = 130/85 mm Hg (p < 0.001). Mean hemoglobin A(1C) levels did not change significantly. After the tobacco cessation CPG, screening and education increased significantly (p < 0.001 and p = 0.04, respectively). CONCLUSIONS: The asthma CPG improved some processes and all outcomes. The diabetes CPG improved two of the eight measured processes but had no effect on outcomes. Education and screening, but not counseling, improved with the tobacco CPG. CPGs appear to improve diagnostic and educational processes more than provider-dependent treatment processes. Outcomes were improved after implementation of the asthma CPG but not after the diabetes CPG.

Lesko S.M. et al. *Asthma morbidity after the short-term use of ibuprofen in children.* Pediatrics. 2002; 109(2) : E20.p Abstract: OBJECTIVE: To test the hypothesis that short-term use of ibuprofen

increases asthma morbidity in children. **METHODS:** A randomized, double-blind, acetaminophen-controlled clinical trial was conducted. Children who had asthma and a febrile illness were randomly assigned to receive either acetaminophen suspension or ibuprofen suspension for fever control. Rates of hospitalization and outpatient visits for asthma during follow-up were compared by randomization group. **RESULTS:** A total of 1879 children receiving asthma medications were studied. Rates of hospitalization for asthma did not vary significantly by antipyretic assignment; compared with children who were randomized to acetaminophen, the relative risk for children who were assigned to ibuprofen was 0.63 (95% confidence interval: 0.25-1.6). However, the risk of an outpatient visit for asthma was significantly lower in the ibuprofen group; compared with children who were randomized to acetaminophen, the relative risk for children who were assigned to ibuprofen was 0.56 (95% confidence interval: 0.34-0.95). **CONCLUSIONS:** Rather than supporting the hypothesis that ibuprofen increases asthma morbidity among children who are not known to be sensitive to aspirin or other nonsteroidal antiinflammatory drugs, these data suggest that compared with acetaminophen, ibuprofen may reduce such risks. Whether the observed difference in morbidity according to treatment group is attributable to increased risk after acetaminophen use or a decrease after ibuprofen cannot be determined. These data provide evidence of the relative safety of ibuprofen use in children with asthma.

Letonturier P. [The future of asthmatics]. *Presse Med.* 2004; 33(15) : 1052.p

Leung T.F. et al. *Nitric oxide synthase polymorphisms and asthma phenotypes in Chinese children.* *Clin Exp Allergy.* 2005; 35(10) : 1288-94.p **Abstract:** **BACKGROUND:** Nitric oxide (NO) is a key factor for balancing T-helper type 1/T-helper type 2 immunity. Single nucleotide polymorphisms (SNPs) in nitric oxide synthase (NOS) genes have been associated with atopy and exhaled NO concentrations in Caucasians. We investigated the association between asthma traits and genetic polymorphisms in neuronal NO synthase (NOS1) and endothelial NO synthase (NOS3) in Chinese children. **METHODS:** Asthmatic children between 5 and 18 years of age and non-allergic controls were recruited. Plasma total IgE was measured by microparticle immunoassay, whereas allergen-specific IgEs were measured by fluorescent enzyme immunoassay. Fractional exhaled NO concentration (FeNO) was measured by a chemiluminescence analyser. NOS1 C5266T and NOS3 G894T were genotyped by restriction fragment length polymorphism, and (AAT)n polymorphism in intron 20 of NOS1 was determined by GeneScan analysis. **RESULTS:** The mean (SD) ages of 295 asthmatics and 174 controls were 11.1 (3.8) years and 11.6 (4.0) years, respectively (P=0.162). NOS1 C5266T and NOS3 G894T were not associated with asthma, atopy or FeNO. However, significantly more subjects with T/T in NOS1 C5266T had increased plasma total IgE as compared with those with C/T or C/C (P=0.017). This SNP was also associated with sensitization to *Dermatophagoides pteronyssinus* (P=0.049). Among asthmatic patients, log-transformed plasma total IgE levels were significantly higher among those homozygous for 5266T of NOS1 [mean (SD): 2.84 (0.44) for T/T, 2.68 (0.42) for C/T, 2.59 (0.69) for C/C; P=0.021]. This study found a significant inter-ethnic difference in the allele frequencies of AAT repeats, and this polymorphism was associated with high plasma total IgE levels (P=0.044) but not FeNO (P=0.158). NOS3 G894T was not associated with any asthma or atopy phenotype. **CONCLUSIONS:** NOS1 C5266T and AAT repeats affect plasma IgE concentrations in Chinese children. On the other hand, neither NOS1 nor NOS3 SNP was associated with FeNO or the risk of having asthma.

Leung T.F. et al. *Thromboxane A2 receptor gene polymorphism is associated with the serum concentration of cat-specific immunoglobulin E as well as the development and severity of asthma in Chinese children.* *Pediatr Allergy Immunol.* 2002; 13(1) : 10-7.p **Abstract:** Thromboxane A2 and its receptor (TBXA2R) are involved

in the constriction of vascular and respiratory smooth muscles. The T924C polymorphism in the TBXA2R gene was recently found to be associated with asthma in Japanese adults but not in children. Its relationship with atopy or asthma severity in children has not been defined. To investigate this further, we first assessed the severity of asthma in Chinese children using a standardized questionnaire modified from the Disease Severity Score and spirometric evaluation. Then, peripheral blood was analyzed for serum total and aeroallergen-specific immunoglobulin E (IgE) levels, and TBXA2R T924C genotypes were determined by restriction fragment length polymorphism (RFLP) analysis. One-hundred and fifty three asthmatic patients and 57 control children were recruited, of respective mean ages 9.9 and 11.0 years (p = 0.07). The mean logarithmic serum total IgE concentration was 2.57 and 2.09, respectively, for the asthmatic group and control group (p < 0.0001). Atopy was detected in 132 (86%) asthmatics and 33 (58%) controls. A significant association was observed between T924C and the diagnosis of atopic asthma (p = 0.044; odds ratio: 1.84). In addition, those asthmatics homozygous for the mutant allele in T924C had a lower forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) (p = 0.032 and 0.002, respectively). Among our asthmatic patients, the TBXA2R T924C polymorphism correlated with the concentration of cat-specific IgE in serum (p = 0.046). Nonetheless, this gene marker did not show an association with the serum total IgE concentration or any clinical indicator of asthma severity. In conclusion, our results suggest that the T924C marker in the TBXA2R gene is associated, in Chinese children, with an increased susceptibility of developing atopic asthma. This marker is also associated with the extent of allergic sensitization to cat, as well as with reduced FEV1 and FVC values.

Leung T.F. et al. *Association between TARC C-431T and atopy and asthma in children.* *J Allergy Clin Immunol.* 2004; 114(1) : 199-202.p

Leung T.F. et al. *The C-159T polymorphism in the CD14 promoter is associated with serum total IgE concentration in atopic Chinese children.* *Pediatr Allergy Immunol.* 2003; 14(4) : 255-60.p **Abstract:** Activation of macrophages through CD14 by microbes is crucial in inducing immunity by type 1 T helper cells. A C-to-T polymorphism at position -159 of CD14 was associated with serum total IgE level in Caucasians but not in Japanese subjects. The objective of this study is to determine whether this polymorphic marker is associated with atopy and asthma phenotypes in Chinese children. Restriction fragment length polymorphism was used to characterize CD14/-159 genotypes. Microparticle immunoassay was used to measure serum total IgE level; fluorescent enzyme immunoassay was performed to measure serum concentrations of specific IgE to aeroallergens; and enzyme-linked immunosorbent assay was used to measure serum levels of soluble CD14 (sCD14). Lung function in asthmatics was assessed by spirometry. Two hundred and fifty-eight patients and 92 control children were recruited. Their mean serum total IgE concentrations were 331 and 74 kIU/l, respectively (p < 0.0001). Atopy, defined as the presence of at least one allergen-specific IgE in serum, was found in 220 (85%) patients and in 41 (45%) controls (p < 0.0001). Serum sCD14 levels were significantly associated with CD14/-159 genotypes (p = 0.004). Atopic subjects with CC genotype in CD14/-159 had the highest serum total IgE levels compared with CT and TT genotypes, with the respective mean values being 661, 427 and 380 kIU/l (p = 0.015). Similarly, a higher proportion of subjects with CC genotype had increased serum total IgE concentration (p = 0.039). This polymorphic marker was not associated with asthma or aeroallergen sensitization in our cohort. Our results suggest that the C-159T of CD14 was associated with serum total IgE concentration in atopic Chinese children.

Leung T.F. et al. *Plasma concentration of thymus and activation-regulated chemokine is elevated in childhood asthma.* *J Allergy Clin*

Immunol. 2002; 110(3) : 404-9.p **Abstract:** BACKGROUND: Thymus and activation-regulated chemokine (TARC) is responsible for the trafficking of T(H)2 lymphocytes into sites of allergic inflammation. Serum TARC levels correlate with the severity of atopic dermatitis. The relationship between this marker and the occurrence and severity of asthma has not been evaluated. OBJECTIVE: We tested whether plasma TARC level is a useful marker for asthma and atopy in children. METHODS: Plasma total IgE levels were measured by means of microparticle immunoassay, and specific IgE levels to common aeroallergens were measured by using a fluorescent enzyme immunoassay. We used a sandwich enzyme immunoassay to measure plasma TARC concentrations. RESULTS: Sixty asthmatic children and 28 age- and sex-matched control subjects were recruited, with mean logarithmic plasma total IgE levels of 2.66 +/- 0.60 kIU/L and 1.74 +/- 0.58 kIU/L, respectively (P <.0001). The median plasma TARC concentration was higher in asthmatic patients without inhaled corticosteroid treatment (131.0 pg/mL) compared with those seen in steroid-treated patients (97.5 pg/mL) and control subjects (76.0 pg/mL; P =.01 and P <.0001, respectively). Plasma TARC concentration was found to correlate with total IgE level in plasma (r = 0.219, P =.04). This marker was also increased in subjects who were sensitized to cat allergen (P =.001) but not in subjects sensitized to other aeroallergens. Disease severity score, FEV(1) value, and atopy were not associated with increased plasma TARC levels. CONCLUSION: Our results suggest that plasma TARC concentrations are elevated in childhood asthma. This marker is also linked to plasma total IgE levels and cat allergen sensitization.

Leung T.F. et al. Plasma TARC concentration may be a useful marker for asthmatic exacerbation in children. Eur Respir J. 2003; 21(4) : 616-20.p **Abstract:** Recent studies suggested the T-helper cells type-2 lymphocytes-specific thymus and activation-regulated chemokine (TARC) and monocyte-derived chemokine (MDC) are useful inflammatory markers for chronic asthma. However, their roles in assessing the severity of acute asthma are unknown. This study aims to evaluate the serial changes of plasma TARC and MDC concentrations in children with asthmatic exacerbation. All patients with acute asthma were treated with systemic corticosteroid for 5 days. The severity of asthmatic exacerbation was classified according to the Global Initiative for Asthma guidelines. Plasma TARC and MDC concentrations were measured by sandwich enzyme immunoassays. Sixteen children, with a median (interquartile range) age of 9.3 (7.2-10.6) yrs and asthmatic exacerbation, were recruited. Plasma TARC concentration showed inverse correlation with peak expiratory flow rate at presentation. The median plasma TARC concentration was highest during the acute attacks (46 pg x mL(-1)) as compared to those levels at 1 (31 pg x mL(-1)) and 5 weeks (32 pg x mL(-1)) following treatment. The median plasma MDC level similarly decreased from 698 pg x mL(-1) at baseline to 261 pg x mL(-1) 1 week later, but increased back to 574 pg x mL(-1) at 5 weeks. These results suggest that plasma T-helper cells type-2 lymphocytes-specific thymus and activation-regulated chemokine but not monocyte-derived chemokine concentration may be a useful inflammatory marker in assessing asthmatic exacerbation in children.

Leung T.F. et al. Increased macrophage-derived chemokine in exhaled breath condensate and plasma from children with asthma. Clin Exp Allergy. 2004; 34(5) : 786-91.p **Abstract:** BACKGROUND: Type 2 helper T lymphocyte-specific chemokines including macrophage-derived chemokine (MDC), thymus and activation-regulated chemokine (TARC) and eotaxin are important mediators for allergic airway inflammation. OBJECTIVE: We investigated whether these chemokines can be detected in exhaled breath condensate (EBC) and their relation to childhood asthma. METHODS: Asthmatics recruited from paediatric clinics of a university teaching hospital were classified into intermittent asthma (IA) and persistent asthma (PA) according to Global Initiative for Asthma guidelines. EBC was collected by a disposable collection kit, whereas fractional exhaled

nitric oxide (FENO) was measured by a chemiluminescence analyser. Concentrations of MDC, TARC and eotaxin in both EBC and plasma were measured using sandwich enzyme immunoassay. The intra-subject reproducibility of exhaled chemokine measurements was determined by co-efficients of variation (CV). RESULTS: Forty-eight patients with PA, 36 children with IA and 18 controls were recruited. MDC and eotaxin were present in EBC from nearly all subjects, whereas TARC could be measured in EBC from 33 (32%) subjects only. The median MDC concentration in EBC was higher in PA (117 pg/mL) as compared with IA (106 pg/mL) and controls (105 pg/mL; P=0.003 for both). The median plasma MDC concentration in PA (648 pg/mL) was also higher than that in IA (520 pg/mL; P=0.002) and controls (490 pg/mL; P=0.008). The median plasma TARC concentration was also increased in PA as compared with IA (72 pg/mL vs. 35 pg/mL; P=0.004). MDC concentrations in EBC were lower in patients with PA who received high-dose inhaled corticosteroid (P=0.005). FENO was significantly higher in asthmatics than controls (P<0.0001), but it was not associated with chemokines in EBC or plasma. The mean (range) CV for measuring MDC, TARC and eotaxin in EBC (n=6) were 5.5 (2.0-7.2%), 8.8 (3.6-14.4%) and 5.2 (2.8-7.9%), respectively. CONCLUSIONS: Our results suggest that MDC in EBC and MDC and TARC in plasma are increased in children with PA as compared with IA or control. MDC concentrations in EBC are suppressed in patients on high-dose inhaled corticosteroid treatment.

Leung T.F. et al. Analysis of growth factors and inflammatory cytokines in exhaled breath condensate from asthmatic children. Int Arch Allergy Immunol. 2005; 137(1) : 66-72.p **Abstract:** BACKGROUND: Vascular endothelial growth factor (VEGF), AA isoform of platelet-derived growth factor (PDGF-AA), and epidermal growth factor (EGF) are involved in the pathogenesis of airway inflammation in asthma. These molecules are closely associated with cytokines such as tumor necrosis factor-alpha (TNF-alpha) and interleukin (IL)-4. This study investigates the relation between childhood asthma and levels of these mediators in exhaled breath condensate (EBC). METHODS: EBC was collected from asthmatic children and controls using a disposable collection kit, and the concentrations of VEGF, PDGF-AA, EGF, TNF-alpha and IL-4 in EBC were measured using sandwich enzyme immunoassays. Exhaled nitric oxide concentration was measured by a chemiluminescence analyzer. RESULTS: Thirty-five asthmatic patients aged between 7 and 18 years and 11 controls were recruited. Sixteen patients had intermittent asthma (IA) whereas 19 of them suffered from persistent asthma (PA). A significant correlation was found between IL-4 and TNF-alpha in EBC (rho = 0.374, p = 0.010). PDGF-AA levels in EBC were higher in subjects with diminished FEV1 (p = 0.023) whereas IL-4 concentrations were increased in asthmatics (p = 0.007) as well as subjects with increased plasma total IgE (p = 0.033). Patients with PA receiving high-dose inhaled corticosteroid (ICS) had higher EBC IL-4 concentration than those on low-dose ICS (p = 0.007). Linear regression revealed that PDGF-AA levels in EBC were negatively associated with FEV1 percentage (beta = -0.459, p = 0.006) among the asthmatic patients. CONCLUSIONS: IL-4 in EBC is increased in childhood asthma, and growth factors are detectable in a significant proportion of these children. Increased PDGF-AA is found in asthmatics with more severe airflow limitation.

Levenson D. Adherence to national asthma guidelines is poor among high-risk children, study says. Rep Med Guidel Outcomes Res. 2001; 12(24) : 7-9.p

Levenson D. NCQA report notes some health plan quality gains and major gaps. Rep Med Guidel Outcomes Res. 2004; 15(21) : 1-2, 5.p

Levesque B. et al. Total and specific immunoglobulin E and their relationship to respiratory symptoms in Quebec children and adolescents. Can Respir J. 2005; 12(8) : 426-32.p **Abstract:**

BACKGROUND: Respiratory disease is a major cause of morbidity in young people. It is now recognized that atopy plays an important role in the development of chronic respiratory symptoms in children. **OBJECTIVE:** To examine the determinants and consequences of serum total and specific immunoglobulin E (IgE) in a general population sample of Quebec children and adolescents. **METHODS:** In 1999, 2349 children and adolescents (nine, 13 or 16 years of age) who had participated in a respiratory symptom and disease questionnaire had their total IgE measured. Of these participants, a subsample of 451 children and adolescents was analyzed to detect antibodies to eight specific allergens (ie, allergens of dust mites [Dermatophagoides farinae and Dermatophagoides pteronyssinus], cat, dog, ragweed, Timothy grass, mould [alternaria] and cockroach). **RESULTS:** The geometric mean of the total IgE was 44.4 U/mL among all participants. Concentrations were higher in boys and increased with age. More than 41% of the participants were sensitized to at least one specific allergen. Such sensitization was strongly associated with the occurrence of respiratory conditions and symptoms, namely asthma, wheezing and rhinitis. Family history, school location and ethnic origin had an impact on the prevalence of atopy and total IgE levels. **CONCLUSIONS:** Allergic sensitization is a major determinant in the development of asthma, wheezing and rhinitis in children and adolescents in the province of Quebec.

Levin M.E. et al. *Anaphylaxis in a milk-allergic child after ingestion of soy formula cross-contaminated with cow's milk protein.* *Pediatrics.* 2005; 116(5) : 1223-5.p **Abstract:** In this report we describe a 9-month-old boy with severe persistent asthma and documented cow's milk allergy (presented with eczema and severe systemic reactions) who had an anaphylactic reaction to a soy formula contaminated with cow's milk protein. Quantitative enzyme-linked immunosorbent assay analysis revealed trace quantities of beta-lactoglobulin in the offending soy formula as well as the dry powder. The patient did not demonstrate clinical reactivity to soy protein (negative challenge, tolerated pure soy formula well). Cross-contamination of the offending soy formula was presumed to have occurred during food manufacturing. This case demonstrates that trace quantities of cow's milk protein can elicit severe systemic reactions in highly milk-allergic individuals. This infant ingested the equivalent of 0.4 mL of cow's milk from the soy formula as documented by an immunoassay for beta-lactoglobulin. This highlights the ease with which cross-contamination can occur during food processing and reinforces the need for better quality control.

Lewis S.A. et al. *Secondhand smoke, dietary fruit intake, road traffic exposures, and the prevalence of asthma: a cross-sectional study in young children.* *Am J Epidemiol.* 2005; 161(5) : 406-11.p **Abstract:** The authors have investigated the independent effects of exposure to secondhand smoke, road vehicle traffic, and dietary fruit intake in a cross-sectional study of asthma in young children. They surveyed all children aged 4-6 years in 235 schools in the East Midlands and East of England regions of the United Kingdom in 2003. Data on respiratory symptoms, diagnoses and treatment, smoking in the home, and dietary fruit intake were collected by parental questionnaire. A geographic information system was used to map postcodes and determine the distance of the home from the nearest main road. Responses were obtained from 11,562 children. Wheeze in the past year and physician-diagnosed asthma were reported by 14.1% and 18.2%, respectively. Both of these outcomes were more common in children who lived with a smoker, and the prevalence of asthma increased with the number of smokers in the home. Asthma prevalence was not associated with proximity of the home to a main road or with dietary fruit intake. The authors conclude that, of the potential risk factors considered in this study, preventing secondhand smoke exposure may be the most effective way of preventing asthma.

Lewis T.C. et al. *Prevalence of asthma and chronic respiratory symptoms among Alaska Native children.* *Chest.* 2004; 125(5) : 1665-73.p **Abstract:** **STUDY OBJECTIVES:** To quantify the prevalence and impact of chronic respiratory symptoms among predominantly Alaska Native (AN)/American Indian (AI) middle school students. **DESIGN:** School-based prevalence assessment using the International Study of Asthma and Allergy in Children survey, with supplemental video material and added questions about productive cough, exposure to tobacco smoke, and the functional impact of symptoms. **SETTING:** The Yukon-Kuskokwim delta region of western Alaska. **PARTICIPANTS:** A total of 466 children in the sixth to ninth grades, 81% of whom are AN/AI (377 children). **INTERVENTIONS:** No study intervention. **RESULTS:** Among the 377 AN/AI children, 40% reported one of the following three categories of chronic respiratory disease: physician-diagnosed asthma, 7.4%; asthma-like symptoms (ALS) without an asthma diagnosis, 11.4%; and chronic productive cough (CPC) without asthma diagnosis or symptoms, 21.5%. Symptom prevalence differed substantially between the largest town in the region and rural villages. After an adjustment for demographic factors, exposure to environmental tobacco smoke, active tobacco smoking, and self-report of atopy, village residents were 63% less likely to have ALS ($p = 0.009$), and had a twofold greater risk of CPC ($p < 0.001$) compared to children living in the town. Children with respiratory symptoms experienced sleep disturbances and accessed clinic visits for respiratory problems more often than did asymptomatic children. **CONCLUSIONS:** Chronic respiratory symptoms are very common among AN children. CPC is an important nonasthmatic respiratory condition in this population. The differing patterns of respiratory illness within this region may help to elucidate the specific risk factors for asthma and chronic bronchitis in children.

Lex C. et al. *Sputum induction in children with difficult asthma: safety, feasibility, and inflammatory cell pattern.* *Pediatr Pulmonol.* 2005; 39(4) : 318-24.p **Abstract:** Difficult childhood asthma is defined by persistent symptoms despite maximal conventional therapy. We aimed to establish a safe method of sputum induction for these children and to study cytology and the relationship to exhaled nitric oxide (eNO). Sputum induction was performed in 38/40 children (aged 6-16 years) with difficult asthma, using 3.5% saline for four 5-min periods after bronchodilator pretreatment. Two children were excluded from sputum induction because postbronchodilator forced expired volume in 1 sec (FEV₁) was <65% predicted. Seven of 38 children had symptoms (dyspnea and wheezing) during induction; of these, 3 experienced a fall in FEV₁ of >20% from postbronchodilator FEV₁, readily reversed with salbutamol. Sputum induction was successful in 28/38 children, with a higher success rate in children ≥ 12 years than in younger children (87% vs. 50%, $P = 0.02$). Only 9/28 had abnormal sputum cytology; of these, 6 had predominant sputum eosinophilia (>2.5% eosinophils, $\leq 54\%$ neutrophils), while 3 had sputum neutrophilia ($\leq 2.5\%$ eosinophils, >54% neutrophils). Of 23 children with elevated eNO values, only 6 had sputum eosinophilia. In conclusion, sputum induction can be used to assess airway inflammation in children with difficult asthma, but abnormal sputum cytology is only present in a minority. Raised nitric oxide is only poorly predictive of sputum eosinophilia in these children.

Li A.M. et al. *Cough frequency in children with stable asthma: correlation with lung function, exhaled nitric oxide, and sputum eosinophil count.* *Thorax.* 2003; 58(11) : 974-8.p **Abstract:** **BACKGROUND:** A study was undertaken to assess the correlation between cough frequency in asthmatic children with lung function and two non-invasive markers of airway inflammation. **METHODS:** Thirty two children of median age 12.0 years (interquartile range (IQR) 9.5-13.4) with stable asthma were recruited. They underwent spirometric testing, exhaled nitric oxide (eNO) measurement, sputum induction for differential cell count, and ambulatory cough monitoring over 17 hours and 40 minutes. Coughing episodes were

counted both as individual spikes and as clusters. RESULTS: Complete cough frequency data were available in 29 children (90%) and their median forced expiratory volume in 1 second (FEV1) and eNO were 88.5% (IQR 79.5-98) and 23.9 ppb (IQR 11.4-41.5), respectively. The median number of cough episodes was 14 (IQR 7.0-24.0) which was significantly higher than that of normal children (6.7 (IQR 4.1-10.5), $p < 0.001$). Sputum induction was successful in 61% of the subjects; the median induced sputum eosinophil count was 0.05% (IQR 0-9.0). Cough frequency was found to have a significant positive correlation with eNO (Spearman's $r = 0.781$, $p < 0.001$) but not with FEV1 or sputum eosinophil count ($r = -0.270$, $p = 0.157$; $r = -0.173$, $p = 0.508$, respectively). CONCLUSIONS: Children with stable asthma have increased cough frequency compared with normal controls and cough frequency was greater during the day than at night. Cough may be a more sensitive marker of airway inflammation than simple spirometry.

Li A.M. et al. *Once-daily fluticasone propionate in stable asthma: study on airway inflammation.* J Asthma. 2006; 43(2) : 107-11.p **Abstract:** Children with stable asthma receiving twice-daily fluticasone propionate (FP) were studied. Spirometry, exhaled nitric oxide (eNO) and sputum eosinophils were measured at baseline and 8 weeks after FP was changed to once-daily use while keeping the same total dosage. Visual analogue scores on asthma severity, symptoms, and dosing regimen preference were obtained. Twenty-nine children of mean age 10.6 years (SD 2.5) were recruited. There was significant improvement in eNO (47.1 ppb [30.3] vs. 39.9 ppb [27.1], $p = 0.037$), and sputum eosinophils (5.7% [6.5] vs. 2.5% [3.9], $p = 0.024$) after 8 weeks. All subjects preferred the once-daily dosing regimen. Once-daily FP is effective in controlling airway inflammation. This frequency of medication use is also the preferred regimen.

Li H. et al. *Genetic polymorphisms in arginase I and II and childhood asthma and atopy.* J Allergy Clin Immunol. 2006; 117(1) : 119-26.p **Abstract:** BACKGROUND: A recent microarray study implicated arginase I (ARG1) and arginase II (ARG2) in mouse allergic asthma models and human asthma. OBJECTIVES: To examine the association between genetic variation in ARG1 and ARG2 and childhood asthma and atopy risk. METHODS: We enrolled 433 case-parent triads, consisting of patients with asthma 4 to 17 years old and their biologic parents, from the allergy clinic of a public hospital in Mexico City between 1998 and 2003. Atopy to 24 aeroallergens was determined by skin prick tests. We genotyped 4 single nucleotide polymorphisms (SNPs) of ARG1 and 4 SNPs of ARG2 with minor allele frequencies higher than 10% by using the TaqMan assay (Roche Molecular Systems, Pleasanton, Calif). RESULTS: ARG1 SNPs and haplotypes were not associated with asthma, but all 4 ARG1 SNPs were associated with the number of positive skin tests ($P = .007-.018$). Carrying 2 copies of minor alleles for either of 2 highly associated ARG2 SNPs was associated with a statistically significant increased relative risk (RR) of asthma (1.5, 95% CI = 1.1-2.1 for arg2s1; RR = 1.6, 95% CI = 1.1-2.3 for arg2s2). The association was slightly stronger among children with a smoking parent (arg2s1 RR = 2.1, 95% CI = 1.2 - 3.9 with a smoking parent; RR = 1.2, 95% CI = 0.8-1.9 without; interaction $P = .025$). Haplotype analyses reduced the sample size but supported the single SNP results. One ARG2 SNP was related to the number of positive skin tests ($P = .027$). CONCLUSION: Variation in arginase genes may contribute to asthma and atopy in children.

Li Y. et al. *Modeling spatial survival data using semiparametric frailty models.* Biometrics. 2002; 58(2) : 287-97.p **Abstract:** We propose a new class of semiparametric frailty models for spatially correlated survival data. Specifically, we extend the ordinary frailty models by allowing random effects accommodating spatial correlations to enter into the baseline hazard function multiplicatively. We prove identifiability of the models and give sufficient regularity conditions.

We propose drawing inference based on a marginal rank likelihood. No parametric forms of the baseline hazard need to be assumed in this semiparametric approach. Monte Carlo simulations and the Laplace approach are used to tackle the intractable integral in the likelihood function. Different spatial covariance structures are explored in simulations and the proposed methods are applied to the East Boston Asthma Study to detect prognostic factors leading to childhood asthma.

Li Y.F. et al. *Intercellular adhesion molecule-1 and childhood asthma.* Hum Genet. 2005; 117(5) : 476-84.p **Abstract:** We investigated the role of intercellular adhesion molecule-1 in childhood asthma by examining associations of functional variants at codons 29 (A --> T), 241 (G --> A), and 469 (A --> G) in Children's Health Study participants. Among African-Americans, 469G carriers had lower risk for asthma (ever asthma OR = 0.4, 95% CI 0.2-0.9) but increased risk among 29T carriers (early onset active asthma OR = 2.2, 95% CI 1.0-4.9). Protective associations with the 241A allele were observed among non-Hispanic and Hispanic whites (ever asthma OR = 0.7, 95% CI 0.6-0.9; early onset active asthma OR = 0.5, 95% CI 0.4-0.8), and these associations were not confounded by population stratification. To gauge the potential impact of confounding by population stratification, we performed analyses by ethnic group and in an independent family-based sample. Regional associations were stable across analyses. Haplotype associations of the four common haplotypes (29A/241G/469A, AGG, TGA, and AAG) with asthma showed that Hispanics with the AAG haplotype had lower asthma risk compared to carriers of two copies of AGA haplotype (OR = 0.6, 95% CI 0.4-0.9). Among non-Hispanic whites, the AAG haplotype was associated with reduced risk for active asthma. For African-Americans, who had a low frequency of the AAG haplotype, carrying one copy of the AGG haplotype was associated with a lower risk of asthma (OR = 0.3, 95% CI 0.1-0.8), as compared with two copies of the AGA haplotype. Consistent with information on variant function, the 241A and 469G variants may indicate haplotypes that are associated with reduced risk for asthma.

Liam C.K. et al. *Skin prick test reactivity to common aeroallergens in asthmatic patients with and without rhinitis.* Respiriology. 2002; 7(4) : 345-50.p **Abstract:** OBJECTIVE: The aim of this study was to investigate the prevalence of skin prick test (SPT) reactivity to common aeroallergens among Malaysian asthmatic patients with and without rhinitis. METHODOLOGY: An SPT using eight aeroallergens (Dermatophagoides pteronyssinus, Dermatophagoides farinae, cat fur, cockroach, Acacia sp., Bermuda grass, Aspergillus fumigatus and Aspergillus niger) was performed on 206 asthmatic patients. RESULTS: One hundred and forty patients (68%) were reactive to at least one of the aeroallergens. Among the SPT-positive patients, a positive prick test reaction to the house dust mites, D. pteronyssinus (93.6%), and D. farinae (81.4%) was most common, followed by cat fur (20.0%), cockroach (7.9%), Bermuda grass (7.9%), Acacia sp. (7.9%), A. fumigatus (0.7%) and A. niger (0.7%). A history of rhinitis was elicited in 111 (53.9%) patients and 95 (85.3%) of these patients were SPT-positive compared with only 45 (47.4%) of 95 patients with asthma symptoms alone ($P < 0.001$). The presence of rhinitis and a young age of onset of asthma were independent factors for positive SPT reaction to at least one of the aeroallergens. CONCLUSIONS: The prevalence of SPT reactivity to common aeroallergens is high among Malaysian asthmatics, particularly in those with an early age of onset and in those with coexisting rhinitis.

Liao M.F. et al. *Evaluation of the serum antioxidant status in asthmatic children.* Acta Paediatr Taiwan. 2004; 45(4) : 213-7.p **Abstract:** Many studies have shown the balance between the oxygen reactive species (ROS) and the antioxidant capacities, and that the massive ROS generation could lead to cell damage and diseases such as atherosclerosis, aging and cancer. Changes in antioxidant capacity

like free radicals scavenging antioxidant agents such as vitamin E, C content, serum concentrations of bilirubin, uric acid, albumin and antioxidant enzyme systems like SOD, and GPx activities have been described to be related to many diseases. However, the research on chronic airway inflammatory disease and the antioxidant defence system is still not enough. Understanding of the antioxidant status and antioxidant enzymes in asthmatic patients is still unclear. In the present controlled study, we investigated the total antioxidant status (TAS) in serum and the antioxidant enzyme (total SOD and GPx) activities in 46 asthmatic children and 52 normal controls. The serum level of TAS in asthmatic children was significantly lower than the controls. The SOD concentration in asthmatic children was higher than the control, however the GPx was much lower than the control children, even though it was not statistical significance. In conclusion, these results suggested the existence of higher oxidative stress and reactive oxygen species (ROS) in asthmatic children, and that the antioxidant capacities in asthmatic children were altered. If the production of ROS was persistent, it would result in chronic inflammation and the imbalance of oxidative-reductive status in those patients.

Liard R. et al. [Development over 3 years of asthma recently diagnosed in a cohort of children (ASMA study). Factors related to improvement in clinical status]. *Presse Med.* 2002; 31(14) : 637-43.p **Abstract:** OBJECTIVE: The objective of the ASMA study was to describe the evolution of light to moderate asthma, newly or recently (12 Pounds months) diagnosed in private pneumology centers, and to search for the predictive factors. METHODS: In 1995, 251 private pneumologists, throughout Metropolitan France, recruited 396 asthmatic children, 6 to 12 years old (64% boys). The 334 patients eligible for the study were examined every 4 months during 3 years (a mean of 6 controls were conducted out of the expected 9). The data were collected on standardized questionnaires completed by the physicians and notebooks filled-in by the patients the week before each control. This questionnaire comprised two asthma 'control' criteria: "control" of the clinical state, defined as asthma attacks < 1 per week AND nocturnal awakening < 1 per week AND absence of asthma symptoms between attacks on every control visit; "control" of the need for b2 mimetics on request, defined as the non-use throughout the week preceding the control visit. RESULTS: The global clinical state of the cohort rapidly improved once care was initiated: the proportion of children exhibiting at least one attack of asthma per week rapidly dropped to 43% on inclusion and to 13% on the first control visit (4 months), 10% on the second control visit, and then fluctuated at around 8% up until the last control visit. A similar evolution was noted regarding nocturnal asthma attacks. The proportion of patients with prescriptions for inhaled corticosteroids and long-lasting b2-mimetics increased over the three years of follow-up. Analysis of the factors related to the individual 'control' of the clinical state showed a negative effect in family histories of asthma (father) and the presence of smokers in the home, but above all a positive effect of compliance to treatment and particularly its understanding (OR = 2.5; p = 0.03) and respect of the doses (OR = 2.7; p < 0.01). The positive effect of compliance was confirmed by analysis of the factors related to the use of b2 mimetics on request. CONCLUSION: Smoking should be avoided in the home. Compliance to treatment could be improved by making sure that the patients and their parents fully understand the disease and its treatment, and by persuading them to strictly follow the treatments prescribed.

Lichenstein R. et al. *Respiratory viral infections in hospitalized children: implications for infection control.* *South Med J.* 2002; 95(9) : 1022-5.p **Abstract:** BACKGROUND: Identification of children with respiratory viral infections may augment infection-control practices on inpatient units. There are clinical syndromes leading to morbidity among hospitalized children, however, in which a viral etiology of the illness might not be considered. METHODS: Virus infection rates among 243 children aged <1 to 19 years hospitalized between

October 1993 and April 1994 with asthma, pneumonia, bronchiolitis, fever, apnea, croup, or respiratory distress were evaluated as part of a University of Maryland Medical Center infection-control protocol. Anonymous data collected included admission diagnoses, age, and virus-identification result. RESULTS: Seventy-one children (29%) had a virus identified, including 19 of 123 (15%) with asthma, 4 of 12 (33%) with pneumonia, 27 of 47 (57%) with bronchiolitis, 13 of 41 (32%) with fever, 4 of 9 (44%) with apnea, 2 of 3 (67%) with croup, and 2 of 8 (25%) with unspecified respiratory distress. CONCLUSION: This study reinforces the concept that clinicians should consider respiratory viruses for a broad range of diagnoses. This heightened awareness may help reduce the number of nosocomial respiratory viral infections.

Lierl M.B. *Exhaled nitric oxide: a useful aide in pediatric asthma management?* *J Pediatr.* 2003; 142(5) : 461-2.p

Lieu T.A. et al. *Cultural competence policies and other predictors of asthma care quality for Medicaid-insured children.* *Pediatrics.* 2004; 114(1) : e102-10.p **Abstract:** OBJECTIVE: More than half of Medicaid enrollees are now in managed care. Scant information exists about which policies of practice sites improve quality of care in managed Medicaid. Children with asthma are a sentinel group for Medicaid quality monitoring because they are at elevated risk for adverse outcomes. The objective of this study was to identify practice-site policies and features associated with quality of care for Medicaid-insured children with asthma. METHODS: A prospective cohort study with 1-year follow-up was conducted in 5 health plans in California, Washington, and Massachusetts. Data were collected via telephone interviews with parents at baseline and 1 year, surveys of practice sites and clinicians, and computerized databases. The practice site survey asked about policies to promote cultural competence, the use of several types of reports to clinicians, support for self-management of asthma, case management and care coordination, and access to and continuity of care. Quality of care was evaluated on the basis of 5 measures: 1) preventive medication underuse based on parent report; 2) the parent's rating of asthma care; 3) the 1-year change in the child's asthma physical status based on a standardized measure; 4) preventive medication underprescribing based on computerized data; and 5) the occurrence of a hospital-based episode. RESULTS: Of the 1663 children in the study population, 67% had persistent asthma at baseline based on parent report of symptoms and medications. At 1-year follow-up, 65% of the children with persistent asthma were underusing preventive medication based on parent report. In multivariate analyses, patients of practice sites with the highest cultural competence scores were less likely to be underusing preventive asthma medications based on parent report at follow-up (odds ratio [OR]: 0.15; 95% confidence interval [CI]: 0.06-0.41 for the highest vs lowest categories) and had better parent ratings of care. The use of asthma reports to clinicians was predictive of less preventive medication underprescribing based on computerized data (OR: 0.33; 95% CI: 0.16-0.69), better parent ratings of care, and better asthma physical status at follow-up. Patients of practice sites with policies to promote access and continuity had less underuse of preventive medications (OR: 0.56; 95% CI: 0.34-0.93). Among the 83 practice sites, the practice site's size, organizational type, percentage of patients insured by Medicaid, mechanism of payment for specialty care, and other primary care features were not consistently associated with quality measures. CONCLUSIONS: Practice-site policies to promote cultural competence, the use of reports to clinicians, and access and continuity predicted higher quality of care for children with asthma in managed Medicaid.

Lim D.L. et al. *An evaluation of asthma morbidity in Singaporean schoolchildren--a teachers' survey.* *Asian Pac J Allergy Immunol.* 2003; 21(2) : 71-4.p **Abstract:** Asthma is the most common chronic illness in childhood. This study evaluated the asthma morbidity among Singaporean schoolchildren. The survey involved

1,744 schoolteachers using a structured written questionnaire. 73.4% of class teachers reported at least 1 asthmatic student in their class. 37.1% of teachers had students absent from school for up to 3 days per month and 5.1% missed school for 4 to 14 days in a month. 87.4% of the physical education (PE) teachers reported at least 1 asthmatic student in their class. 65.2% reported an average of 1-3 students sitting out at each PE lesson and 15.1% reported students who were exempted from PE for more than 3 months in a year due to asthma. The morbidity of asthma in Singaporean schoolchildren in terms of school absenteeism and exemption from PE classes is substantial. The data supports a need to improve asthma control amongst our schoolchildren.

Lin H.C. et al. *Length of stay and costs for asthma patients by hospital characteristics--a five-year population-based analysis.* J Asthma. 2005; 42(7) : 537-42.p **Abstract:** This study sets out to explore the relationship between hospital characteristics, asthma length of stay (LOS), and costs per discharge. The study adopts hospitalization data from the Taiwan National Health Insurance Research Database covering the period from 1997 to 2001. Study subjects were identified from the database by principal diagnosis of asthma or asthmatic bronchitis, with a total of 139,630 cases being included in the study. Multiple-regression analyses were performed to explore the relationship between LOS, costs per discharge and hospital characteristics, adjusting for age, gender, and discharge status of patients, as well as complications or comorbidities. The regression analyses showed that, compared with district hospitals, medical centers and regional hospitals have longer and more statistically significant LOS, as well as higher costs. Hospitals operating on a for-profit basis have shorter LOS and lower costs than public and not-for-profit hospitals. This study shows the existence of wide variations in LOS and costs per discharge for asthma hospitalizations, between the various types of hospitals in Taiwan.

Lin H.C. et al. *No association between TAP1 DpnII polymorphism and bronchopulmonary dysplasia.* Acta Paediatr Taiwan. 2005; 46(6) : 341-5.p **Abstract:** The possibility that a family history of asthma may have a role in susceptibility to bronchopulmonary dysplasia (BPD) had been raised in several reports, and there was evidence of a strong association between transporter associated with antigen processing (TAP1) polymorphism and asthma in Taiwanese population. To test whether TAP polymorphism has a role in the BPD, we investigated the association between TAP1 polymorphism and BPD by analyzing the results of genotype distribution. The study included 224 ventilated preterm infants (<30 weeks) who had respiratory distress syndrome (RDS) and needed intermittent mandatory ventilation (IMV) during Jan. 1999 to July 2003. The typing of TAP1 polymorphism was performed by polymerase chain reaction (PCR)-based restriction analysis. The demography between two groups of these ventilated preterm infants was not different. We observed no significant differences in genotype distribution or allele frequency of the TAP1 polymorphisms between BPD and their respective control infants. There was also no significant difference in genotype distribution of the TAP1 polymorphism with duration of IMV. Therefore, we conclude that TAP1 polymorphism is not a useful marker for predicting the susceptibility or severity to BPD for Taiwanese.

Lin M. et al. *Gaseous air pollutants and asthma hospitalization of children with low household income in Vancouver, British Columbia, Canada.* Am J Epidemiol. 2004; 159(3) : 294-303.p **Abstract:** Associations of gaseous air pollutants (including carbon monoxide, sulfur dioxide, nitrogen dioxide, and ozone) with asthma hospitalization, stratified by sex and socioeconomic status, were examined among children 6-12 years of age in Vancouver, British Columbia, Canada, between 1987 and 1998. Relative risks for an exposure increment corresponding to the interquartile range for each gaseous air pollutant were estimated for asthma hospitalization after adjustment for

weather conditions, including daily maximum and minimum temperatures as well as average relative humidity. Similar results were obtained by using locally weighted smoothing functions (LOESS) with default convergence criteria and by using natural cubic splines with a more stringent setting. Exposures to nitrogen dioxide were found to be significantly and positively associated with asthma hospitalization for males in the low socioeconomic group but not in the high socioeconomic group. For females, this same pattern of association was observed for exposures to sulfur dioxide. No significantly positive associations were found between carbon monoxide and ozone and asthma hospitalization in either low or high socioeconomic groups.

Lin S. et al. *Childhood asthma hospitalizations and ambient air sulfur dioxide concentrations in Bronx County, New York.* Arch Environ Health. 2004; 59(5) : 266-75.p **Abstract:** The association between asthma hospitalizations and ambient sulfur dioxide (SO₂) concentrations was examined in a case-control study in Bronx County, New York. Cases comprised 2629 children aged 0-14 yr who were admitted to hospitals for asthma. There were 2236 controls who were admitted for reasons other than asthma. Daily ambient SO₂ concentrations were categorized into quartiles of both average and maximum levels and various exposure windows (i.e., day of admission and 1-, 2-, and 3-d lags). Cases were exposed to higher daily average concentrations of SO₂ than controls. The authors compared the highest exposure quartile with the lowest, and the odds ratios were 1.66, 1.90, 2.05, and 2.21 (all p < 0.01 for same-day, 1-, 2-, and 3-d lags, respectively), with a similar finding for daily SO₂ maximum exposure. The results suggest a consistent positive association between SO₂ exposure and hospitalizations for childhood asthma.

Lin S. et al. *Childhood asthma hospitalization and residential exposure to state route traffic.* Environ Res. 2002; 88(2) : 73-81.p **Abstract:** This study investigated whether pediatric hospitalization for asthma was related to living near a road with heavy traffic. In this case-control study, cases (N=417) consisted of white children aged 0-14 years who were admitted for asthma and who resided in Erie County, New York, excluding the city of Buffalo. Controls (N=461) were children in the same age range admitted during the same time period for nonrespiratory diseases. Subjects' residential addresses were linked to traffic information provided by the New York State Department of Transportation. After adjustments for age and poverty level were made, children hospitalized for asthma were more likely to live on roads with the highest tertile of vehicle miles traveled (VMT) (odds ratio (OR): 1.93, 95% confidence interval (CI): 1.13-3.29) within 200 m and were more likely to have trucks and trailers passing by within 200 m of their residence (OR=1.43, 95% CI: 1.03-1.99) compared to controls. However, childhood asthma hospitalization was not significantly associated with residential distance from state roads, annual VMT within 500 m, or whether trucks or trailers passed by within 500 m. This study suggests that exposure to high volumes of traffic/truck within 200 m of homes contributes to childhood asthma hospitalizations.

Lin S. et al. *Upper respiratory symptoms and other health effects among residents living near the World Trade Center site after September 11, 2001.* Am J Epidemiol. 2005; 162(6) : 499-507.p **Abstract:** The authors investigated changes in respiratory health after September 11, 2001 ("9/11") among residents of the area near the World Trade Center (WTC) site in New York City as compared with residents of a control area. In 2002, self-administered questionnaires requesting information on the presence and persistence of respiratory symptoms, unplanned medical visits, and medication use were sent to 9,200 households (22.3% responded) within 1.5 km of the WTC site (affected area) and approximately 1,000 residences (23.3% responded) in Upper Manhattan, more than 9 km from the site (control area). Residents of the affected area reported higher rates of

new-onset upper respiratory symptoms after 9/11 (cumulative incidence ratio = 2.22, 95% confidence interval (CI): 1.88, 2.63). Most of these symptoms persisted 1 year after 9/11 in the affected area. Previously healthy residents of the affected area had more respiratory-related unplanned medical visits (prevalence ratio = 1.73, 95% CI: 1.13, 2.64) and more new medication use (prevalence ratio = 2.89, 95% CI: 1.75, 4.76) after 9/11. Greater impacts on respiratory functional limitations were also found in the affected area. Although bias may have contributed to these increases, other analyses of WTC-related pollutants support their biologic plausibility. Further analyses are needed to examine whether these increases were related to environmental exposures and to monitor long-term health effects.

Lin S.J. et al. *Decreased intercellular adhesion molecule-1 (CD54) and L-selectin (CD62L) expression on peripheral blood natural killer cells in asthmatic children with acute exacerbation.* *Allergy.* 2003; 58(1): 67-71.p **Abstract:** **BACKGROUND:** The capacity of inflammatory cells to adhere involves an array of adhesion molecules, and is critical to the inflammatory responses seen in childhood asthma. We aimed to determine the changes of intercellular adhesion molecule-1 (ICAM-1) and L-selectin expressed on peripheral blood (PB) T lymphocytes and natural killer (NK) cells in asthmatic children with acute exacerbation and after prednisolone therapy. **METHODS:** Flow cytometric analysis was performed to determine the expression of ICAM-1 (CD54) and L-selectin (CD62L) on T (CD3+) cells and NK (CD3-/CD56+) cells of PB from children with allergic asthma with acute exacerbation and in a stable condition after prednisolone therapy. Atopic subjects without asthma and age-matched controls were also included for comparison. **RESULTS:** Percentages of PB non-CD3, CD56+ NK cells, but not CD3+ T cells, increased in asthmatic children with acute exacerbation, compared to those assessed in a stable condition after a course of prednisolone. However, significant decrease of ICAM-1 ($P = 0.01$) and L-selectin ($P = 0.01$) expression on PB NK cells, but not on T cells, were found in children with acute asthma compared to those in a stable condition. NK cells in children with acute asthma showed minimal expression of CD69 and CD25. **CONCLUSIONS:** Results suggests that either NK cells expressing ICAM-1 and L-selectin selectively migrated into inflamed lung tissues, or subsets of NK cells not expressing ICAM-1/L-selectin were expanded during acute exacerbation of childhood asthma.

Lindbaek M. et al. *Socioeconomical conditions as risk factors for bronchial asthma in children aged 4-5 yrs.* *Eur Respir J.* 2003; 21(1): 105-8.p **Abstract:** A number of factors are associated with the development of childhood asthma. The purpose of this study was to establish the prevalence of childhood asthma and to explore the socioeconomic background factors associated with childhood asthma in a Norwegian cohort of children aged 4-5 yrs. A questionnaire was given to parents in connection with the ordinary child control of 4-5-yr-old children in Vestfold county, Norway. In addition to the question "Has the child at present or ever had asthma?", a number of medical and socioeconomic background factors were registered. Of the 2,430 parents, 1,913 (79%) responded. Of the 163 (cumulative prevalence 8.7%) children with confirmed asthma, 19 did not use any medication and were regarded as having outgrown their asthma. Several background factors were significantly associated with asthma in a logistic regression analysis: few rooms at home, psychosocial problems, fever more than three times during the last year, hay fever, reaction to food and mother or father with chronic disease. The findings indicate that socioeconomic background factors are associated with asthma in childhood, in addition to other known risk factors.

Linna O. et al. *Central airways stenosis in school-aged children: differential diagnosis from asthma.* *Acta Paediatr.* 2002; 91(4): 399-402.p **Abstract:** This study assessed the value of spirometry and chest X-rays in the diagnosis of airways stenosis in the tracheal

or laryngeal regions at school age. A series of 14 patients was studied. Six of them had vascular ring anomalies, four subglottic stenosis, two aberrant innominate artery, one tracheal stenosis and one a laryngeal web. Four patients were suffering from chronic cough and ten from dyspnoea, noisy breathing and cough upon physical exercise. Two had had their symptoms since infancy and five since 3-6 y of age, whereas seven had had their first symptoms at school age. Nine patients had previously been suspected of having asthma, and five of them had been using inhaled corticosteroids, one inhaled sodium cromoglycate and one peroral terbutaline without any effect. The ratio of forced expiratory volume in 1 s (FEV1) to peak expiratory flow (PEF) was abnormally high in most of the patients. All six children with vascular ring anomalies also had an abnormal aortic configuration on a chest X-ray, and narrowing of the trachea was seen in two of the four with subglottic stenosis. Two children had both chest X-rays and spirometry values within the normal limits. **Conclusion:** The results show that children with stenosis in the laryngeal or tracheal region may not have their first symptoms until school age. Many patients are falsely suspected of having asthma. Simple spirometry and chest X-rays will help the physician to make the correct diagnosis in these patients.

Lipworth B.J. *Designer inhaled corticosteroids: are they any safer?* *Chest.* 2005; 128(3): 1081-4.p

Lipworth B.J. et al. *Effect of plastic spacer handling on salbutamol lung deposition in asthmatic children.* *Br J Clin Pharmacol.* 2002; 54(5): 544-7.p **Abstract:** **AIMS:** To study the effects of electrostatics in a plastic spacer on the lung deposition of salbutamol in asthmatic children. **METHODS:** Twenty-five children (5-12 years) with mild asthma were given salbutamol hydrofluoroalkane pressurized metered dose inhaler 400 micro g via a 750 ml plastic spacer on separate days. Blood samples were taken for plasma salbutamol at 5, 10, 15 and 20 min after inhalation to measure lung bioavailability as a surrogate for relative lung dose. With immediate inhalation following actuation, a new rinsed spacer (NewRinsed) was compared with a used spacer after repeated daily use (Used), a spacer rinsed after repeated use (UsedRinsed) and a spacer primed with benzalkonium chloride to avoid electrostatics (Primed1). In addition, spacers were evaluated using a 15 s inhalation delay following actuation with primed (PrimedDelay) and rinsed (RinsedDelay) spacers. Data were log transformed and expressed as geometric mean fold difference for the average plasma salbutamol concentration (Cav) over 20 min. **RESULTS:** There were significant differences ($P < 0.05$) in Cav (as geometric mean fold difference and 95% CI) between Primed1 vs NewRinsed 1.92 fold (95% CI 1.15, 3.20) and between Used vs NewRinsed 1.75 fold (1.11, 2.76). There were no significant differences comparing Primed1, Used or UsedRinsed. There were also significant differences ($P < 0.05$) between Primed1 vs PrimedDelay 2.34 fold (1.31, 4.19), or vs RinsedDelay 3.59 fold (2.15, 5.99); and for Used vs PrimedDelay 2.14 fold (1.24, 3.69), or vs RinsedDelay 3.28 fold (2.13, 5.04). **CONCLUSIONS:** The relative lung dose of salbutamol from a plastic spacer may differ considerably depending on spacer handling suggesting that nonelectrostatic spacers may be the best way forward.

Liu C.A. et al. *Prenatal prediction of infant atopy by maternal but not paternal total IgE levels.* *J Allergy Clin Immunol.* 2003; 112(5): 899-904.p **Abstract:** **BACKGROUND:** The atopic history of parents has long been used to predict infant atopy. However, bias from questionnaires of allergic history are also frequently suspected, because a large number of vasomotor rhinitis, intrinsic asthma, and seborrheic dermatitis cases are probably misinterpreted to be atopic diseases. **OBJECTIVE:** We attempted to identify a risk factor other than parental atopic history to predict elevated infant IgE levels and infant atopy. **METHODS:** A total of 655 core families were prenatally recruited, and finally 545 families completed the study for the prospective analysis of infant atopy at 6 months of age. Atopic history and blood samples of parents were collected in the third

trimester during pregnancy. Cord blood (CB) was collected immediately after birth. Infant blood samples and history of infant eczema were collected in the 6-month physical checkup clinic. Blood total IgE and specific IgE levels were determined by use of the Pharmacia CAP system. RESULTS: In univariate analysis, maternal, but not paternal, atopic history correlated with elevated CB IgE levels and the occurrence of infant eczema. Elevated maternal, but not paternal, total IgE levels (>150 KU/L) significantly correlated with increases of CB IgE levels (median, 0.54 vs 0.17 KU/L, $P < .001$), infant IgE levels (log-transformed mean values, 1.32 +/- 0.51 vs 1.13 +/- 0.51 KU/L, $P < .001$), and infant eczema ($P = .008$). Multivariate logistical regression analysis, however, showed that only maternal total IgE levels correlated with CB and infant IgE levels and the development of infant eczema. CONCLUSIONS: The maternal, but not paternal, total IgE level correlates with elevated infant IgE levels and infant atopy. This provides a high specificity (83%) and a sensitivity of 34% for prediction of infant atopy. This suggests that maternal factors, placental factors, or both have an impact on perinatal allergic sensitization.

Liu L.J. et al. *Exposure assessment of particulate matter for susceptible populations in Seattle.* Environ Health Perspect. 2003; 111(7) : 909-18.p **Abstract:** In this article we present results from a 2-year comprehensive exposure assessment study that examined the particulate matter (PM) exposures and health effects in 108 individuals with and without chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), and asthma. The average personal exposures to PM with aerodynamic diameters < 2.5 microm (PM_{2.5}) were similar to the average outdoor PM_{2.5} concentrations but significantly higher than the average indoor concentrations. Personal PM_{2.5} exposures in our study groups were lower than those reported in other panel studies of susceptible populations. Indoor and outdoor PM_{2.5}, PM₁₀ (PM with aerodynamic diameters < 10 microm), and the ratio of PM_{2.5} to PM₁₀ were significantly higher during the heating season. The increase in outdoor PM₁₀ in winter was primarily due to an increase in the PM_{2.5} fraction. A similar seasonal variation was found for personal PM_{2.5}. The high-risk subjects in our study engaged in an equal amount of dust-generating activities compared with the healthy elderly subjects. The children in the study experienced the highest indoor PM_{2.5} and PM₁₀ concentrations. Personal PM_{2.5} exposures varied by study group, with elderly healthy and CHD subjects having the lowest exposures and asthmatic children having the highest exposures. Within study groups, the PM_{2.5} exposure varied depending on residence because of different particle infiltration efficiencies. Although we found a wide range of longitudinal correlations between central-site and personal PM_{2.5} measurements, the longitudinal r is closely related to the particle infiltration efficiency. PM_{2.5} exposures among the COPD and CHD subjects can be predicted with relatively good power with a microenvironmental model composed of three microenvironments. The prediction power is the lowest for the asthmatic children.

Liu X. et al. *Improving the quality of care of patients with asthma: the example of patients with severely symptomatic disease.* J Eval Clin Pract. 2001; 7(3) : 261-9.p **Abstract:** The increasing economic burden of asthma care is incurred partly by patients with more severe symptoms. However, little is known about the characteristics of these severe asthma patients. This study examined sociodemographic, disease-specific characteristics and health care utilization that are related to asthma disease severity, for the purpose of identifying areas for treatment improvement. A total of 2927 asthma patients (12 years or older), who were continuously enrolled in one of three participating health plans for a 6-month study period and who responded to an asthma survey, were included in the study. Univariate and multivariate analyses were performed to examine the sociodemographic, disease-specific characteristics and health care utilization by asthma severity. About 25% of the patients reported experiencing severe asthma symptoms. They were more likely to be

African-Americans, Hispanics, women, patients with less than a college education, residents in the south-west, current smokers, and those receiving care from non-specialists. Severe asthmatics reported having less of an understanding of the clinical manifestation of asthma and the means to manage asthma exacerbation. Outpatient contacts did not differ significantly between severe and other patients, although their utilization of emergency room and inpatient care was significantly greater. This study suggests that a significant proportion of asthma patients is experiencing severe symptoms and barriers other than access to care prevent appropriate control of asthma. Poor control appears to be related to smoking, deficits in knowledge about self-care, not receiving medical care from a specialist, and inadequate use of medications.

Lloyd J.B. *Re: Baby car seats.* RCM Midwives J. 2002; 5(4) : 140.p

Lo Y.C. et al. *Food-specific immunoglobulin E among children with atopic dermatitis: a retrospective study.* J Microbiol Immunol Infect. 2005; 38(5) : 338-42.p **Abstract:** This retrospective study included 133 children aged between 2 and 16 years with elevated serum food-specific immunoglobulin E (IgE), including 59 children clinically diagnosed with atopic dermatitis (AD) and 74 children clinically diagnosed with atopic disease without AD (asthma, allergic rhinitis, or both). Six common serum food-specific IgEs were detected by the Pharmacia ImmunoCAP test, including: egg white, milk, peanut, soybean, shrimp and egg yolk. Serum total IgE was also measured. The results showed that both AD and non-AD atopic children had the highest sensitization rate to shrimp. AD children had significantly higher serum total IgE and average number of positive food sensitization items than atopic children without AD. Three serum food-specific IgEs, including peanut, soybean and egg yolk, were significantly higher in children with AD than in those without AD. Furthermore, 3 pairs of food-specific IgEs were correlated with each other in AD children: egg white IgE correlated with peanut IgE, egg white IgE correlated with egg yolk IgE, and peanut IgE correlated with soybean IgE. In logistic regression analysis of the serum of 6 food allergen-specific IgEs in AD children, we found that elevated peanut- and egg yolk-specific IgE were risk factors of AD in elevated serum food-specific IgE children whose serum total IgE was less than 1000 kU/L but not in those with total IgE greater than 1000 kU/L.

Lobdell D.T. et al. *Development of a biomarkers database for the National Children's Study.* Toxicol Appl Pharmacol. 2005; 206(2) : 269-73.p **Abstract:** The National Children's Study (NCS) is a federally-sponsored, longitudinal study of environmental influences on the health and development of children across the United States (). Current plans are to study approximately 100,000 children and their families beginning before birth up to age 21 years. To explore potential biomarkers that could be important measurements in the NCS, we compiled the relevant scientific literature to identify both routine or standardized biological markers as well as new and emerging biological markers. Although the search criteria encouraged examination of factors that influence the breadth of child health and development, attention was primarily focused on exposure, susceptibility, and outcome biomarkers associated with four important child health outcomes: autism and neurobehavioral disorders, injury, cancer, and asthma. The Biomarkers Database was designed to allow users to: (1) search the biomarker records compiled by type of marker (susceptibility, exposure or effect), sampling media (e.g., blood, urine, etc.), and specific marker name; (2) search the citations file; and (3) read the abstract evaluations relative to our search criteria. A searchable, user-friendly database of over 2000 articles was created and is publicly available at: . PubMed was the primary source of references with some additional searches of Toxline, NTIS, and other reference databases. Our initial focus was on review articles, beginning as early as 1996, supplemented with searches of the recent primary research literature from 2001 to 2003.

We anticipate this database will have applicability for the NCS as well as other studies of children's environmental health.

Lodrup Carlsen K.C. *The environment and childhood asthma (ECA) study in Oslo: ECA-1 and ECA-2.* *Pediatr Allergy Immunol.* 2002; 13 Suppl 15 : 29-31.p **Abstract:** An observed increase in asthma admissions in Oslo during the 1980s prompted a prospective birth cohort study to ask the following question: was air pollution (outdoor and indoor) (in a broad sense) associated with asthma development in young children? During 12 months from 1 January 1992, 3,754 children (birth weight \geq 2,000 g) in Oslo were enrolled at birth into the Environment and Childhood Asthma (ECA) study and followed to 2 years of age (ECA-part I). Cord blood, a detailed questionnaire (family and pregnancy history of disease, environmental exposures, socio-economic status) completed by the mother and lung function measurements ($n = 803$) were collated at birth. Detailed questionnaires completed every 6 months for 2 years included the child's disease history, feeding habits and environmental exposures. A nested case-control study comprised 306 children with confirmed minimum two episodes of bronchial obstruction (rBO) and 306 controls (without lower respiratory tract disease) with clinical investigations (including tidal breathing lung function, beta-2 responsiveness and allergy assessment) and environmental exposure assessments (indoor and outdoor). Home dampness and low ventilation, as well as maternal smoking in pregnancy, but not outdoor air pollution increased the risk of rBO. Lung function at birth was decreased among newborns whose mother smoked during pregnancy. To understand better the early risk factors for asthma and allergy development, a follow-up study started (in 2001; ECA-part II) of all cases and controls, and those with lung function measured at birth (total 1,230 invited) (9-10 years of age). This involved clinical investigation, allergy assessments, lung function, airway hyper responsiveness measures, exhaled nitric oxide and immunological as well as allergen exposure investigations.

Logan D. et al. *The Illness Management Survey: identifying adolescents' perceptions of barriers to adherence.* *J Pediatr Psychol.* 2003; 28(6) : 383-92.p **Abstract:** **OBJECTIVE:** To develop a self-report measure of barriers to adherence and to evaluate its reliability and validity in a sample of adolescents with asthma. **METHODS:** The Illness Management Survey (IMS) was developed through item generation, expert panel review, and focus group administration. Adolescents with asthma ($N = 152$) completed the measure. Participants reported on perceived drawbacks to medication, risk-taking behavior, and social desirability tendencies. Providers rated adolescents' illness severity and adherence. Reliability and validity of the IMS were assessed, and factor structure was examined. **RESULTS:** The 27-item IMS shows high internal consistency ($\alpha = .87$). Scores correlate with perceived medication drawbacks, risk taking, and self- and provider reports of adherence. Principal-components analysis indicates five domains of barriers, accounting for 52.4% of the variance: disease/regimen issues, cognitive difficulties, lack of social support/lack of self-efficacy, denial/distrust, and peer/family issues. **CONCLUSIONS:** Preliminary data indicate that the IMS reliably and validly assesses perceived barriers to adherence within this sample of adolescents with asthma. It shows promise as a tool for identifying subgroups of nonadherent adolescents.

Logminiene Z. et al. *Avoidable mortality in Lithuania: 1991-1999 compared with 1970-1990.* *Public Health.* 2004; 118(3) : 201-10.p **Abstract:** This paper assesses the changes in avoidable mortality in Lithuania in 1991-1999 compared with 1970-1990. Causes of death were disaggregated into causes most amenable to treatment and those amenable to prevention. Trends in age-standardised death rates were calculated. In 1970-1990, avoidable causes of death accounted for 26.3% of all deaths. By 1991-1999 this figure had decreased slightly to 24.6%. At the same time, age-standardised death rates from

avoidable causes increased by 8%, from 118.1 per 100000 in 1970-1990 to 127.9 in 1991-1999. Avoidable mortality among men was considerably higher than for women in both periods. There was considerable fluctuation in both treatable and preventable mortality during the 1990s, reflecting diversity in trends in different causes of death. Increases occurred in death rates from tuberculosis, cervical cancer and liver cirrhosis and, immediately after independence, also in hypertensive and cerebrovascular diseases and, among men, lung cancer, followed by subsequent declines. Deaths from chronic rheumatic heart disease, asthma and other respiratory diseases, appendicitis, abdominal hernia, cholelithiasis and maternal mortality consistently declined. In conclusion, avoidable mortality declined as a proportion of total mortality in Lithuania during 1991-1999 compared with 1970-1990. This reflected the combined impact of an initial rise in death rates from treatable and, to a lesser extent, preventable causes, followed by subsequent declines. While this indicates some success in the development of medical care, it emphasises the need for more effective public health policies directed at the major determinants of health.

Loh L.C. et al. *Asthma prescribing practices of government and private doctors in Malaysia--a nationwide questionnaire survey.* *Asian Pac J Allergy Immunol.* 2005; 23(1) : 7-17.p **Abstract:** A self-answered, anonymously completed questionnaire survey was performed between June 2002 and May 2003 where doctors from government and private sectors in Malaysia were invited to participate by post or during medical meetings. One hundred and sixteen government doctors and 110 private doctors provided satisfactorily completed questionnaires (effective respondent rate: 30.1%). The most preferred medications for 'first-line', 'second-line' and 'third-line' treatment were for government doctors: inhaled short-acting beta2-agonist (SABA) (98%), inhaled corticosteroids (CS) (75%), and leukotriene antagonist (52%); and for private doctors: oral SABA (81%), inhaled CS (68%), and oral CS (58%). The first choice inhaler device for most government and private doctors were metered dose inhalers, with cost and personal preferences (for private doctors), and technical ability (for government doctors) as the key considerations when deciding on the choice of device. This benchmark data on the asthma prescribing practices of a healthcare delivery system fully dichotomized into government and private sector, provides evidence for practice differences affected by the nature of the healthcare system, and might have implications on healthcare systems of other countries that share similarities with that of Malaysia.

Lonnkvist K. et al. *Increased eosinophil transmigration after nasal allergen challenge in children with allergic asthma and rhinitis.* *Allergy.* 2002; 57(12) : 1200-4.p **Abstract:** **BACKGROUND:** Eotaxin and interleukin-5 together provide the signal essential for eosinophil transmigration to airway tissue in allergic reactions. However, it is not known whether peripheral blood eosinophils (PBE) possess an increased transmigration capacity in vitro after allergen challenge in vivo before they leave the circulation. We aimed to determine whether PBE in cat-sensitized children have increased spontaneous and/or eotaxin-induced transmigration capacity in vitro, and to what extent allergen challenge alters this feature. **METHODS:** Fourteen cat-allergic children and four healthy controls underwent nasal challenge with cat-allergen. Blood samples were drawn prechallenge and at 2 h and 24 h postchallenge. We analyzed the in vitro transmigration of PBE, with and without eotaxin as a chemoattractant. We used a transmigration assay with fibronectin-coated membranes. Eosinophil cationic protein (ECP) and PBE counts were run in parallel. **RESULTS:** The spontaneous transmigration capacity of eosinophils in vitro was significantly higher at 2 h after allergen challenge ($P < 0.01$ vs. prechallenge) and returned to prechallenge levels at 24 h postchallenge ($P < 0.02$ vs. 2 h postchallenge). Addition of eotaxin further augmented the increased transmigration. In concordance, no accompanying changes were measured in the levels of eosinophils in blood or ECP in serum. Furthermore no spontaneous or eotaxin-induced eosinophil

transmigration was detected in healthy controls. CONCLUSION: PBE possess increased spontaneous (and eotaxin-induced) capacity to transmigrate as early as 2 h after allergen challenge in allergic children, without accompanying signs of eosinophil activation in terms of increased PBE count or ECP level. This is probably due to the increased stage of activation of the eosinophil, often referred to as "priming".

Lopez Chacon A. [Identification of the learning needs of asthmatic diseases in relatives of pediatric patients]. *Rev Alerg Mex.* 2005; 52(1) : 18-24.p Abstract: BACKGROUND: Information on asthma is fundamental for an adequate control and management of patients who suffer from it, or for their relatives; hence, new educational programs are being carried out in order to achieve this aim. OBJECTIVE: To identify learning requirements for its subsequent use in the development of an educational program. Material and methods: A descriptive study was carried out. 326 surveys were applied to relatives of pediatric patients seen at the allergology department of Hospital Leonor Perez, from April to September 2003. Frequencies, percentages, as well as Pearson's chi-square test were used in order to compare groups. RESULTS: An inadequate knowledge of treatment was observed in 69.3% of the cases, of its physiopathology in 84.7%, of its preventive medication and of crisis in 51.7 and 59.5%, respectively, as well as from the importance of both treatments in 65.3% of them. Most of the relatives included in this study recognized the importance of being instructed in the disease process (94.8%). There were no significant differences between the group of relatives with prior specialized attention and the group who attended consultation for the first time; except for preventive medication to treat crisis, where the first one showed better knowledge of the disease ($p = 0.002$). Difference on the overall knowledge was also better in the first group, although lower than expected. CONCLUSIONS: It is important to apply an educational program aimed at improving levels of knowledge on specific aspects of asthma.

Lord A. et al. *The value of asthma camps for young people in Victoria, Australia.* *Contemp Nurse.* 2001; 11(2-3) : 133-41.p Abstract: PURPOSE: This paper investigates the impact of the Asthma Foundation of Victoria's educational camp program on children's knowledge of asthma and its management, their feelings about asthma, and their attitudes toward physical and social activities. Parents' observations of changes in their child's behaviour and attitudes are also reported. DESIGN AND METHODS: This research was descriptive and applied. It used questionnaires at four stages (directly pre- and post-camp, three-four months and ten-15 months post-camp) of an asthma education camp program to assess child asthma knowledge levels. At three months post-camp, parental observations of children's attitudes and behaviours were assessed using a questionnaire. Children's feelings toward asthma were also assessed using a questionnaire pre- and post-camp. RESULTS: The children surveyed displayed a better knowledge of asthma and how to manage their condition immediately after the camp. This knowledge tended to return to pre-camp levels after ten months. The children also reported less anxiety and fear about their illness, a greater sense of wellbeing, and more confidence in participating in a whole range of physical and social activities. Many parents also noted positive changes in their children in terms of activities and asthma management at three months post-camp. CLINICAL IMPLICATIONS: Although there were limitations to sustaining knowledge gained in the asthma camping program, the camping experience provided a benefit for children in terms of promoting their mental and social wellbeing. When readers consider modernising asthma education (e.g. shorter camps, education in everyday social settings such as schools), they need to consider retaining the key ingredients of the more traditional camping program that supports good asthma management, wellbeing and social participation.

Loughlin J.E. et al. *Prevalence of serious eosinophilia and incidence of Churg-Strauss syndrome in a cohort of asthma patients.* *Ann Allergy Asthma Immunol.* 2002; 88(3) : 319-25.p Abstract: BACKGROUND: Some leukotriene receptor antagonists, such as zafirlukast and montelukast, have been associated with systemic eosinophilia, with interest focused on Churg-Strauss syndrome (CSS). OBJECTIVE: To calculate the background incidence rate of CSS and prevalence of eosinophilia among people with asthma who have not used leukotriene receptor antagonists. METHODS: We conducted a cohort study in the setting of three geographically diverse UnitedHealthcare health plans. We identified 36,230 people who received a diagnosis of asthma during the period October 1994 through September 1997. We identified 241 potential cases from the claims data. Using a standardized hospital record abstract form, nurses abstracted relevant clinical data from the hospital charts of potential cases. We applied several a priori case definitions to the abstracted clinical data and computed incidence rates of CSS among patients with asthma. We additionally used these data to compute the prevalence of serious eosinophilia. RESULTS: Incidence rates of definite CSS among asthma patients ranged from zero (90% confidence interval 0.0 to 23.0) to 67 (90% confidence interval 22.5 to 160.6) cases per 1,000,000 person-years, depending on the definition used. All patients who met the criteria for CSS expressed symptoms consistent with mild asthma. CONCLUSIONS: This report is the first direct measurement of the incidence rate of CSS among asthma patients. We believe that the prevalence and incidence information that we report is a useful description of population rates in the United States for these conditions.

Louie D. et al. *Physiological changes at altitude in nonasthmatic and asthmatic subjects.* *Can Respir J.* 2004; 11(3) : 197-9.p Abstract: Exercised-induced asthma is not due to exercise itself per se, but rather is due to cooling and/or drying of the airway because of the increased ventilation that accompanies exercise. Travel to high altitudes is accompanied by increased ventilation of cool, often dry, air, irrespective of the level of exertion, and by itself, this could represent an 'exercise' challenge for asthmatic subjects. Exercise-induced bronchoconstriction was measured at sea level and at various altitudes during a two-week trek through the Himalayas in a group of nonasthmatic and asthmatic subjects. The results of this study showed that in mild asthmatics, there was a significant reduction in peak expiratory flow at very high altitudes. Contrary to the authors' hypothesis, there was not a significant additional decrease in peak expiratory flow after exercise in the asthmatic subjects at high altitude. However, there was a significant fall in arterial oxygen saturation postexercise in the asthmatic subjects, a change that was not seen in the nonasthmatic subjects. These data suggest that asthmatic subjects develop bronchoconstriction when they go to very high altitudes, possibly via the same mechanism that causes exercise-induced asthma.

Lowe A.J. et al. *Atopic disease and breast-feeding--cause or consequence?* *J Allergy Clin Immunol.* 2006; 117(3) : 682-7.p Abstract: BACKGROUND: A number of studies have observed an association between breast-feeding and increased risk of development of asthma and eczema. It has been proposed that these results might be due to early signs of atopic disease in the infant causing mothers to prolong breast-feeding. OBJECTIVE: We sought to determine whether early symptoms of atopic disease (eczema, food reaction, or asthma) or positive skin prick test responses reduce the likelihood of ceasing breast-feeding. METHODS: A prospective birth cohort of 620 infants from Melbourne, Australia, was used. Telephone interviews every 4 weeks were conducted until 64 weeks and then again at 78 and 104 weeks to determine duration of breast-feeding (both exclusive and total) and evidence of atopic disease. Because of the varying time of onset of atopic symptoms, they were modeled as time-varying covariates in Cox models. RESULTS: Only 52 (8.4%) infants did not establish breast-feeding, whereas an additional 103 (25.0%) did not establish exclusive breast-feeding.

Early signs of atopic disease or sensitization were independently associated with an approximately 28% reduction in risk of ceasing exclusive breast-feeding (adjusted hazard ratio, 0.72; 95% CI, 0.53-0.97); $P=0.029$), but there was no evidence for a relationship with risk of ceasing breast-feeding completely (adjusted hazard ratio, 1.12; 95% CI, 0.92-1.37; $P=0.262$). **CONCLUSION:** Early signs of atopic disease might prolong the duration of exclusive breast-feeding. This could mask a protective effect of breast-feeding or even result in breast-feeding appearing to be a risk factor for the development of atopic diseases. Future investigation of the relationship between breast-feeding and atopic diseases should consider this possibility.

Lowe G.L. et al. *Undiagnosed and untreated wheezing in a cohort of adolescents with a family history of allergic disease.* Br J Gen Pract. 2001; 51(469) : 664-5.p **Abstract:** Wheezing is a common symptom among adolescents. A cross-sectional survey was undertaken of a prospective cohort of teenagers with a close family history of allergy. The results demonstrate the prevalence of wheezing, the diagnosis of asthma, and the treatment of symptoms in this group. The findings suggest that undiagnosed and inadequately or untreated wheezing is as common among adolescents with a family history of allergic disease as in the general adolescent population, and can be associated with severe symptoms.

Lowe L. et al. *Specific airway resistance in 3-year-old children: a prospective cohort study.* Lancet. 2002; 359(9321) : 1904-8.p **Abstract:** **BACKGROUND:** The development of a method to assess lung function in young children may provide new insight into asthma development. Plethysmographic measurement of specific airway resistance (sR_{aw}) is feasible in this age group. We aimed to identify risk factors associated with low lung function in early childhood in a prospective birth cohort. **METHODS:** Children were prenatally assigned to risk group according to parental atopic status (high risk, both parents atopic; medium risk, one parent atopic; low risk, neither parent atopic) and followed prospectively until age 3 years. We measured sR_{aw} in 503 symptom-free children using whole-body plethysmography during tidal breathing. **FINDINGS:** 803 of 868 children attended the clinic, of whom 503 obtained satisfactory sR_{aw} readings. 200 who wheezed at least once during first 3 years of life had significantly higher sR_{aw} than the 303 who had never wheezed (mean difference 5.8%, 95% CI 2.2-9.3, $p=0.002$). For children who had never wheezed there were significant differences in sR_{aw} between risk groups ($p<0.001$). Children at high risk ($n=87$) had a higher sR_{aw} (geometric mean 1.17 kPa/s, 1.12-1.22) than children at medium risk ($n=162$; 1.02 kPa/s, 1.00-1.05) and at low risk (54; 1.04 kPa/s, 0.99-1.11). Atopic children ($n=62$) had significantly higher sR_{aw} (1.15 kPa/s, 1.09-1.21) than those who were not atopic (232; 1.05 kPa/s, 1.02-1.07, $p=0.002$). For non-atopic children, those at high risk (58) had higher sR_{aw} (1.13 kPa/s, 1.07-1.18) than those at medium risk (125, 1.01 kPa/s, 0.98-1.05) or at low risk (49, 1.04 kPa/s, 0.97-1.10, $p=0.003$). We showed a significant interaction between history of maternal asthma and child's atopic status ($p=0.006$). **INTERPRETATION:** Even in the absence of respiratory symptoms, children of atopic parents and those with personal atopy have impaired lung function in early life.

Lu L.R. et al. *Snoring in preschool children: prevalence and association with nocturnal cough and asthma.* Chest. 2003; 124(2) : 587-93.p **Abstract:** **INTRODUCTION:** The association between snoring, nocturnal cough, and allergic symptoms in young children is not known. **OBJECTIVE:** To measure the prevalence of habitual snoring and its association with nocturnal cough, asthma, and hay fever in preschool children. **SETTING:** A cross-sectional study. **SUBJECTS:** Preschool children aged 2 to 5 years. **METHOD:** The data were collected in a cross-sectional study. A total of 974 children were randomly selected from two areas of Lismore and Wagga Wagga in New South Wales, Australia. **RESULTS:** The prevalence of snoring was 10.5%, with no gender difference ($p = 0.99$) or trend association

with age ($p = 0.58$). The association between snoring and nocturnal cough was highly significant (odds ratio [OR], 3.68; 95% confidence interval [CI], 2.41 to 5.63; $p = 0.001$). This association was significant in both the nonasthmatic and asthmatic groups when examined separately. Snoring was also significantly associated with asthma (OR, 2.03; 95% CI, 1.34 to 3.10; $p = 0.001$). In subjects without hay fever, the association between snoring and asthma was also highly significant (41.2% vs 24.8%; OR, 2.12; 95% CI, 1.34 to 3.37; $p = 0.001$). **CONCLUSION:** The prevalence of snoring in preschool children was 10.5% for both genders. Snoring was significantly associated with both nocturnal cough and asthma. Because snoring, asthma, and nocturnal cough may have a common etiology, it is possible that effective treatment of one symptom may lead to reductions in the presence or severity of the other symptoms.

Luethviksson B.R. et al. *Allergic diseases and asthma in relation to serum immunoglobulins and salivary immunoglobulin A in pre-school children: a follow-up community-based study.* Clin Exp Allergy. 2005; 35(1) : 64-9.p **Abstract:** **BACKGROUND:** We have previously reported an association between low IgA and allergic manifestations in early childhood (0-2 years) and have now followed our cohort for an additional 2 years. **OBJECTIVE:** To evaluate in a longitudinal community-based cohort study the association between maturation of Ig production and allergic manifestations in the first 4 years of life. **METHODS:** A cohort of 161 randomly selected children was followed from birth to the age of 42-48 months and evaluated at 18-23 months (EV1; $n = 179$) and again at the age of 42-48 months (EV2; $n = 161$). Diagnoses were made with the help of a clinical questionnaire, physical examination and skin prick tests (SPTs) to 10 common allergens. Serum immunoglobulins were measured at EV1 and EV2, and salivary IgA (sal-IgA) at EV2. **RESULTS:** Serum IgA, IgE, IgG1, IgG2 and IgG4 increased from 2 to 4 years of age ($P < 0.001$) and their levels showed close correlations ($P \leq 0.01$ for most comparisons). Children with one or more positive SPTs had lower serum IgA ($P = 0.004$) and IgG4 ($P = 0.05$) at EV2 than those who did not respond, and children who developed allergic rhinitis between EV1 and EV2 had low sal-IgA ($P = 0.006$) and IgG3 ($P < 0.05$) at EV2. Atopic eczema was associated with low sal-IgA at EV2, and children who developed eczema between EV1 and EV2 had significantly lower sal-IgA than those who recovered after EV1 ($P = 0.02$). **CONCLUSION:** Allergic manifestations in predisposed children may be influenced by the rate of maturation of immunological components that counteract sensitization or inhibit effector mechanisms of allergy.

Luskin A.T. et al. *Symptom control and improved functioning: the effect of omalizumab on asthma-related quality of life (ARQL).* J Asthma. 2005; 42(10) : 823-7.p **Abstract:** This investigation evaluated variability in asthma-related quality-of-life (ARQL) outcomes among patients randomized to omalizumab or placebo. Pooled data on the Asthma Quality of Life Questionnaire (AQLQ) from two trials were used ($n = 948$). Variability in AQLQ outcomes was determined by categorizing AQLQ score changes according to minimal clinically important difference (MCID: 0.5 points) and large clinically important difference (LCID: 1.5 points) score changes. A greater proportion of patients achieved improvement in every domain of AQLQ scores during all periods with omalizumab compared with placebo. Omalizumab-treated patients showed greater clinically important improvement in ARQL compared with patients receiving placebo.

Lwebuga-Mukasa J.S. et al. *Association between traffic volume and health care use for asthma among residents at a U.S.-Canadian border crossing point.* J Asthma. 2004; 41(3) : 289-304.p **Abstract:** Little information is available about health impacts of the North American Free Trade Agreement (NAFTA) traffic-related pollution on residents near the major traffic corridors along the U.S.-Canadian border. Here we report on a 10 year (1991-2000) retrospective study

of commercial traffic volumes across the Peace Bridge and health care use for asthma in a residential community, which serves as a conduit for traffic crossing between Fort Erie, Ontario, Canada, and Buffalo, New York. We hypothesized that commercial traffic pollution was impacting on residents in close proximity to the trade corridor. Commercial traffic volumes, hospital discharges for asthma, and outpatient visits to area hospitals and clinics were analyzed before and after implementation of NAFTA. Results showed a positive association between increased commercial traffic volume and increased health care use for asthma. Zip codes 14201 and 14213, which surround the Peace Bridge Plaza Complex (PBC), had the highest prevalence rates and health care use rates for asthma. Statistical analysis showed the findings to be significant ($p < 0.05$) in that residential proximity to the PBC was associated with greater hospital discharge rates for asthma. The findings were strongest ($p < 0.000$) in the zip codes where the PBC was located (14213) and the major highway I-190 passed through (14201). A yearly excess of 230.2 adult asthma hospital discharges was associated with an increase in traffic volume during the period from 1991 to 1996 in the study area. This is in contrast to an overall decrease in the national rate of hospitalizations for asthma by 7.5% in the same period. The results suggest that NAFTA-related commercial traffic has a negative health impact on asthmatics living in close proximity to the trade corridor. Health and social costs due to traffic pollution need to be included in cost estimates of transport decisions related to the NAFTA corridors. Similar health effects due to NAFTA traffic need to be studied at other U.S.-Canada border crossing points.

Lwebuga-Mukasa J.S. et al. *Risk factors for asthma prevalence and chronic respiratory illnesses among residents of different neighbourhoods in Buffalo, New York.* J Epidemiol Community Health. 2004; 58(11) : 951-7.p **Abstract:** STUDY OBJECTIVE: The aim of this study is to identify risk factors for asthma prevalence and chronic respiratory illnesses in Buffalo's neighbourhoods after previous studies reported increased levels of asthma among residents on Buffalo's west side. DESIGN: Cross sectional surveys. SETTING: Buffalo neighbourhoods along a US-Canada border crossing point. SUBJECTS: A systematic random survey of 82% of the 2000 targeted households was conducted between January and August 2002. MAIN RESULTS: A multivariate logistic regression model shows that the risk of persons with asthma and chronic respiratory illnesses is significantly ($p < 0.05$) high among children and young adults living in Buffalo's west side, newer housing units, and of Latino ethnicity. In a separate analysis of the nine risk factors, it was observed that location, gender, age, and race were significant risk factors even after adjusting for age of housing, pets, moulds, animal trigger, and smoking. CONCLUSIONS: These findings confirm the hypothesis that a considerable risk of asthma and chronic respiratory illnesses exists particularly among Buffalo's west side residents. Further evaluation of these risk factors is warranted to determine the severity of asthma and the reasons for such a significant disease burden.

Lyon H. et al. *IL10 gene polymorphisms are associated with asthma phenotypes in children.* Genet Epidemiol. 2004; 26(2) : 155-65.p **Abstract:** IL10 is an anti-inflammatory cytokine that has been found to have lower production in macrophages and mononuclear cells from asthmatics. Since reduced IL10 levels may influence the severity of asthma phenotypes, we examined IL10 single-nucleotide polymorphisms (SNPs) for association with asthma severity and allergy phenotypes as quantitative traits. Utilizing DNA samples from 518 Caucasian asthmatic children from the Childhood Asthma Management Program (CAMP) and their parents, we genotyped six IL10 SNPs: 3 in the promoter, 2 in introns, and one in the 3' UTR. Using family-based association tests, each SNP was tested for association with asthma and allergy phenotypes individually. Population-based association analysis was performed with each SNP locus, the promoter haplotypes and the 6-loci haplotypes. The 3' UTR SNP was significantly associated with FEV(1) as a percent of

predicted (FEV(1)PP) ($P=0.0002$) in both the family and population analyses. The promoter haplotype GCC was positively associated with IgE levels and FEV(1)PP ($P=0.007$ and 0.012 , respectively). The promoter haplotype ATA was negatively associated with lnPC(20) and FEV(1)PP ($P=0.008$ and 0.043 , respectively). Polymorphisms in IL10 are associated with asthma phenotypes in this cohort. Further studies of variation in the IL10 gene may help elucidate the mechanism of asthma development in children.

Lyttle B. et al. *Fluticasone propionate 100 microg bid using a non-CFC propellant, HFA 134a, in asthmatic children.* Can Respir J. 2003; 10(2) : 103-9.p **Abstract:** BACKGROUND: Secondary to phasing out chlorofluorocarbons (CFCs), the fluticasone propionate (FP) pressurized metered-dose inhaler has been formulated in a nonozone-depleting propellant, hydrofluoralkane (HFA) 134a. OBJECTIVES: To demonstrate equivalent efficacy and safety of FP 200 microg daily propelled by HFA 134a to FP 200 microg daily propelled by CFCs 11 and 12 over a four-week treatment period in pediatric asthmatic patients. METHODS: The study was multinational, randomized, double blind and of parallel group design. Eligible patients aged 16 years and younger were steroid naive or receiving 500 microg/day or less of beclomethasone dipropionate, budesonide or flunisolide, or 250 microg/day or less of inhaled FP. The primary efficacy variable was mean morning peak expiratory flow with equivalence determined if the 90% CIs for the treatment differences between groups were within ± 15 L/min. RESULTS: Three hundred fifteen patients (mean age 9.3 ± 2.8 years) were randomly assigned; 158 patients received FP HFA 134a and 157 patients received FP CFC. Over the four-week treatment period, mean morning peak expiratory flow increased from baseline in both groups (14 L/min and 17 L/min, respectively), with a mean treatment difference of -2 L/min. Equivalence was demonstrated between the groups (90% CI -6 to +3 L/min; $P=0.589$). Both formulations were well tolerated with no serious drug-related events. CONCLUSIONS: FP propelled by HFA 134a has equivalent efficacy and comparable safety to FP propelled by CFC propellants at a microgram equivalent dose in pediatric asthmatic patients.

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Ma H.R. et al. *Clinical observation between chronic sustained cough with asthma and childhood inguinal hernia.* J Microbiol Immunol Infect. 2003; 36(4) : 275-7.p **Abstract:** Inguinal hernias are common and cause problems for the health services. Several factors are thought to influence their development. Patients under 16 years old who had received hernioplasty at National Taiwan University Hospital were enrolled in a study to analyze the correlation between preceding recurrent cough with asthma and later hernia development. Patients aged 5 and 6 years old (when admitted for hernioplasty in 2000) were particularly focused. This entailed further analysis of their birth history, family atopic history, specific allergic diseases (allergic rhinitis, atopic dermatitis, asthma), hernia type (direct or indirect), the onset of chronic cough and asthma. One hundred and sixty three patients (2.66%) from a total hernioplasty population of 6130 were found to have had preceding asthma with recurrent cough before having the hernioplasty intervention. One hundred twenty-five patients were aged 5 to 6 years old, among whom 8 (6.4%) patients were found to have asthma, and 20 (16%) patients were noted to have recurrent sustained cough. All the hernia types were indirect and were received with high suture ligation. In conclusion, the incidence of asthma was not significantly higher in the group of individuals receiving hernioplasty. However, a higher incidence of recurrent sustained cough was noted, which could be a relatively important factor for the hernia development. Further reliable cough measurements would be needed to evaluate the severity of recurrent sustained cough as the potential risk for the hernia development.

Ma J. et al. *US physician adherence to standards in asthma pharmacotherapy varies by patient and physician characteristics.* J Allergy Clin Immunol. 2003; 112(3) : 633-5.p

Maarsingh E.J. et al. *Airflow limitation in asthmatic children assessed with a non-invasive EMG technique.* Respir Physiol Neurobiol. 2002; 133(1-2) : 89-97.p **Abstract:** The aim of the study was to investigate the association between electromyography (EMG) of the diaphragm and intercostal muscles and the forced expiratory volume in 1 s (FEV(1)) at different levels of histamine-induced airflow limitation, and the response to salbutamol. Moreover, we assessed the reproducibility of the EMG measurements on 2 different occasions during different levels of airflow limitation in asthmatic school children. Fourteen children with asthma performed 2 histamine challenges with a 24-h time interval and 1 child performed 1 histamine challenge. The EMG signals were derived from surface electrodes. The logarithm of the EMG-activity-ratio (log EMGAR; mean peak-bottom ratio of respiratory muscle activity) was used as EMG parameter. The log EMGAR of the diaphragm (di) and the log EMGAR of the intercostal muscles (int) associated well with the histamine-induced fall in FEV(1) at 5% steps from the baseline value. After administration of salbutamol log EMGAR_{di} and log EMGAR_{int} returned to baseline mean peak-bottom values (for all leads P<0.001). The EMGAR_{di} and EMGAR_{int} values were reproducible at different levels of airflow limitation. This study showed that EMGAR_{di} and EMGAR_{int} as a parameter for a change in electrical activity of the diaphragm and intercostal muscles associated well with FEV(1), was reversible after salbutamol and was reproducible at different levels of histamine-induced airflow limitation in asthmatic school children.

Macaubas C. et al. *Association between antenatal cytokine production and the development of atopy and asthma at age 6 years.* Lancet. 2003; 362(9391) : 1192-7.p **Abstract:** **BACKGROUND:** Various lines of evidence suggest that antenatal factors are important in determining susceptibility to atopy and asthma. One possible mechanism is cytokines, production of which in the placenta is high throughout gestation and which protect placental integrity via control of local immunological homeostasis. We investigated antenatal cytokine concentrations in a prospective birth cohort, intensively monitored for atopy and asthma outcomes at age 6 years. **METHODS:** Cryopreserved cord-blood serum samples from 407 children were assayed for interleukins 4, 5, 6, 10, 12, and 13, interferon gamma, and tumour necrosis factor alpha (TNFalpha). Associations between family, antenatal, and perinatal factors, cord-blood cytokine concentrations, and atopy or asthma outcomes were analysed by logistic regression. Causal effects of cytokines on outcomes were estimated by propensity scores based on family, antenatal, and perinatal factors. **FINDINGS:** Detectable cord-blood concentrations of interleukin 4 and interferon gamma were each associated with lower risk of physician-diagnosed asthma (adjusted odds ratios 0.60 [95% CI 0.37-0.99] and 0.60 [0.37-0.97] respectively), current asthma (0.59 [0.33-1.00] and 0.39 [0.22-0.71]), and current wheeze (0.55 [0.32-0.93] and 0.52 [0.31-0.90]) and atopy (sensitisation to some inhalant allergens) outcomes at 6 years. High concentrations of TNFalpha were associated with lower risk of atopy but not with asthma risk. These associations were broadly unaltered by propensity-score adjustment. Maternal smoking was associated with higher risk of both wheeze at 6 years and lower concentrations of interleukin 4 and interferon gamma in cord blood. **INTERPRETATION:** The mechanism underlying attenuated T-helper-1/T-helper-2 cytokine production in high-risk children also apparently operates in control of cytokine production in the fetoplacental unit. The finding that this mechanism is dysregulated by maternal smoking suggests it is a target for antenatal environmental factors relevant to asthma aetiology.

Macdessi J.S. et al. *Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma.* Med J Aust. 2003; 178(5) : 214-6.p **Abstract:** Three children presented with adrenal crises, manifested by vomiting and hypoglycaemia, after protracted courses of high-dose inhaled corticosteroids for asthma. Significant dose reduction was possible in all three without loss of asthma control, emphasising the importance of back-titration to minimise dose. Parents of children taking high doses of inhaled corticosteroids should be alerted to the clinical features of adrenal insufficiency. If suspected, prompt medical assessment should be arranged, including serum glucose and cortisol measurement.

Mahabee-Gittens E.M. et al. *ED environmental tobacco smoke counseling.* Am J Emerg Med. 2005; 23(7) : 916-8.p

Mahabee-Gittens M. *Smoking in parents of children with asthma and bronchiolitis in a pediatric emergency department.* Pediatr Emerg Care. 2002; 18(1) : 4-7.p **Abstract:** **OBJECTIVES:** To determine smoking habits, levels of nicotine-addiction, readiness to quit, and beliefs about the effects of environmental tobacco smoke (ETS) of parents of children with bronchiolitis and asthma who present to a children's emergency department (ED). **DESIGN/METHODS:** This was a cross-sectional prevalence study of parents or legal guardians of children with asthma or bronchiolitis presenting to a pediatric ED. **RESULTS:** Two hundred forty-nine parents/legal guardians comprised the study group. The mean age (+/-SD) was 30.0 (+/-8.9) years; 88% were female; 51% were nonwhite; 37% were educated beyond high school. The self-reported smoking prevalence was 41% (95% CI = 32-51). Smoking prevalence among parents of wheezing children varied according to education, income, and race, but not according to gender, age, or employment status. Of the 102 smokers in the sample, 84 (82.4%, 95% CI = 73-88) reported that they wanted to quit; 78 (76.5%, 95% CI = 68-84) stated that they wanted to quit within the next month. Forty-nine percent (95% CI = 39-59) scored above 4 on the Fagerstrom Test for Nicotine Dependence and were considered nicotine-dependent. The majority of smokers admitted to smoking around their children (66.7%, 95% CI = 57-75). Many parents knew that ETS might contribute to the development of the following illnesses: colds/upper respiratory tract infections - 77.5%, otitis media - 68.6%, pneumonia - 50%, wheezing/asthma attacks - 86.3%, and SIDS - 31.4%. **CONCLUSION:** The prevalence of smoking and nicotine addiction among parents of children with asthma or bronchiolitis who bring their children to a pediatric ED is high. Many parents have some knowledge about the effects of ETS, and the majority would like to quit. Future studies to help determine the best way to deliver advice to parents on ETS exposure reduction and smoking cessation are warranted.

Mahachoklertwattana P. et al. *Decreased cortisol response to insulin induced hypoglycaemia in asthmatics treated with inhaled fluticasone propionate.* Arch Dis Child. 2004; 89(11) : 1055-8.p **Abstract:** **AIMS:** To assess adrenal function in asthmatic children treated with inhaled fluticasone propionate for up to 16 weeks. **METHODS:** Children with asthma and bronchial hyperresponsiveness to inhaled methacholine were treated with inhaled fluticasone 250-750 microg/day via Volumatic spacer. The insulin tolerance test (ITT) was performed to assess adrenal function. **RESULTS:** Eighteen asthmatic patients (10 boys, 8 girls), aged 7-17 years received inhaled fluticasone therapy at a median dose of 477 microg/m² per day for 5-16 weeks. Adrenal suppression, defined as 60 minute serum cortisol less than 500 nmol/l, was found in 9 of 18 children. Following the ITT, the median basal and 60 minute serum cortisol concentrations of the suppressed group were 135.0 and 350.0 nmol/l, respectively; the corresponding values for the unsuppressed group were 242.2 and 564.7 nmol/l. Repeat ITT in the suppressed group 2-3 months after discontinuation of fluticasone revealed that all patients had a 60 minute serum cortisol greater than 500 nmol/l. **CONCLUSION:** After therapy for asthma with inhaled fluticasone at

approximately 500 microg daily for up to 16 weeks, half the children had evidence of adrenal suppression.

Mahut B. et al. *Increase in alveolar nitric oxide in the presence of symptoms in childhood asthma.* *Chest.* 2004; 125(3) : 1012-8.p **Abstract:** STUDY OBJECTIVES: To determine respective contributions of alveolar and proximal airway compartments in exhaled nitric oxide (NO) output (QNO) in pediatric patients with asthma and to correlate their variations with mild symptoms or bronchial obstruction. PATIENTS AND DESIGN: In 15 asthmatic children with recent mild symptoms, 30 asymptomatic asthmatic children, and 15 healthy children, exhaled NO concentration was measured at multiple expiratory flow (V) rates allowing the calculation of alveolar and proximal airway contributions in QNO, using two approaches, ie, linear and nonlinear models. MEASUREMENTS AND RESULTS: Asymptomatic and recently symptomatic patients were not significantly different regarding FEV(1) and maximum V between 25% and 75% of FVC (MEF(25-75)): FEV(1), 93.3 +/- 13.4% vs 90 +/- 7.5%; MEF(25-75), 70 +/- 22% vs 68 +/- 28% of predicted values, respectively (mean +/- SD). Maximal airway QNO output was significantly higher in recently symptomatic vs asymptomatic patients ($p < 0.0001$), and in asymptomatic patients vs healthy children ($p < 0.02$): 134 +/- 7 nl/min, 55 +/- 43 nl/min, and 19 +/- 8 nl/min, respectively. In a multiple regression analysis, variables that influenced airway QNO output were symptoms ($p < 0.0001$) and distal airway obstruction as assessed by MEF(25-75) ($p < 0.05$). Alveolar NO concentration (FANO) was significantly ($p < 0.03$) higher in recently symptomatic than in patients without symptoms, whereas it was not significantly different between asymptomatic patients and healthy children: 7.2 +/- 2.4 parts per billion (ppb), 5.5 +/- 2.7 ppb, and 4.2 +/- 2.0 ppb, respectively. CONCLUSIONS: An increase in FANO was observed in the presence of symptoms, and proximal airway NO output was correlated with distal obstruction during asthma.

Mai X.M. et al. *Leptin and asthma in overweight children at 12 years of age.* *Pediatr Allergy Immunol.* 2004; 15(6) : 523-30.p **Abstract:** Obesity is suggested as a risk factor for asthma, but the mechanisms are unclear. The relationship between obesity and asthma has not been considered in children born with very low-birth weight (VLBW). We hypothesized that overweight was a contributing factor for asthma in VLBW children, and that leptin and leptin-associated cytokines might play roles in overweight-related asthma. Seventy-four VLBW and 64 normal birth weight (NBW) children participated in a 12-yr follow up study assessing asthma and allergy. Twenty-seven (12 VLBW) of the 138 children were overweight according to the proposed international definition. The diagnosis of current asthma was made by a pediatrician. Serum levels of leptin and interferon (IFN)-gamma were analyzed by enzyme-linked immunosorbent assay (ELISA). Leptin levels were considerably higher in the overweight than in the non-overweight children (median value: 18.1 vs. 2.8 ng/ml, $p < 0.001$). In the overweight children, current asthmatics had twice as high levels of leptin as children without current asthma (median value: 30.8 vs. 14.3 ng/ml, $p = 0.14$), but this was not the case in the non-overweight children. IFN-gamma was more often detected in the overweight than in the non-overweight children (61% vs. 12%, $p < 0.001$), and there was a positive correlation between the levels of leptin and the levels of IFN-gamma ($Rho = 0.40$, $p < 0.001$). In the VLBW group, the overweight children had a significantly increased risk for current asthma compared with the non-overweight children after adjustment for the neonatal risk factors [adjusted odds ratio (OR) 5.8, 95% confidence interval (CI): 1.2-27]. Thus, overweight was associated with asthma in the VLBW children. Our hypothesis remained that leptin might be involved in the pathogenesis of asthma in the overweight children, and IFN-gamma might be a pathway in the process of leptin-induced inflammation.

Mai X.M. et al. *Early rapid weight gain and current overweight in relation to asthma in adolescents born with very low birth weight.* *Pediatr Allergy Immunol.* 2005; 16(5) : 380-5.p **Abstract:** Early catch-up growth and subsequent overweight are suggested to be associated with later cardiovascular diseases and later type II diabetes. However, the impact of early catch-up growth and childhood overweight on the development of asthma has been less studied, particularly in children born with very low birth weight (VLBW). A birth cohort of 74 VLBW children (birth weight $< \text{or} = 1500 \text{ g}$) was followed from birth and investigated on asthma at 12 yr of age. Early rapid weight gain was in one way defined as an increase of weight $> \text{or} = 1$ standard deviation score (SDS) at 6 months of corrected postnatal age. Current overweight was defined by body mass index (BMI) exceeding 21.2 and 21.7 kg/m², respectively, for boys and girls at 12 yr of age. Current asthma was diagnosed by a pediatrician, according to asthma ever in combination with a positive response to hypertonic saline bronchial provocation test and/or wheeze at physical examination at 12 yr old. Being overweight at 12 yr of age was associated with an increased risk for current asthma in the VLBW children [crude odds ratio (OR): 5.5, 95% confidence interval (CI): 1.3-22.2]. After adjustment for early weight gain and neonatal risk, the OR of overweight increased nearly three times (adjusted OR: 15.3, 95% CI: 2.5-90.6). Early rapid weight gain seemed to be inversely associated with current asthma (adjusted OR: 0.49 for an increase of weight equal to 1 SDS, 95% CI: 0.23-1.02, $p = 0.06$). In addition, early rapid weight gain was inversely associated with the magnitude of bronchial responsiveness at 12 yr (coefficient -1.15, $p < 0.01$). There was a strong and positive association between overweight and asthma at 12 yr of age in the VLBW children. This strong association had been reduced by early rapid weight gain, possibly via the reduction of bronchial responsiveness.

Mai X.M. et al. *Hypertonic saline challenge tests in the diagnosis of bronchial hyperresponsiveness and asthma in children.* *Pediatr Allergy Immunol.* 2002; 13(5) : 361-7.p **Abstract:** The hypertonic saline challenge test is the recommended method to assess bronchial hyperresponsiveness in the International Study of Asthma and Allergies in Childhood (ISAAC). The sensitivity of this procedure to assess asthma symptoms, however, has been reported to vary among study centers. The purpose of our study was to evaluate the value of this provocation test in an epidemiological survey in children, and to relate the degree of bronchial hyperresponsiveness to the severity of asthma symptoms. All 11-13-year-old children from 16 randomly selected schools in Linköping, Sweden received a questionnaire regarding respiratory symptoms and allergic disease. Skin prick tests with eight inhalant allergens were performed. In addition, all children with wheeze over the past 12 months (current wheeze) and a random sample of children without current wheeze were invited to perform hypertonic saline provocation tests. A complete data set was available for 170 children, including 50 with and 120 without current wheeze. Bronchial hyperresponsiveness (BHR) was defined as at least 15% decline in FEV1. The degree of BHR was represented by the response/dose ratio, i.e. the fall in FEV1 divided by total dose of inhaled saline. The severity of asthma symptoms was classified by the number of wheezing episodes over the past 12 months. 'Asthma ever' was defined by a combination of symptoms in the questionnaires. Children with 'asthma ever' and current wheeze were considered as having current asthma. Current atopic asthma was defined as current asthma with at least one positive skin prick test. The sensitivity of the procedure to detect 'asthma ever', current asthma and current atopic asthma was 62, 61 and 83%, and the specificity 83, 81 and 60%, respectively. The positive challenge rate was 52, 34, 13 and 7% among current wheezers, previous wheezers, non-wheezers with a history of allergy and healthy children. The degree of bronchial hyperresponsiveness increased with the number of wheezing episodes. Thus, the median and range of the response/dose ratio were 4.8%/ml (2.1-14.8), 2.6%/ml (0.7-8.6) and 1.3%/ml (0.8-2.7), respectively, for children with ≥ 4 episodes, 1-3 episodes and no wheezing episodes over the past 12 months ($p < 0.001$). In conclusion, hypertonic saline provocation test is useful

as a tool to detect asthma in epidemiological studies in children. The degree of bronchial hyperresponsiveness, as represented by the response/dose ratio, reflects the severity of asthma symptoms.

Maitra A. et al. *Mode of delivery is not associated with asthma or atopy in childhood.* Clin Exp Allergy. 2004; 34(9) : 1349-55.p Abstract: BACKGROUND: Caesarean-section delivery has been associated with the subsequent development of atopy and wheezing in childhood. OBJECTIVE: To examine the association between mode of delivery (vaginal vs. caesarean section) and development of atopy, asthma and wheezing disorders in a population-based cohort of children. METHODS: The Avon Longitudinal Study of Parents and Children is a longitudinal birth cohort of children born 1 April 1991 to 31 December 1992. Mode of delivery was categorized as vaginal (including forceps and ventouse extractions) or caesarean section (elective and emergency). Primary outcomes were parental report of asthma or wheezing between 69 and 81 months of age, physician-diagnosed asthma (PDA) at 91 months of age and atopy at 7 years by skin prick testing. Possible confounding factors were considered in a multivariable logistic regression model. RESULTS: Total livebirths were 14,062, from which were selected 12 367 born to mothers resident in a defined area and delivered in one of two major obstetric hospitals. Of these infants, 10,980 (88.8%) were delivered vaginally and 1387 (11.2%) by caesarean section. Outcome data were available for 7495 (61%) subjects (asthma 69-81 months); 7389 (60%) (wheeze 69-81 months); 7196 (58%) (PDA 91 months) and 5916 (48%) (atopy 7 years). Adjusted odds ratios [95% confidence interval] for caesarean section compared with vaginal delivery were not statistically significant for any outcome we considered: asthma 69-81 months 1.16 [0.9, 1.5]; wheeze 69-81 months 0.95 [0.7, 1.3]; PDA 1.14 [0.9, 1.4]; atopy 1.04 [0.8, 1.3]. CONCLUSION: Delivery by caesarean section was not associated with the subsequent development of asthma, wheezing or atopy in later childhood in this population.

Majani G. et al. *Impact of children's respiratory allergies on caregivers.* Monaldi Arch Chest Dis. 2005; 63(4) : 199-203.p Abstract: BACKGROUND: Despite the great attention that has been paid to HRQoL in children with respiratory allergy, few studies have addressed this aspect in relation to caregivers. The aim of our study was to evaluate the impact of childhood respiratory allergies on caregivers by means of a new method. METHODS: 119 parents of children suffering from allergies (75 suffering from asthma and 44 suffering from rhinitis) were recruited from three Italian Allergy Units. Parents were asked to complete the Disease Impact On Caregiver (DIOC), a new non disease specific questionnaire, validated on the Italian population. The questionnaire consists of 31 items grouped in four factors (Performance, Personal gratification, Psychophysical endurance, Socio-emotional domain) and covers the life aspects that could be affected by the assistance duties towards an ill family member. RESULTS: Child's asthma resulted to have a worse impact on many aspects of a parents' life than rhinitis. Differences resulted to be statistically significant in 19 aspects out of the 31 assessed. The worse impact of asthma versus rhinitis was confirmed in the following domains: Performance (24.0 +/- 18.2 vs 11.5 +/- 17.8), Personal gratification (26.3 +/- 20.5 vs 12.1 +/- 16.5) and Psychophysical endurance (35.0 +/- 24.8 vs 18.8 +/- 21.7). In the Socio-emotional domain no difference emerged. CONCLUSIONS: Compared to parents of rhinitics, parents of asthmatic children appear to be more compromised in their resistance to stress, mood, emotional stability, amount of spare time and leisure activities. Our results suggest the need of giving the due attention to these problems both in clinical practice and in research, in order to avoid possible interferences of the caregiver's distress in the optimization of treatment outcome.

Makarova S.I. et al. *Atopy parameters in asthmatic children increase with accumulation of null-alleles of glutathione-S-transferase M1.* Bull

Exp Biol Med. 2004; 138(5) : 460-2.p Abstract: Atopy parameters (total IgE, skin prick test, and peripheral blood eosinophil count) in children with atopic bronchial asthma depend on the number of glutathione-S-transferase M1 mutant alleles in the genotype and on family history of asthma.

Makino S. et al. *Pharmacologic control of asthma.* Int Arch Allergy Immunol. 2005; 136 Suppl 1 : 14-49.p

Malik R. et al. *Counseling hospitalized pediatric patients with asthma.* Am J Health Syst Pharm. 2002; 59(19) : 1829, 1833.p

Mallol J. *[Satellite symposium: Asthma in the World. Asthma among children in Latin America].* Allergol Immunopathol (Madr). 2004; 32(3) : 100-3.p Abstract: The prevalence of respiratory symptoms related to asthma in children from Latin America has been largely ignored. This region participated in phases I and III of the International Study of Asthma and Allergies in Childhood (ISAAC) with 17 participating centers in phase I and 78 centers in phase III. Data were obtained on asthma, rhinitis and eczema from countries and centers with markedly different climactic, cultural and environmental conditions and socioeconomic development. The results for phase I are presented herein because data from phase III are currently being revised at the ISAAC international data control center and will be officially available in the second half of 2004. Phase I provided important information on the prevalence of asthma in the participating countries and demonstrated wide variation among centers in the same country and among countries. The participating Latin American countries are all developing countries and share more or less the same problems related to low socioeconomic status. Therefore, the results and figures should be analyzed within that context. The range for accumulative and current asthma symptoms in children from the Latin American countries that participated in phase I (89,000) were as follows: the prevalence of asthma ranged from 5.5% to 28% in children aged 13-14 years and from 4.1% to 26.9% in children aged 6-7 years. The prevalence of wheezing in the previous 12 months ranged from 6.6% to 27% in children aged 13-14 years and from 8.6% to 32.1% in children aged 6-7 years. The high figures for asthma in a region with a high level of gastrointestinal parasites infestation, a high burden of acute respiratory and gastrointestinal infections occurring early in life, severe environmental and hygiene problems, suggest that these factors, considered as protective in other (developed) regions of the world, do not have the same effect in this region. Furthermore, those aggressive environmental conditions acting together from very early in life might condition different asthmatic phenotypes with more severe clinical presentation in infancy (first 2 years of life), lower atopy and enhanced airways reactivity. The present study indicates that the prevalence of asthma and related symptoms in Latin America is as high and variable as described previously for industrialized or developed regions of the world and that the environmental risk factors, mainly related with poverty, could be responsible for the different clinical and functional presentations of asthma in children from developing regions.

Malmberg L.P. et al. *Exhaled nitric oxide rather than lung function distinguishes preschool children with probable asthma.* Thorax. 2003; 58(6) : 494-9.p Abstract: BACKGROUND: Respiratory function and airway inflammation can be evaluated in preschool children with special techniques, but their relative power in identifying young children with asthma has not been studied. This study was undertaken to compare the value of exhaled nitric oxide (FE(NO)), baseline lung function, and bronchodilator responsiveness in identifying children with newly detected probable asthma. METHODS: Ninety six preschool children (age 3.8-7.5 years) with asthmatic symptoms or history and 62 age matched healthy non-atopic controls were studied. FE(NO) was measured with the standard online single exhalation technique, and baseline lung

function and bronchodilator responsiveness were measured using impulse oscillometry (IOS). RESULTS: Children with probable asthma (n=21), characterised by recent recurrent wheeze, had a significantly higher mean (SE) concentration of FE(NO) than controls (22.1 (3.4) ppb v 5.3 (0.4) ppb; mean difference 16.8 ppb, 95% CI 12.0 to 21.5) and also had higher baseline respiratory resistance, lower reactance, and larger bronchodilator responses expressed as the change in resistance after inhalation of salbutamol. Children with chronic cough only (n=46) also had significantly raised mean FE(NO) (9.2 (1.5) ppb; mean difference 3.9 ppb, 95% CI 0.8 to 7.0) but their lung function was not significantly reduced. Children on inhaled steroids due to previously diagnosed asthma (n=29) differed from the controls only in their baseline lung function. The analysis of receiver operating characteristics (ROC) showed that FE(NO) provided the best power for discriminating between children with probable asthma and healthy controls, with a sensitivity of 86% and specificity of 92% at the cut off level of 1.5 SD above predicted. CONCLUSIONS: FE(NO) is superior to baseline respiratory function and bronchodilator responsiveness in identifying preschool children with probable asthma. The results emphasise the presence of airway inflammation in the early stages of asthma, even in young children.

Malone R. et al. *The safety of twice-daily treatment with fluticasone propionate and salmeterol in pediatric patients with persistent asthma.* Ann Allergy Asthma Immunol. 2005; 95(1) : 66-71.p **Abstract:** BACKGROUND: For children older than 5 years with asthma who remain symptomatic despite inhaled corticosteroid (ICS) therapy, the preferred treatment is to add an inhaled long-acting beta2-agonist vs increasing the ICS dose. OBJECTIVE: To compare the safety of twice-daily treatment with inhaled fluticasone propionate plus the inhaled long-acting beta2-agonist salmeterol with that of fluticasone propionate used alone in children aged 4 to 11 years with persistent asthma. METHODS: A randomized, multicenter, double-blind, active-controlled, parallel-group study in 203 children with persistent asthma who were symptomatic during ICS therapy. Patients received fluticasone propionate-salmeterol (100/50 microg) or fluticasone propionate (100 microg) alone twice daily for 12 weeks. RESULTS: The safety profile of fluticasone propionate-salmeterol was similar to that of fluticasone propionate alone. The overall incidence of adverse events was 59% for fluticasone propionate-salmeterol and 57% for fluticasone propionate. Both treatments were well tolerated. Two patients receiving fluticasone propionate-salmeterol and 5 receiving fluticasone propionate withdrew from the study because of worsening asthma. Changes in heart rate, blood pressure, and laboratory variables were infrequent and were similar between treatments. No patients had clinically significant abnormal electrocardiographic findings during treatment. Geometric mean 24-hour urinary cortisol excretion at baseline and after 12 weeks of treatment was comparable within and between groups; no patient in either group had abnormally low 24-hour urinary cortisol excretion after 12 weeks of treatment. The incidence of withdrawals due to asthma exacerbations was 2% in the fluticasone propionate-salmeterol group and 5% in the fluticasone propionate group. CONCLUSIONS: In pediatric patients with persistent asthma, fluticasone propionate-salmeterol twice daily was well tolerated, with a safety profile similar to that of fluticasone propionate used alone.

Mander A. et al. *Altered phospholipid composition and aggregate structure of lung surfactant is associated with impaired lung function in young children with respiratory infections.* Am J Respir Cell Mol Biol. 2002; 27(6) : 714-21.p **Abstract:** Alterations to pulmonary surfactant structure, composition, and function contribute to the severity of respiratory infections. Analysis of bronchoalveolar lavage fluid (BALF) from children undergoing diagnostic bronchoscopy for structural abnormalities (control group, n = 24), asthma (n = 18), lung infection (n = 30), and cystic fibrosis (CF, n = 15) showed that BALF phospholipid concentration decreased with age for the control

group and was elevated in all disease groups. The fractional concentration of the major surface active component, dipalmitoyl phosphatidylcholine (PC16:0/16:0), correlated ($r(2) = 0.608$, $P < 0.01$) with airway resistance (FEV(1%) predicted), and decreased PC16:0/16:0 was accompanied by increased concentrations of phospholipid components characteristic of cell membranes (PC16:0/18:1 and PI18:0/20:4). Median minimal surface tension, measured by pulsating bubble surfactometer, was elevated ($P < 0.01$) in both infection (17.5 mN/m) and CF (17.1 mN/m) compared with the control group (1.5 mN/m). Centrifugation (60,000 x g, 40 min) of BALF indicated that infection was accompanied by accumulation of large aggregate forms of surfactant, in contrast to previous reports of increased conversion to inactive small aggregate surfactant particles in ventilated patients with respiratory failure. This accumulation of surface-inactive, large aggregate forms of surfactant, possibly due to mixing with membrane material from inflammatory cells, may contribute to severity of lung disease in children with respiratory infections.

Mandhane P.J. et al. *Sex differences in factors associated with childhood and adolescent-onset wheeze.* Am J Respir Crit Care Med. 2005; 172(1) : 45-54.p **Abstract:** RATIONALE: Factors predicting the development of wheeze may differ between sexes and between childhood and adolescence. METHODS: A New Zealand birth cohort of 1,037 children was followed to age 26. For this analysis, those reporting recurrent wheezing at two or more assessments were classified as "wheezers." We examined risk factors for development of wheeze before age 10 (childhood) and subsequently (adolescent-onset) for males and for females separately using Cox regression modeling. RESULTS: Males more often developed childhood wheeze ($p = 0.002$) and females adolescent-onset wheeze ($p < 0.001$). Maternal atopy (asthma or hay fever) was a risk factor for childhood wheeze in both sexes (hazard ratio [HR], 1.48, $p < 0.05$ for males; HR, 2.37, $p < 0.001$ for females). Paternal atopy also influenced childhood wheeze, significantly for males (HR, 1.72; $p = 0.01$), and similarly but not significantly for females (HR, 1.70; $p = 0.08$). For adolescent-onset wheeze, neither maternal (HR, 1.41; $p = 0.19$) nor paternal history (HR, 0.73; $p = 0.42$) was a risk factor in males, but maternal history (HR, 2.08; $p < 0.01$) was a significant risk factor for females. When both age ranges were combined, providing greater power for analysis, paternal history was a stronger risk factor for wheeze in females (HR, 1.62; $p = 0.02$) than in males (HR, 1.35; $p = 0.12$). CONCLUSION: The influence of parental atopy on the development for wheeze differs between males and females and between childhood- and adolescent-onset wheeze.

Mangione-Smith R. et al. *Measuring the effectiveness of a collaborative for quality improvement in pediatric asthma care: does implementing the chronic care model improve processes and outcomes of care?* Ambul Pediatr. 2005; 5(2) : 75-82.p **Abstract:** OBJECTIVE: To examine whether a collaborative to improve pediatric asthma care positively influenced processes and outcomes of that care. METHODS: Medical record abstractions and patient/parent interviews were used to make pre- and postintervention comparisons of patients at 9 sites that participated in the evaluation of a Breakthrough Series (BTS) collaborative for asthma care with patients at 4 matched control sites. SETTING: Thirteen primary care clinics. PATIENTS: Three hundred eighty-five asthmatic children who received care at an intervention clinic and 126 who received care at a control clinic (response rate = 76%). INTERVENTION: Three 2-day educational sessions for quality improvement teams from participating sites followed by 3 "action" periods over the course of a year. RESULTS: The overall process of asthma care improved significantly in the intervention group but remained unchanged in the control group (change in process score +13% vs 0%; $P < .0001$). Patients in the intervention group were more likely than patients in the control group to monitor their peak flows (70% vs 43%; $P < .0001$) and to have a written action plan (41% vs 22%; $P = .001$). Patients in the intervention group had better general health-

related quality of life (scale score 80 vs 77; $P = .05$) and asthma-specific quality of life related to treatment problems (scale score 89 vs 85; $P < .05$). **CONCLUSIONS:** The intervention improved some important aspects of processes of care that have previously been linked to better outcomes. Patients who received care at intervention clinics also reported higher general and asthma-specific quality of life.

Mangunkusumo R.T. et al. *Internet versus paper mode of health and health behavior questionnaires in elementary schools: asthma and fruit as examples.* J Sch Health. 2006; 76(2) : 80-6.p **Abstract:** The Internet has become an inevitable tool for collecting health and health behavior questionnaires. This study compared the feasibility, presence of score differences, and subjective evaluations by children between Internet and identical paper (asthma/fruit) questionnaires in elementary schools. A randomized crossover design was applied, with children starting with one administration mode before completing (5 minutes later) the other mode. Ten Dutch elementary schools with 270 school children (fifth grade, 10-12 years) were approached to participate. Response was 92%. The Internet mode had significantly less missing/nonunique answers than the paper mode ($p < .01$). The completion times did not differ significantly between the Internet and the paper mode. Except for perceived self-efficacy to eat sufficient fruit ($p < .05$), no differences in the asthma and fruit scores were found when comparing between the 2 modes. All variables showed strong intraclass correlation coefficients (166 $>or=$ 0.64) between modes. Most items had good to very good agreement (kappa 0.61-0.95). The percentages for global and exact agreement ranged per item from 61.3 to 100. Most children preferred the Internet mode on "general preference" and "ease of use" aspects but rated no preference on "understandability." The majority rated the evaluation aspects of the Internet mode positively. Thus, Internet administration of a health and health behavior questionnaire is feasible at elementary schools, gives comparable responses, and is well accepted and preferred by children compared to the paper version. Therefore, it is recommended to use Internet as a tool in health and health behavior research among children.

Mann M. et al. *Serious asthma exacerbations in asthmatics treated with high-dose formoterol.* Chest. 2003; 124(1) : 70-4.p **Abstract:** **OBJECTIVE:** To review three prospective, randomized, placebo-controlled, double-blind clinical studies of formoterol (Foradil Aerolizer; Novartis Pharmaceuticals; Basel, Switzerland) at dosages of 12 microg and 24 microg bid for the treatment of patients with asthma. **DATA SOURCES:** Clinical studies submitted to the US Food and Drug Administration in support of the approval of Foradil Aerolizer for marketing in the United States. **RESULTS:** More patients treated regularly with formoterol, 24 microg bid, had a serious asthma exacerbation than did patients who had been treated with placebo. In the first study, 4 of 135 adult patients (3%) who had been treated with formoterol, 24 microg bid, had a serious asthma exacerbation compared to none of 136 placebo-treated patients. In the second study, 5 of 136 patients (3.7%) treated with formoterol, 24 microg bid, had a serious asthma exacerbation compared to 2 of 141 placebo-treated patients (1.4%). In the third study, 11 of 171 pediatric patients (6.4%) treated with formoterol, 24 microg bid, had a serious asthma exacerbation compared to none of 176 placebo-treated patients. **CONCLUSION:** Regular use of high-dose inhaled formoterol (24 microg bid) may be associated with more frequent serious asthma exacerbations.

Manning P. et al. *Asthma control and management: a patient's perspective.* Ir Med J. 2005; 98(10) : 231-2, 234-5.p **Abstract:** Irish asthma guidelines, published in 2000, are based on the Global Initiative for Asthma (GINA) international asthma management guidelines and provide recommendations for optimal asthma management and control. Using the same methodology as employed in the Asthma Insights and Reality in Europe (AIRE) survey, which

assessed whether specific goals of asthma management based on GINA were being realised, 400 patients with current asthma in Ireland were interviewed in the Asthma Insights and Reality in Ireland (AIRI) survey to determine their healthcare utilisation, symptom severity, activity limitations and level of asthma control. Of those surveyed, acute services were utilised by a significant number of respondents. Over the previous year, 27% had either an emergency visit to the hospital or their general practitioner (GP) and 7% were hospitalised for asthma. In terms of asthma control, 19% experienced sleep disturbance at least once a week, 29% missed work or school and 37% of respondents experienced symptoms during physical activity over the previous 4-week period. Based on these findings, the level of asthma control and asthma management in Ireland falls short of recommended national and international asthma guidelines.

Manolio T.A. et al. *Correlates of sensitization to *Blomia tropicalis* and *Dermatophagoides pteronyssinus* in asthma in Barbados.* Int Arch Allergy Immunol. 2003; 131(2) : 119-26.p **Abstract:** **BACKGROUND:** Sensitivity to the mite *Blomia tropicalis* is related to asthma in tropical climates, but correlates of sensitivity to *B. tropicalis* and its relationship to *Dermatophagoides pteronyssinus* sensitivity have not been widely examined in families with asthma. The main objective of this study was to determine prevalence and correlates of sensitivity to these mites in families with asthma and characteristics of persons sensitized to both. **METHODS:** Antibodies to major antigens (Blo t 5 and Der p 1) of these mites were measured by immunochemiluminescent assay in 481 members of 29 families from Barbados ascertained through two asthmatic siblings. **RESULTS:** Blo t 5 sensitivity was present in 261 subjects (46%) and was associated with younger age, higher total serum IgE level, and more than a three-fold increased prevalence of asthma (42 vs. 13%). Der p 1 sensitivity was less common (27%) and showed similar associations with age, IgE, and asthma. Of the 261 subjects sensitized to Blo t 5, 116 were also sensitized to Der p 1; they were younger, had higher total and Blo t 5 specific IgE levels, and had more than twice the asthma prevalence as those sensitized to Blo t 5 alone (59 vs. 29%). Der p 1 sensitivity without Blo t 5 sensitivity was uncommon; 90% of those sensitized to Der p 1 were also sensitized to Blo t 5. Geometric mean total IgE levels were lowest in the 207 participants without any mite sensitization (102 U/ml), intermediate in 158 sensitized to either Blo t 5 OR Der p 1 (609 U/ml), and highest in 116 sensitized to both (1,869 U/ml). **CONCLUSIONS:** Blo t 5 is the predominant sensitizing mite allergen in these Barbadian families with correlates similar to Der p 1. Concomitant sensitization to Der p 1 appears to identify a more reactive subgroup of individuals at a higher risk of asthma.

Mansur A.H. et al. *Linkage/association study of a locus modulating total serum IgE on chromosome 14q13-24 in families with asthma.* Thorax. 2004; 59(10) : 876-82.p **Abstract:** **BACKGROUND:** A study was undertaken to validate a locus modulating total serum IgE levels on 14q13-24. **METHODS:** A linkage and association study was performed between total serum IgE and a panel of seven microsatellites which map to the 14q13-24 region in 69 families with asthma recruited from Leeds, UK. **RESULTS:** Non-parametric, multipoint, sib pair analysis showed no evidence of genetic linkage between the quantitative trait "log IgE" and any of the tested markers. However, a significant association was observed between locus D14S63 (14q23) and total serum IgE ($p = 0.017$). Allelic analysis showed an association between low total IgE and allele 157 of D14S63 ($p = 0.01$, OR = 0.63, 95% CI 0.44 to 0.90). Modelling of allele 157 genotypes as a continuous covariate indicated evidence of a significant inverse linear trend across the three genotypes where 157 homozygotes had the lowest mean log IgE ($p = 0.045$). Association of D14S63 with log IgE was confirmed in the analysis of a combined dataset of 53 families from Southampton, UK and the 69 families from Leeds (total 122 families). An association was observed at the locus level ($p = 0.022$) and the allelic level where allele 165 showed an association with high total IgE ($p = 0.001$, OR

= 3.79, 95% CI 1.54 to 9.7) and allele 157 showed an association with low total IgE ($p = 0.041$, OR = 0.77, 95% CI 0.6 to 0.99). The transmission disequilibrium test was positive for allele 165 ($p < 0.05$) and negative for allele 157 ($p > 0.05$). CONCLUSIONS: Despite the lack of linkage, the findings of this study support the previous observation of a gene(s) at 14q23 that modulates total serum IgE.

Mantymaa M. et al. *Infant-mother interaction as a predictor of child's chronic health problems.* Child Care Health Dev. 2003; 29(3) : 181-91.p **Abstract:** BACKGROUND: Psychological stress is associated with physical illnesses like asthma or infections. For an infant, situations perceived as stressful are highly dependent on the relationship with the caregiver. Constantly poor mother-infant interaction increases the child's vulnerability to stressful conditions and experiences. The aim of the study was to investigate the impact of the quality of early mother-infant interaction on the subsequent physical health of the child. Poor mother-infant interaction was hypothesized to be associated with chronic or recurrent health problems in the child. PARTICIPANTS: Fifty-seven mother-infant dyads from families at risk of psychosocial problems and 63 from non-risk families, altogether 120 dyads, participated in the study. Families were drawn from normal population, from well-baby clinics in the city of Tampere, Finland. Infants were full-term and healthy, families with severe risks like psychotic illnesses of the parents or a history of child protection concerns were excluded from the study. METHODS: After the initial interview with the mother, the mother-infant interaction was videotaped when the infants were 8-11 weeks of age and the interaction was assessed using the Global Rating Scale for Mother-Infant Interaction (Murray et al. 1996a). After the 2-year follow-up mothers were interviewed again and the health problems of the child were elicited. RESULTS: Poor dyadic mother-infant interaction and infant's poor interactive behaviour assessed at two months were separately associated with the physical health of the child during the two-year follow-up. After adjusting for other factors in the logistic regression analysis infant's poor interactive behaviour remained as a significant predictor of chronic or recurrent health problems in the child. Infant's health problems at the time of the initial interview and day care centre attendance were also significant predictors. CONCLUSIONS: The results suggest that interactional issues between a mother and her infant are related to the child's subsequent physical health. Children with recurrent or chronic health problems may have relationship difficulties with which they need help. Also, early avoidant behaviour of the infant should be regarded as an indicator of the infant's distress with possibly adverse outcomes in the child's physical health, among other consequences.

Mantzouranis E.C. et al. *Throat clearing - a novel asthma symptom in children.* N Engl J Med. 2003; 348(15) : 1502-3.p

Marcal L.E. et al. *Superoxide release and cellular glutathione peroxidase activity in leukocytes from children with persistent asthma.* Braz J Med Biol Res. 2004; 37(11) : 1607-13.p **Abstract:** Asthma is an inflammatory condition characterized by the involvement of several mediators, including reactive oxygen species. The aim of the present study was to investigate the superoxide release and cellular glutathione peroxidase (cGPx) activity in peripheral blood granulocytes and monocytes from children and adolescents with atopic asthma. Forty-four patients were selected and classified as having intermittent or persistent asthma (mild, moderate or severe). The spontaneous or phorbol myristate acetate (PMA, 30 nM)-induced superoxide release by granulocytes and monocytes was determined at 0, 5, 15, and 25 min. cGPx activity was assayed spectrophotometrically. The spontaneous superoxide release by granulocytes from patients with mild ($N = 15$), moderate ($N = 12$) or severe ($N = 6$) asthma was higher at 25 min compared to healthy individuals ($N = 28$, $P < 0.05$, Duncan test). The PMA-induced superoxide release by granulocytes from patients with moderate ($N = 12$) or severe ($N = 6$) asthma was higher at 15 and 25 min compared to healthy individuals ($N = 28$, $P < 0.05$ in both times of incubation,

Duncan test). The spontaneous or PMA-induced superoxide release by monocytes from asthmatic patients was similar to healthy individuals ($P > 0.05$ in all times of incubation, Duncan test). cGPx activity of granulocytes and monocytes from patients with persistent asthma ($N = 20$) was also similar to healthy individuals ($N = 10$, $P > 0.05$, Kruskal-Wallis test). We conclude that, under specific circumstances, granulocytes from children with persistent asthma present a higher respiratory burst activity compared to healthy individuals. These findings indicate a risk of oxidative stress, phagocyte auto-oxidation, and the subsequent release of intracellular toxic oxidants and enzymes, leading to additional inflammation and lung damage in asthmatic children.

Marchal F. et al. *Filtering artefacts in measurements of forced oscillation respiratory impedance in young children.* Physiol Meas. 2004; 25(5) : 1153-66.p **Abstract:** Respiratory mechanical impedance measured at a single frequency is of great interest to describe change in airways dimensions with time in young children with asthma. Adequate filtering is mandatory in order to eliminate spurious values at rapid flow transient or during glottis closure. The aim of the study was to test a new filtering procedure. Respiratory impedance was measured at 12 Hz using the head generator technique in 33 asthmatic children aged 3.5-7.5 years. Two separate measurements were obtained at baseline and one 10 min after salbutamol inhalation. Assuming corrupted data would correspond to major distortion in flow oscillation, the tested procedure calculated an index expressing departure of each flow oscillation from an ideal sinusoid (flow shape index filter (FSIF)). Cut-offs ranging from 5 to 20% were compared to the visual identification and 'by hand' elimination of corrupted data (visual filtering). Sensitivity and specificity of FSIF versus visual filtering indicated an optimal range of cut-off values between 10 and 15% (FSIF10 and FSIF15). Compared with visual filtering, respiratory conductance in inspiration (Grs) was marginally but significantly lower with FSIF10 ($p < 0.01$) but not FSIF15 and had slightly larger (within measurement) coefficient of variation with either FSIF10 or FSIF15 ($p < 0.01$). Between-measurement repeatability of Grs and Grs change induced by salbutamol were similarly estimated by FSIF10, FSIF15 or visual filtering. It is concluded that FSIF appears as a valid alternative to visual filtering. The 10% cut-off is a good compromise considering sensitivity (72%), amount of rejected data (<20%) and effect on Grs and variability.

Marchal F. et al. *Respiratory impedance response to a deep inhalation in children with history of cough or asthma.* Pediatr Pulmonol. 2002; 33(6) : 411-8.p **Abstract:** The aim of this study was to describe the change in respiratory impedance induced by a deep inhalation (DI) in children who developed a positive response to inhalation of methacholine (Mch). Eighteen children aged 4.5-12.5 years, presenting with chronic cough or doctor-diagnosed asthma, were studied at baseline after inhalation of Mch and after inhalation of a bronchodilator. Respiratory resistance (Rrs) and reactance (Xrs) were measured by the forced oscillation technique, varying transrespiratory pressure at 12 Hz around the head. The tidal flow (V') and volume (V) dependence of Rrs before and after the DI was characterized according to the equation $Rrs = K1 + K2 \times V' + K3 \times V$. DI induced no significant change at baseline or after inhalation of a bronchodilator. During Mch challenge, Rrs and K1 were significantly lower, and K3 and Xrs significantly less negative after DI than before, during both inspiration and expiration; there was no change in K2. We conclude that DI results in a decrease in Rrs in children with induced bronchoconstriction. The associated changes in Xrs, K1, and K3, and lack of decrease in K2, suggest that dilatation of airways occurs at the bronchial level, with little contribution of the upper airways or of a change in breathing patterns.

Mari A. *Allergy-like asthma and rhinitis. A cross-sectional survey of a respiratory cohort and a diagnostic approach using the autologous*

serum skin test. Int Arch Allergy Immunol. 2004; 133(1) : 29-39.p

Abstract: BACKGROUND: Chronic idiopathic urticaria is considered an allergy-like skin disorder, and in some cases an auto-reactivity caused by mast cell degranulating factors has been demonstrated. A positive reaction to the autologous serum skin test (ASST), reflecting the presence of factors capable to degranulate the mast cells, is regarded as a reliable in vivo diagnostic test in chronic urticaria patients. About one out of three patients complaining for rhinitis or asthma does not show sensitization to any allergenic source. No data are available on the application of ASST to respiratory patients. METHODS: A cohort of respiratory patients, aged 1 to 80 years, complaining about suspected respiratory symptoms was screened using a panel of inhalant allergens by means of SPT and IgE. Current and past information on skin and respiratory symptoms were recorded for each patient. Patients were divided in 'allergy' and 'allergy-like' whether or not they react to at least one allergenic source. Age and gender distribution were analyzed. A control group fulfilling criteria for chronic idiopathic urticaria (CIU) was selected as well. The ASST was applied to the control CIU group, to the allergy-like and allergy subsets, and to a group of 58 healthy adult subjects. RESULTS: Allergy and allergy-like patients were differently distributed in relation to age and gender. Allergy-like children were prevalent before age six, whereas the prevalence of allergics steadily increased with age representing the large majority of patients in late childhood. The ratio of allergy/allergy-like subjects continues to increase in adult males, whereas adult females represent the large majority of the adult patients mainly within the allergy-like subset. Fifty-eight percent of CIU control patients reacted to the ASST. Among allergy-like patients ASST was positive in 47% of the adults (male 26%, female 54%), and in 84% of the children (no gender differences). The percentage of reactive subjects increased in the adult allergy-like subset if a CIU was associated (65%). Eighty-six percent of the pediatric patients and 61% of the adults having an allergy respiratory disease associated with an allergy-like condition had a positive ASST reactivity. Pure allergy patients reacted in 73% and 40% of the cases in the children and adults subgroups, respectively. Forty-five percent of healthy controls reacted to the ASST as well, and statistically significant gender differences were still recorded. CONCLUSIONS: An ASST reactivity is reported for the first time in allergy-like respiratory patients. A higher prevalence of reactive subjects has been recorded in all the pediatric subsets without gender differences, whereas female reactivity is prevalent among adults. The ASST reactivity seems to parallel the patient distribution within the entire respiratory cohort. Further studies are needed to demonstrate that the serum factors causing the ASST reactivity in respiratory patients are the same as for CIU affected subjects. In the light of recent in vitro findings, the ASST reactivity of healthy subjects could lead to a new interpretation of the autologous serum reactivity.

- Marin V. et al.** *Allergic memory of patients sensitized to castor bean after a long stimulation-free period.* J Asthma. 2006; 43(3) : 193-8.p **Abstract:** We have taken advantage of the temporary exposure of Marseilles population to castor bean seed proteins to follow 26 allergic patients more than 20 years after sensitization. Skin tests, specific immunoglobulin E (IgE) antibody assays, and specific immunoblots were performed. Skin test reactivity to Ricinus Communis and specific IgE concentrations decreased progressively and almost completely disappeared after 20 years. Specific IgE concentration displayed a fairly exponential decrease, with a half-life of 4.7 years. Thus, in the absence of any antigenic stimulation, directly by castor bean, or indirectly by cross-reactivity to other Euphorbiaceae, especially latex, IgE sensitization is bound to disappear.
- Marinho S. et al.** *Barnacle allergy: allergen characterization and cross-reactivity with mites.* J Investig Allergol Clin Immunol. 2006; 16(2) : 117-22.p **Abstract:** BACKGROUND: Barnacles are a type of seafood with worldwide distribution and abundant along the shores

of temperate seas. They are particularly appreciated and regularly consumed in Portugal as well as in Spain, France and South America, but barnacle allergy is a rare condition of which there is only one reference in the indexed literature. The molecular allergens and possible cross-reactivity phenomena implicated (namely with mites) have not been established. OBJECTIVE: To demonstrate the IgE-mediated allergy to barnacle and to identify the proteins implicated as well as possible cross-reactivity phenomena with mites. METHODS: We report the clinical and laboratory data of five patients with documented IgE-mediated allergy to barnacle. The diagnosis was based on a suggestive clinical history combined with positive skin prick tests (SPT) to barnacle-prick to prick method. Two barnacle extracts were prepared (raw and cooked barnacle) and sodium dodecylsulphate polyacrylamide gel electrophoresis (SDS-PAGE) and IgE-immunoblotting were performed. An immunoblotting inhibition assay with Dermatophagoides pteronyssinus was also done in order to evaluate cross-reactivity. RESULTS: All patients had mite-related asthma and the allergic rhinoconjunctivitis; they all experienced mucocutaneous symptoms. All of them had positive SPT to barnacle, and the immunoblotting showed several allergenic fractions with a wide molecular weight range (19 - 94 kDa). The D. pteronyssinus extract inhibited several IgE-binding protein fractions in the barnacle extract. CONCLUSIONS: We describe five patients with IgE-mediated barnacle allergy. We also describe a group of IgE-binding-proteins between 30 and 75 kDa as the allergenic fractions of this type of Crustacea. Cross-reactivity with D. pteronyssinus was demonstrated in two cases.

- Markovitz B.** *Does magnesium sulphate have a role in the management of paediatric status asthmaticus?* Arch Dis Child. 2002; 86(5) : 381-2.p
- Marks G.B. et al.** *Asthma in Australia 2005.* Med J Aust. 2005; 183(9) : 445-6.p **Abstract:** A recent report outlines the good and the bad news about asthma.
- Marks G.B. et al.** *A nationwide perspective on asthma in older Australians.* Med J Aust. 2005; 183(1 Suppl) : S14-6.p **Abstract:** WHAT WE NEED TO KNOW: What is the prevalence of impaired lung function among older people in Australia? How can we differentiate between asthma and other causes of breathlessness in population-based health surveys of older people? What are the effects of ageing on people with asthma? WHAT WE NEED TO DO: Improve existing survey measures and accuracy of diagnosis. Incorporate measures of spirometric function into health surveys of representative samples of the general population. Use spirometry in the diagnostic work-up of older patients with dyspnoea.
- Marshall L.J. et al.** *Free secretory component from cystic fibrosis sputa displays the cystic fibrosis glycosylation phenotype.* Am J Respir Crit Care Med. 2004; 169(3) : 399-406.p **Abstract:** Secretory IgA contributes to humoral defense mechanisms against pathogens targeting mucosal surfaces, and secretory component (SC) fulfills multiple roles in this defense. The aims of this study were to quantify total SC and to analyze the form of free SC in sputa from normal subjects, subjects with asthma, and subjects with cystic fibrosis (CF). Significantly higher levels of SC were detected in CF compared with both other groups. Gel filtration chromatography revealed that SC in CF was relatively degraded. Free SC normally binds interleukin (IL)-8 and inhibits its function. However, in CF sputa, IL-8 binding to intact SC was reduced. Analysis of the total carbohydrate content of free SC signified overglycosylation in CF compared with normal subjects and subjects with asthma. Monosaccharide composition analysis of free SC from CF subjects revealed overfucosylation and undersialylation, in agreement with the reported CF glycosylation phenotype. SC binding to IL-8 did not interfere with the binding of

IL-8 to heparin, indicating distinct binding sites on IL-8 for negative regulation of function by SC and heparin. We suggest that defective structure and function of SC contribute to the characteristic sustained inflammatory response in the CF airways.

Martignon G. et al. *Does childhood immunization against infectious diseases protect from the development of atopic disease?* *Pediatr Allergy Immunol.* 2005; 16(3) : 193-200.p **Abstract:** The argument of whether early immunization against infections promotes allergy or protects from it is presently under debate. The relationship between childhood immunization and the development of atopic diseases (asthma, allergic rhinitis and eczema) was examined in a population-based sample of 718 adolescents by taking individual data drawn from personal paediatric records on the schedule and the type of vaccination into account. Atopic diseases were determined using a standardized questionnaire. After adjustment for sex, age, father's socioeconomic status and active smoking, adolescents having been vaccinated (n = 694) had a significant lower risk to suffer from asthma or atopic diseases than non-vaccinated adolescents did (n = 24) [odds ratio (OR) = 0.30; 95% CI: 0.10, 0.92]. The relationship did not depend on the disease against which the vaccine was used as prophylaxis, the observance of the vaccination schedule or the number of inoculations. A higher protection was observed in the case of live attenuated vaccines (oral poliomyelitis and bacilli Camille-Guerin; OR = 0.26; 95% CI: 0.08, 0.83). These results, in agreement with previous ecological data, support the hypothesis that early vaccines could promote Th1 proliferation in response to the infectious agent contained in it, which inhibits the enhancement of atopic manifestations. Further studies are needed to confirm the phenomenon.

Martin I.R. et al. *To skin prick test or not to skin prick test - this is the question.* *N Z Med J.* 2002; 115(1161) : U166.p

Martin Iglesias M.A. et al. *Asthma camp. Quality of life questionnaires.* *Allergol Immunopathol (Madr).* 2003; 31(4) : 231-5.p **Abstract:** Asthma is one of the most common chronic childhood disease. Asthmatic children need a self-management educational program, besides the medical treatment and clinical control. Camps are the ideal place to complete the educational program, to get the right control of the disease and to build the child confidence. Madrid Castilla la Mancha Allergy Society organizes every year a summer camp in a town, near Madrid. Fifty-four children stay for one week with certified allergists, fellows-in-training, nurses and cheerleaders. Fifty-four children from 8 to 14 years old, with moderate to severe asthma participate in the camp. The camp includes educational, athletic and social activities. Campers participate daily in instructive and didactic teaching sessions. We evaluate quality of life with a questionnaire filled in the camp and two months later. Results are analysed into two age groups, one between 8-10 years old and the other from 11 to 14 years old. The first group get a good management and improve their vision of the disease, quite the contrary, adolescents face up to a chronic disease with daily treatment, feeling asthma as a restriction of their autonomy. Even so, they identify crisis and learn to control them in an special risky life period. Asthma camps is a good experience for both groups and also for sanitary equipment.

Martin M. et al. *Improving asthma research in an inner-city Latino neighborhood with community health workers.* *J Asthma.* 2005; 42(10) : 891-5.p **Abstract:** This study tests the feasibility of a partnership between an academic medical center and community health workers to perform mutually beneficial research investigating asthma in an urban Latino neighborhood. Community health workers participated in the study design, instrument development, implementation, and analysis. The 103 participants recruited by the community health workers were primarily Mexican with very low

education and acculturation levels. After the 1-year enrollment period, the community health workers described the challenges of data collection and gave explanations for the access to care outcomes. This academic-community partnership showed that community health workers can be effective research partners.

Martindale S. et al. *Antioxidant intake in pregnancy in relation to wheeze and eczema in the first two years of life.* *Am J Respir Crit Care Med.* 2005; 171(2) : 121-8.p **Abstract:** Two thousand women were recruited for a prospective investigation of the influence of maternal antioxidant intake in pregnancy on the development of asthma and eczema in children. A food frequency questionnaire was used to characterize diet during pregnancy and blood antioxidant levels were measured. Postal questionnaires were used to follow up the 1,924 singleton children born to the cohort at 6, 12, and 24 months of age. There were no associations between maternal antioxidant intake and wheezing symptoms and eczema in the children's first year. In the children's second year, maternal vitamin E intake during pregnancy was negatively associated with wheeze in the absence of a "cold" (p for trend 0.010) and, in children whose mothers were atopic, there was a negative association between maternal vitamin E intake and childhood eczema (p for trend 0.024). Maternal vitamin C intake during pregnancy was positively associated with "ever wheeze" and eczema during the children's second year. This study suggests that maternal dietary antioxidant intakes during pregnancy may modify the risks of developing wheeze and eczema during early childhood. Further follow up of the cohort will determine whether maternal diet during pregnancy is associated with asthma and atopic disease in later childhood.

Martinez F.D. *Toward asthma prevention--does all that really matters happen before we learn to read?* *N Engl J Med.* 2003; 349(15) : 1473-5.p

Martins L.M. et al. *The Helix aspersa (brown garden snail) allergen repertoire.* *Int Arch Allergy Immunol.* 2005; 136(1) : 7-15.p **Abstract:** BACKGROUND: Ingestion of snails can induce strong asthmatic or anaphylactic responses, mainly in house-dust-mite-sensitized patients. The aim of this study was to identify the *Helix aspersa* (Hel a), *Theba pisana* (The p) and *Otala lactea* (Ota l) allergens and the extent of their cross-reactivity with the *Dermatophagoides pteronyssinus* (Der p) mite. PATIENTS AND METHODS: In 60 atopic patients, skin prick tests (SPT) to snail and D. pteronyssinus, total and specific IgE, specific IgE immunoblots, RAST and immunoblot inhibition assays were performed. RESULTS: Mean total IgE was >1,000 kU/l. Mean specific IgE (class 6 for Der p and class 2 for Hel a) SPT were positive in 44 patients for snail and in 56 for mite. Isoelectric focusing (IEF) and SDS-PAGE followed by immunoblotting of *H. aspersa* extract enabled the identification of 27 and 20 allergens, respectively. Myosin heavy chains from snails (molecular weight >208 kDa) disclosed two major allergens. Hel a and Der p RAST were strongly inhibited by their homologous extracts, with Hel a RAST being inhibited by the Der p extract to a much greater extent (72.6%) than the inverse (5.6%). A complete inhibition of the immunoblots by their homologous extract was obtained. However, Hel a extract did not inhibit Der p IEF separated recognition. On the other hand, mite extract extensively inhibited snail immunoblots from both IEF and SDS-PAGE separations. Immune detection on chicken, pig, rabbit, cow and horse myosins did not reveal any IgE cross recognition with snail. CONCLUSIONS: In most cases of snail allergy, mite appeared to be the sensitizing agent. Nevertheless, snails may also be able to induce sensitization by themselves. This hypothesis is supported by the finding of specific IgE to Hel a in 2 patients who did not show specific IgE to Der p, and one of them was suffering from asthma after snail ingestion.

Marvez E. et al. *Predicting adverse outcomes in a diagnosis-based protocol system for rapid sequence intubation.* Am J Emerg Med. 2003; 21(1) : 23-9.p **Abstract:** Our ED at Louisiana State University developed a unique approach to airway management by having four diagnosis-based protocols for rapid sequence intubation (RSI). This study examines protocol use and outcome from RSI in an academic ED. The study objective was to identify variables that are predictive of adverse outcomes in patients requiring RSI. This was a 4-year prospective, observational, data-gathering study of all intubations in an academic ED setting with >250,000 patient visits per year. Four protocols were established for 1) children <10 years of age, 2) adults with increased intracranial pressure, 3) adults with chronic obstructive pulmonary disease/asthma, and 4) other adults not fitting B or C. A special continuing quality improvement (CQI) committee was established to examine each case of RSI. Prospective data were collected, including age, race, gender, protocol, diagnostic group, intubation indication, and preintubation oxygen saturation. Diagnostic group was categorized as medical, blunt trauma, or penetrating trauma. Adverse outcome was defined as any case with hemodynamic changes, those requiring surgical or bronchoscopic intervention, and those requiring more than three attempts at intubation. Data were analyzed using univariate analysis, logistic regression, and a binomial regression tree analysis with SPSS 9.0 (Chicago, IL) and Answer Tree (SPSS). A total of 1,320 consecutive intubated patients were included. Protocol A was used in 4%, B in 43%, C in 15%, and D in 38%. Significant differences in number of cases with adverse outcome were based on protocol ($P = .03$) and final diagnosis ($P < .03$). Protocol C was less likely to be associated with adverse outcome than protocol D (odds ratio [OR] = 0.2, 95% confidence interval [CI] = 0.1-0.7). Penetrating trauma was more likely to be associated with adverse outcome (OR = 1.8, 95%, CI = 1.1-3.2) than blunt trauma. A regression tree analysis yielded the following, all cases using protocol A or C or medical cases using B had an adverse event in 11 of 458 (2.4%), whereas nonmedical cases using protocols B or D and medical cases using D had adverse outcomes in 73 of 862 cases (8.5%). The decision rules lead to a better classification of cases with adverse outcomes (2.4 vs 8.5%, of = 6.1%, 95% CI = 3.7-8.4). Adult trauma patients who fit the protocols B or D or adult medical patients who fit protocol B were at higher risk for adverse outcomes with RSI. This could alert the physician to a population at higher risk for adverse outcomes. Variables available in a diagnosis-based protocol RSI system can be used to predict adverse outcome among patients requiring RSI.

Mashalane M.B. et al. *Prevalence of exercise-induced bronchospasm in Thokoza schoolchildren.* S Afr Med J. 2006; 96(1) : 67-70.p **Abstract:** BACKGROUND: Asthma is a common childhood illness, with a prevalence of 1 in 10 children. Exercise-induced bronchospasm (EIB) is a common feature of asthma and is found more often in children than in adults. OBJECTIVE: To determine the prevalence and potential impact of various factors on the prevalence of EIB in Thokoza schoolchildren. METHODS: Data were collected on respiratory health and the home environment of children living in Thokoza, Gauteng. A total of 475 9- and 10-year-old children performed the free-running asthma screening test (FRAST). An abnormal response to FRAST was defined as a reduction in the post-exercise peak flow of more than 15% of the pre-exercise value, at 3- and 10- minute intervals. All children who had a fall in post-exercise flow rate (PEFR) of more than 15% on 2 occasions after FRAST were classified as having EIB. RESULTS: Using the above criteria to diagnose EIB, an overall prevalence rate of 7.26% (95% confidence interval (CI): 4.5 - 10.3%) was recorded. A less rigorous definition of EIB as a fall in PEFR of more than 10% on 2 occasions after FRAST, and if this was used then the prevalence of EIB was 15.69% (95% CI: 10.6 - 20.8%). Difficulty breathing and a tight chest were the most prevalent respiratory symptoms in children with EIB (odds ratio (OR): 1.79, 95% CI: 0.49 - 6.49 and OR 1.69, 95% CI: 0.72 - 3.99, respectively). The use of gas and electricity as domestic fuels was the strongest risk factor associated with EIB, as shown by logistical regression analysis using an adjusted OR in a reduced model (OR

2.44, 95% CI: 0.71 - 8.44 and OR 2.33, 95% CI: 0.59 - 9.24, respectively). CONCLUSION: The prevalence of EIB reported in this study is higher than that reported in studies from other African countries, with the exception of a study from Kenya. Findings of the present study suggest that there may be a trend towards increasing prevalence of EIB in South African urban areas.

Masoli M. et al. *Fluticasone given once versus twice a day: meta-analysis.* Respiriology. 2005; 10(2) : 183-8.p **Abstract:** OBJECTIVE: The aim of this study was to examine the efficacy of fluticasone administered once daily compared to twice daily in asthma. METHODOLOGY: A meta-analysis was performed of randomized double-blind trials of at least 4 weeks duration that compared fluticasone administered once versus twice a day and presented data on at least one clinical outcome measure. RESULTS: Six studies of 1517 children and adults with asthma met the inclusion criteria. Studies were predominantly in subjects with moderate asthma, treated with doses of fluticasone ranging from 200 to 500 microg per day. Twice-daily dosing was associated with significantly greater efficacy compared with once-daily dosing, for all outcome measures except night awakenings. The mean (95% CI) differences between twice and once-daily administration for FEV1 and peak expiratory flow were 0.11 L (0.07-0.16) and 12.9 L/min (8.6-17.1), respectively. Twice-daily fluticasone was associated with significantly fewer withdrawals due to asthma than once-daily fluticasone, with an odds ratio of 0.44 (0.30-0.67). CONCLUSION: The findings suggest that twice-daily administration of fluticasone will provide greater therapeutic benefit than a once-daily morning regimen.

Masoli M. et al. *Clinical dose-response relationship of fluticasone propionate in adults with asthma.* Thorax. 2004; 59(1) : 16-20.p **Abstract:** BACKGROUND: A study was undertaken to examine the dose-response relation of inhaled fluticasone in adolescents and adults with asthma. METHODS: A meta-analysis was carried out of randomised clinical trials that presented data on at least one outcome measure of asthma and that used at least two doses of fluticasone given twice daily. The main outcome measures were forced expiratory volume in 1 second (FEV1), morning peak expiratory flow (amPEF), beta agonist use, and withdrawals due to exacerbations of asthma. RESULTS: Seven studies of 2431 adolescents and adults with moderate to severe asthma met the inclusion criteria for the meta-analysis. Four studies examined a dose of >500 microg/day. For all outcome measures there were no statistically significant differences between a dose of 200 v 500 microg/day, 500 v 1000 microg/day, and 200 v > or =500 microg/day, although the point estimates favoured the higher doses. The mean improvement for FEV1 and amPEF resulting from an increase in dose from 200 to > or =500 microg/day was 0.07 l (95% CI -0.01 to 0.14) and 5.9 l/min (95% CI -3.0 to 15.3), respectively. The odds ratio for withdrawals with 200 microg/day compared with > or =500 microg/day was 1.27 (95% CI 0.78 to 2.07). CONCLUSIONS: In adolescents and adults with asthma, most of the therapeutic benefit of fluticasone is achieved with a total daily dose of 200 microg/day with minimal further clinical benefit achieved with higher doses. This conclusion is qualified by the recognition that there is considerable individual variability in the response to inhaled corticosteroids in asthma, which would suggest that some patients may obtain a greater clinical benefit at higher doses.

Massie J. et al. *Implementation of evidence based guidelines for paediatric asthma management in a teaching hospital.* Arch Dis Child. 2004; 89(7) : 660-4.p **Abstract:** AIMS: To evaluate a systematic approach to the development and implementation of evidence based asthma management guidelines. METHODS: Comparative study of children (2-18 years) with acute asthma; a control cohort (cohort 1) was recruited before implementation of the guidelines and two cohorts were recruited after implementation (cohorts 2 and 3). RESULTS: There was no difference in the proportion of patients who reattended

in the six months following initial presentation for cohort 1 (21.5%), cohort 2 (27.8%), or cohort 3 (25.4%) and no difference in readmission rates (11.4%, 11.3%, 11.0% respectively). There was no difference in measures of asthma morbidity between the cohorts at 3 and 6 months across three domains: interval symptoms, exercise limitation, and bronchodilator use. Of those who did not have a management plan before presentation, one was provided to 46.9% of cohort 1, 74.8% of cohort 2, and 81.1% of cohort 3. There was no difference comparing cohort 2 or cohort 3 with cohort 1 regarding quality of life for either the subjects or their parents. CONCLUSIONS: Implementation of our evidence based guidelines was associated with the improved provision of asthma management plans, but there was no effect on reattendance or readmission to hospital, asthma morbidity, or quality of life. Future efforts to improve asthma management should target specific components of asthma care.

Mathieu-Nolf M. *Poisons in the air: a cause of chronic disease in children.* J Toxicol Clin Toxicol. 2002; 40(4) : 483-91.p Abstract: Children represent the largest subpopulation of those susceptible to the adverse effects of air pollution. Compared to adults, children express a greater vulnerability, which can be explained by differences in: the circumstances of exposure related to age, their activities, their child status, differences in lung anatomy and physiology, differences in the clinical expression of disease, and their organ maturity. Many factors have to be assessed in order to evaluate the severity of toxic exposures: pollutant solubility, particle size, concentration, reactivity of pollutants, and pattern of ventilation. Within the numerous air pollutants, some are of special concern for children. For example, ozone has been shown to affect the lungs of healthy school children, especially asthmatics. Airborne particles, nitrogen oxides, sulfur oxides, and acid aerosols have also been shown to induce acute respiratory symptoms, asthma, and bronchitis. Of particular importance is carbon monoxide, which, under certain circumstances, may be found in highly toxic concentrations indoors where children spend most of their time. Special attention has to be given to children's unique differences in order to evaluate the clinical consequences of their toxic exposures. This circumstance emphasizes the key roles of poison centers, clinical toxicologists, and pediatricians, all of whom can collaborate on the identification, assessment, and surveillance of toxic risk for child health and development.

Matsuda K. et al. *Ghrelin and leptin: a link between obesity and allergy?* J Allergy Clin Immunol. 2006; 117(3) : 705-6.p

Matsui E.C. et al. *Cockroach allergen exposure and sensitization in suburban middle-class children with asthma.* J Allergy Clin Immunol. 2003; 112(1) : 87-92.p Abstract: BACKGROUND: Exposure to cockroach allergen is prevalent in inner-city homes and is associated with an increased risk of cockroach sensitization. OBJECTIVE: We sought to determine the prevalence of cockroach allergen exposure in suburban middle-class homes and to study its relationship to cockroach sensitization. METHODS: Children with asthma, 6 to 17 years of age, were recruited from 3 pediatric practices located in counties surrounding Baltimore city and from 1 practice located within Baltimore city limits. Participants underwent skin prick testing and completed baseline questionnaires. In addition, their homes were inspected, and settled dust samples were collected for allergen analysis. RESULTS: Forty-one percent of the total study population (n = 339) had kitchen Bla g 1 levels of greater than 1 U/g. Forty-nine percent were white, 53% had annual incomes of greater than US dollars 50000, and 48% of mothers had college degrees. Seventy-seven percent of the study population resided in a suburban or rural location, and 30% of kitchens in these homes had Bla g 1 levels of greater than 1 U/g. Among the suburban-rural subgroup, 21% were sensitized to cockroach compared with 35% of the city group. In multivariate analysis, exposure to kitchen Bla g 1 levels of greater than 1 U/g was associated with cockroach sensitization for

both the total study population (odds ratio, 2.29; 95% CI, 1.28-4.11) and the suburban-rural subgroup (odds ratio, 2.37; 95% CI, 1.23-4.57). CONCLUSIONS: Cockroach allergen exposure might be more common in suburban middle-class homes of asthmatic children than previously thought. Moreover, the data suggest that low-level cockroach exposure is a risk factor for cockroach sensitization.

Matsumoto Y. et al. *Identification of highly expressed genes in peripheral blood T cells from patients with atopic dermatitis.* Int Arch Allergy Immunol. 2002; 129(4) : 327-40.p Abstract: BACKGROUND: Analysis of genes that are differentially expressed in patients with atopic dermatitis (AD) and normal individuals will provide important information on the underlying molecular pathogenetic mechanisms of AD. METHODS: Transcript of freshly isolated peripheral blood T cells from 59 individuals were analyzed with a fluorescent differential display (FDD) method. Ninety-two differentially expressed genes were identified in this manner. Additionally, real-time quantitative RT-PCR was employed to investigate the expression of the FDD-selected genes and also genes related to T cell function. RESULTS: A number of genes, including CC chemokine receptor 4, T cell-specific tyrosine kinase (Emt/Itk), integrin beta1, integrin alpha6, IQGAP1 and MAR/SAR DNA-binding protein (SATB1), were shown to be more highly expressed in patients with moderate and/or severe AD than in controls or patients with mild AD. Because the products of these upregulated genes influence chemotaxis, adhesion, migration and Th2 polarization, it is suggested that in more severe AD, circulating T cells may function differently in this regard. Several other genes, the role of which in T cell function is currently unknown, were also found to be differentially expressed in AD. These included the heat shock protein 40 and vasopressin-activated calcium-mobilizing receptor 1. CONCLUSION: The upregulated genes identified in this work may serve as useful markers for moderate to severe AD as opposed to normal or mild AD and also as markers indicating progression to more severe AD. Further functional characterization will provide a better understanding of the pathophysiology of circulating T cells in AD.

Mattila P.S. et al. *Predisposition to atopic symptoms to inhaled antigens may protect from childhood type 1 diabetes.* Diabetes Care. 2002; 25(5) : 865-8.p Abstract: OBJECTIVE: To assess the inverse association between type 1 diabetes and asthma to establish whether environmental and/or genetic factors predisposing to asthma or to atopic symptoms to inhaled antigens protect from diabetes. RESEARCH DESIGN AND METHODS: Questionnaires were returned by 306 probands with childhood type 1 diabetes, their 506 nonaffected siblings, and 406 age- and sex-matched unaffected population control subjects. The main outcome measures were self-reported physician-diagnosed asthma and atopic symptoms to animal dust and pollen. RESULTS: Risk of diabetes was inversely associated with asthma (odds ratio 0.49 [95% CI 0.24-1.00]), allergy to animal dust (0.67 [0.45-0.99]), and to a lesser degree to pollen (0.74 [0.51-1.07]) when the probands were compared with the population control subjects. Among the children of the families of an affected proband, the risk of diabetes appeared to be inversely associated with asthma (0.54 [0.27-1.09]) but not with allergy to animal dust (0.99 [0.66-1.47]) nor allergy to pollen (0.88 [0.62-1.27]). CONCLUSIONS: The frequency of asthma and atopic symptoms to some inhaled antigens is decreased in individuals with childhood type 1 diabetes. Factors predisposing to atopic symptoms to inhaled antigens may protect from childhood type 1 diabetes.

Maziak W. *Endotoxin and asthma.* N Engl J Med. 2003; 348(2) : 171-4; author reply 171-4.p

Maziak W. *The hygiene hypothesis and the evolutionary perspective of health.* Prev Med. 2002; 35(4) : 415-8.p

McCann D. et al. *The prevalence and management of asthma in primary-aged schoolchildren in the south of England.* Health Educ Res. 2002; 17(2) : 181-94.p **Abstract:** A postal questionnaire survey of headteachers in 149 Infant, Junior and Primary schools (response rate: 63.8%) indicated poor asthma record keeping and a need for regular staff training in asthma. Dealing with an emergency was a major concern of headteachers. In 25 of the schools surveyed, an International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire was distributed to parents of children in Years 3 and 4 (7-9 years). Headteacher-reported asthma prevalence was 11.9% in these schools, while ISAAC parental reports indicated a current or previous diagnosis of asthma in 24.3% children, with 17.8% receiving asthma treatment and 18.9% reporting wheeze in the previous 12 months. Of six wheezing children per Year 3/4 class, one was receiving no treatment for asthma, three had experienced four or more attacks of wheeze in the previous year with one wheezing child per two Year 3/4 classes experiencing more than 12 such attacks. Four in six children experienced exercise-related wheeze, while only one in five schools allowed asthma medication at Physical Education lessons. A whole school policy on asthma together with some regularly updated staff education and training by an asthma-trained nurse would address many of the issues raised in this study.

McCarthy M.J. et al. *Empowering parents through asthma education.* *Pediatr Nurs.* 2002; 28(5) : 465-73.p **Abstract:** Asthma is the most common chronic illness in children and has a significant impact on children and their families. Asthma management requires a multi-faceted approach, including an effective educational component. The purpose of this pilot study was to compare outcomes for parents who participated in empowering and traditional approaches to asthma education. Specific outcomes that were examined included (a) knowledge, (b) sense of control, (c) ability to make decisions, and (d) ability to provide care. The sample consisted of 57 families who participated in a multi-session educational intervention. Twenty-nine families participated in the empowering approach; the remaining 28 families received the traditional approach. Data were collected before, immediately after, and 6 months following the educational intervention. Significant differences were found regarding sense of control, ability to make decisions, and ability to provide care for parents who participated in the empowering approach. Both approaches resulted in increased knowledge. These findings have implications for asthma education and for the education of health professionals.

McConnell R. et al. *Asthma in exercising children exposed to ozone: a cohort study.* *Lancet.* 2002; 359(9304) : 386-91.p **Abstract:** **BACKGROUND:** Little is known about the effect of exposure to air pollution during exercise or time spent outdoors on the development of asthma. We investigated the relation between newly-diagnosed asthma and team sports in a cohort of children exposed to different concentrations and mixtures of air pollutants. **METHODS:** 3535 children with no history of asthma were recruited from schools in 12 communities in southern California and were followed up for up to 5 years. 265 children reported a new diagnosis of asthma during follow-up. We assessed risk of asthma in children playing team sports at study entry in six communities with high daytime ozone concentrations, six with lower concentrations, and in communities with high or low concentrations of nitrogen dioxide, particulate matter, and inorganic-acid vapour. **FINDINGS:** In communities with high ozone concentrations, the relative risk of developing asthma in children playing three or more sports was 3.3 (95% CI 1.9-5.8), compared with children playing no sports. Sports had no effect in areas of low ozone concentration (0.8, 0.4-1.6). Time spent outside was associated with a higher incidence of asthma in areas of high ozone (1.4, 1.0-2.1), but not in areas of low ozone. Exposure to pollutants other than ozone did not alter the effect of team sports. **INTERPRETATION:** Incidence of new diagnoses of asthma is associated with heavy exercise in communities with high

concentrations of ozone, thus, air pollution and outdoor exercise could contribute to the development of asthma in children.

McConnell R. et al. *Cockroach counts and house dust allergen concentrations after professional cockroach control and cleaning.* *Ann Allergy Asthma Immunol.* 2003; 91(6) : 546-52.p **Abstract:** **BACKGROUND:** It is known that cockroach allergen exposure is both frequent in inner-city homes and associated with asthma severity in children living in those homes. However, there have been few studies of interventions to reduce exposures in this setting. **OBJECTIVE:** To evaluate the effect of short-term professional cockroach control and intensive cleaning on allergen concentrations. **METHODS:** Families of children from a school-based asthma treatment program who had skin test results positive to cockroach allergen were enrolled if the home had cockroaches. Forty-nine homes were randomly assigned to receive professional cleaning with bait traps containing insecticide, professional cleaning with bait traps without insecticide, or no cleaning or bait traps. In all homes, dust was collected repeatedly to evaluate cockroach allergen Bla g 2 in the kitchen and bedroom, and cockroaches were trapped and counted repeatedly for more than 11 weeks. **RESULTS:** Median cockroach counts were reduced in the homes treated with insecticide bait traps but not in other groups. There were significant reductions in allergen concentration in the kitchen in homes that received professional cleaning and had higher initial cockroach counts (54), regardless of whether bait traps had insecticide or not. **CONCLUSIONS:** We conclude that intensive cleaning can produce significant reductions in cockroach allergen in homes with heavy initial cockroach infestations.

McDermott M.F. et al. *Adequacy of medical chart review to characterize emergency care for asthma: findings from the Illinois Emergency Department Asthma Collaborative.* *Acad Emerg Med.* 2006; 13(3) : 345-8.p **Abstract:** **OBJECTIVES:** To assess the intermethod reliability of medical chart review compared with directly observed care in patients presenting to emergency departments (EDs) for asthma care. **METHODS:** ED care practices for persons with asthma were evaluated by comparing chart review with trained observers. Fifty-one patients from five EDs participating in the Illinois Emergency Department Asthma Collaborative were studied. Practices in assessment, treatment, education, and referral were measured. Eighteen elements of care were assessed. Concordance between chart and observation was measured by using the kappa statistic. **RESULTS:** Of 51 subjects studied, nine were children. Kappa values varied depending on content. Kappa values ranged from 0.22 to 0.91 for items reflecting asthma assessment. Good concordances (kappa = 0.50 to 0.82) were found for items reflecting treatment practices. The lowest concordances were for items assessing educational activities (kappa = 0.04 to 0.34). Referral practices had fair to moderate concordances (kappa = 0.21 to 0.45). **CONCLUSIONS:** Intermethod reliability of medical chart review and directly observed care varied depending on the element of care being measured. The use of chart review to measure quality of ED-based asthma care may only be appropriate for a limited number of care processes that are reliably and validly captured from chart review.

McDonald N.J. et al. *Anticholinergic therapy for chronic asthma in children over two years of age.* *Cochrane Database Syst Rev.* 2003; (3) : CD003535.p **Abstract:** **BACKGROUND:** In the intrinsic system of controlling airway calibre, the cholinergic (muscarinic) sympathetic nervous system has an important role. Anticholinergic, anti muscarinic bronchodilators such as ipratropium bromide are frequently used in the management of childhood airway disease. In asthma, ipratropium is a less potent bronchodilator than beta-2 adrenergic agents but it is known to be a useful adjunct to other therapies, particularly in status asthmaticus. What remains unclear is the role of anticholinergic drugs in the maintenance treatment of

chronic asthma. **OBJECTIVES:** To determine the effectiveness of anticholinergic drugs in chronic asthma in children over the age of 2 years. **SEARCH STRATEGY:** The Cochrane Airways Group trials register and reference lists of articles were searched in January 2002. **SELECTION CRITERIA:** Randomised controlled trials in which anticholinergic drugs were given for chronic asthma in children over 2 years of age were included. Studies including comparison of: anticholinergics with placebo, and anticholinergics with any other drug were included. **DATA COLLECTION AND ANALYSIS:** Eligibility for inclusion and quality of trials were assessed independently by two reviewers. **MAIN RESULTS:** Eight studies met the inclusion criteria. Three papers compared the effects of anticholinergic drugs with placebo, and a meta-analysis of these results demonstrated no statistically significant benefit of the use of anticholinergic drugs over placebo in any of the outcome measures used. The results of one of these trials could not be included in the meta-analysis but the authors did report significantly lower symptom scores with inhaled anticholinergics compared with placebo. However, there was no significant difference between ipratropium bromide and placebo in the percentage of symptom-free nights or days. Two trials studied the effects of anticholinergics on bronchial hyper responsiveness to histamine, by measuring the provocation dose of histamine needed to cause a fall of 20 % in FEV1 (PD 20). One study (comparing anticholinergics with placebo) reported a statistically significant increase in PD 20 but this was not found in another study (comparing anticholinergics with a beta-2 agonist). Both trials also examined the effect of anticholinergic drugs on diurnal variation in peak expiratory flow rate (PEFR) and reported no significant effect. Two studies compared the addition of an anticholinergic drug to a beta-2 agonist with the beta-2 agonist alone. Both trials failed to show any significant benefit from the long term use of combined anticholinergics with beta-2 agonists compared with beta-2 agonists alone. One trial compared the effects of oral and inhaled anticholinergic drugs with placebo. No statistically significant differences were found in any of the outcome measures except for a higher FEV1 / VC ratio and RV / TLC ratio with oral anticholinergic therapy when compared with placebo. **REVIEWER'S CONCLUSIONS:** The present review summarises the best evidence available to date. Although there were some small beneficial findings in favour of anticholinergic therapy, there is insufficient data to support the use of anticholinergic drugs in the maintenance treatment of chronic asthma in children.

McGovern V. *Poor environment creates wealth of problems.* Environ Health Perspect. 2002; 110(6) : A292.p

McHugh P. et al. *Buteyko breathing technique and asthma in children: a case series.* NZ Med J. 2006; 119(1234) : U1988.p

McIvor R.A. *Pharmacoeconomics in pediatric asthma.* Chest. 2001; 120(6) : 1762-3.p

McKeever T.M. et al. *Serum nutrient markers and skin prick testing using data from the Third National Health and Nutrition Examination Survey.* J Allergy Clin Immunol. 2004; 114(6) : 1398-402.p **Abstract:** **BACKGROUND:** Diet nutrients and allergic sensitization both affect the development and severity of asthma, but the interrelationship between oral intake and allergic sensitization is not well characterized, although previous work suggests that a higher vitamin E intake may be protective against allergic sensitization. **OBJECTIVE:** To determine whether serum levels of dietary antioxidants, lipids, and other nutrients are associated with the presence of allergen skin sensitization. **METHODS:** Cross-sectional logistic regression analysis of 30 serum nutrient levels in relation to 10 skin test allergens in adults and children in the Third National Health and Nutrition Survey. **RESULTS:** In adults, allergic skin sensitization was less common in participants with higher serum levels of vitamin E: the adjusted odds ratio (OR) per SD difference in vitamin E level was 0.93 (95% CI, 0.87-0.99). Two of the

carotenoids, beta-cryptoxanthin and alpha-carotene, were also inversely associated with allergic skin sensitization (OR, 0.89; 95% CI, 0.83-0.95; and OR, 0.95; 95% CI, 0.91-0.99, respectively). Among adults, serum lycopene had a positive association with allergen sensitization. In youths, however, vitamin A was associated with an increased risk, and high-density lipoprotein cholesterol was associated with a decreased risk of allergic sensitization. The use of vitamin or mineral supplements had little effect on the magnitude of all reported associations. **CONCLUSION:** Overall, there were no strong or consistent associations between serum levels of potentially anti-allergic nutrients, and the occurrence of allergic skin sensitization in these data. However limited, findings suggest that increases in vitamin E, carotenoids, and high-density lipoprotein cholesterol may reduce the risk of allergic skin sensitization.

McKeever T.M. et al. *The importance of prenatal exposures on the development of allergic disease: a birth cohort study using the West Midlands General Practice Database.* Am J Respir Crit Care Med. 2002; 166(6) : 827-32.p **Abstract:** The etiology of allergic disease is not understood, but a decreased exposure to infection may play an important role. There are few published data on the impact of change in microbial exposure during pregnancy on the child's risk of developing allergic disease. Using a birth cohort of 24,690 children, derived from the West Midlands General Practice Research Database, we investigated a number of perinatal exposures on the incidence of asthma, eczema, and hay fever. Our findings suggest that exposure to antibiotics in utero is associated with an increased risk of asthma in a dose-related manner (more than two courses of antibiotics compared with none adjusted hazard ratio [HR] 1.68; 95% confidence interval [CI], 1.51-1.87), and similar associations are present for eczema (adjusted HR 1.17; 95% CI, 1.06-1.29) and hay fever (adjusted HR 1.56; 95% CI, 1.22-2.01). Exposure to a range of infections in utero was also associated with a small increased risk of developing allergic disease. Strong protective effects of older siblings on the incidence of allergy are present within this cohort, but previous pregnancies that did not result in a live birth were not protective. Our findings suggest that exposure to antibiotics and to infections in utero is a potentially important risk factor in the development of allergic disease.

McKeever T.M. et al. *Vaccination and allergic disease: a birth cohort study.* Am J Public Health. 2004; 94(6) : 985-9.p **Abstract:** **OBJECTIVES:** We examined the effect of vaccination for diphtheria; polio; pertussis and tetanus; or measles, mumps, and rubella on the incidence of physician-diagnosed asthma and eczema. **METHODS:** We used a previously established birth cohort in the West Midlands General Practice research database. **RESULTS:** We found an association between vaccination and the development of allergic disease; however, this association was present only among children with the fewest physician visits and can be explained by this factor. **CONCLUSIONS:** Our data suggest that currently recommended routine vaccinations are not a risk factor for asthma or eczema.

McKenzie S.A. *Systemic effects of inhaled steroids.* Thorax. 2001; 56(12) : 981.p

McLean D.E. et al. *Asthma among homeless children: undercounting and undertreating the underserved.* Arch Pediatr Adolesc Med. 2004; 158(3) : 244-9.p **Abstract:** **BACKGROUND:** In the United States, children of color, children who live in urban medically underserved communities, and children whose families have limited economic resources have excessively high rates of asthma. The identification of high-risk subgroups of underserved children is crucial for understanding the determinants and scope of the childhood asthma epidemic and for developing successful interventions. **OBJECTIVE:** To determine the population prevalence of asthma among homeless children. **DESIGN:** Cross-sectional study. **SETTING:** Three family

shelters in New York City. **PARTICIPANTS:** A total of 740 children whose families entered 3 family shelters from June 30, 1998, to September 18, 1999. **MAIN OUTCOME MEASURES:** Prior physician asthma diagnosis, current asthma symptoms using National Asthma Education and Prevention Program symptom criteria, current medications, and emergency department use in the past year. **RESULTS:** Of the children, 26.9% had a prior physician diagnosis of asthma. In addition, 12.9% of the children without a prior physician diagnosis of asthma reported symptoms consistent with moderate or severe persistent asthma. Overall, 39.8% of homeless children in New York City are likely to have asthma. Few children with persistent asthma received any anti-inflammatory treatment. Almost 50% (48.6%) of children with severe persistent asthma had at least 1 emergency department visit in the past year; 24.8% of children with symptoms of mild intermittent asthma had at least 1 visit. **CONCLUSIONS:** The prevalence of asthma among a random sample of homeless children in New York City is likely to be 39.8%-more than 6 times the national rate for children. Asthma in homeless children is also likely to be severe and substantially undertreated.

McNally A.J. et al. *Application of asthma action plans to childhood asthma: national survey repeated.* N Z Med J. 2004; 117(1196) : U932.p **Abstract:** **AIMS:** Define the way childhood asthma action plans are currently being used in New Zealand; determine New Zealand doctor's recommendations about the use of an increased dose of inhaled steroids in asthma action plans; and determine if there has been any change (during the last 7 years) in the way asthma action plans are used. **METHODS:** A postal survey was sent to all 297 paediatricians and paediatric registrars in New Zealand, and to a random sample of 500 general practitioners (GPs). The questions related to asthma action plan use, the inclusion of an increased dose of inhaled steroid in those plans, and details of the way doctor's adjusted inhaled steroid dose. Comparisons were made for selected questions between this survey and the same survey conducted in 1995. **RESULTS:** Valid responses were received from 179 (60%) paediatricians and paediatric registrars, and 233 (47%) GPs. 165 (70.8%) GPs and 137 (76.5%) paediatricians/paediatric registrars indicated that they used written action plans for children with asthma in their care. 184 (61.5%) respondents who used asthma action plans included a step involving an increase in the dose of inhaled steroid, compared to 83.6% in 1995 ($p<0.001$). GPs in 2002 were less likely to use action plans ($p<0.001$) and include a step with an increased dose of inhaled steroid ($p=0.003$) Paediatricians and paediatric registrars in 2002 were just as likely to use action plans ($p=0.549$), but less likely to include a step with an increased dose of inhaled steroid ($p<0.001$). GPs in 2002 were significantly more likely (than paediatricians and paediatric registrars) to include a step involving an increased dose of inhaled steroid ($p<0.001$) There has been a change in the practice of New Zealand GPs, paediatricians, and paediatric registrars--with a decreased tendency to double the dose of inhaled steroids in childhood action plans, thus suggesting doctors are cognisant of conclusions drawn by 'evidence-based medicine'. **CONCLUSIONS:** There has also been a decline in the proportion of asthmatic children receiving a written asthma action plan, and this is inconsistent with recommendations contained in consensus documents.

McPherson A. et al. *The asthma files: evaluation of a multimedia package for children's asthma education.* Paediatr Nurs. 2002; 14(2) : 32-5.p **Abstract:** Children's knowledge of asthma triggers and the impact on children's knowledge of using 'The Asthma Files', an interactive, educational computer program, were evaluated in this pilot study. Thirty-one children aged between seven and 14 years and diagnosed with asthma were recruited to the study. Ten boys participated in evaluating the triggers section and a questionnaire was used to determine their feelings about the program and retention of information. Children enjoyed using the package and knowledge about asthma triggers increased significantly. 'The Asthma Files' shows promise as an additional tool to augment existing education.

McPherson A.C. et al. *A randomized, controlled trial of an interactive educational computer package for children with asthma.* Pediatrics. 2006; 117(4) : 1046-54.p **Abstract:** **OBJECTIVE:** The purpose of this study was to evaluate the impact and acceptability of an educational multimedia program designed to promote self-management skills in children with asthma. **METHODS:** We conducted a randomized, controlled trial with measures at baseline and 1- and 6-month follow-up. The trial was conducted in pediatric outpatient respiratory clinics in 3 United Kingdom hospitals. Participants included 101 children aged 7 to 14 years under the care of hospital-based asthma services. The children were randomly assigned to receive an asthma information booklet alone or the booklet plus The Asthma Files, an interactive CD-ROM for children with asthma. Asthma knowledge was the primary outcome measure. Other measures included asthma locus of control, lung function, use of oral steroids, and school absence. **RESULTS:** At the 1-month follow-up ($n = 99$), children in the computer group had improved knowledge compared with the control group and a more internal locus of control. There were no differences in objective lung-function measures, hospitalizations, or oral steroid use. The study participants were positive in their evaluation of the intervention. At the 6-month follow-up ($n = 90$), significantly fewer children in the intervention group had required oral steroids and had had time off school for asthma in the previous 6 months. The difference did not reach statistical significance in the intention-to-treat analysis for both steroid use and school absence. **CONCLUSION:** The Asthma Files was found to be an effective and popular health education tool for promoting asthma self-management skills within pediatric care.

McQuaid E.L. et al. *Environmental tobacco smoke exposure in pediatric asthma: overview and recommendations for practice.* Clin Pediatr (Phila). 2003; 42(9) : 775-87.p

Medina Segura E. et al. *[Clinical characteristics of atopic dermatitis in a group of patients attending to the Regional Center of Allergy and Clinical Immunology of Monterrey, Mexico].* Rev Alerg Mex. 2004; 51(2) : 45-8.p **Abstract:** **BACKGROUND:** Atopic dermatitis is a chronic inflammatory disease of the skin which mainly affects children. It is characterized by itch and cutaneous hyperactivity with typical lesions that depend on the affected age group and the disease stage. It is frequently associated to rhinitis and asthma. **OBJECTIVE:** To identify the clinical characteristics of atopic dermatitis in patients treated at the Regional Center of Allergy and Clinical Immunology of Monterrey, NL, Mexico. **MATERIAL AND METHODS:** A retrospective and descriptive study was done by the review of clinical files of patients with atopic dermatitis diagnosis from January 1997 to May 2002. The statistical analysis was done by central tendency measures. **RESULTS:** We reviewed 119 clinical files, 53 (44.5%) were male and 66 (55.5%) female. The most frequent clinical manifestations were pruritus and eczematous lesions, both in 117 patients (98.3%). Fifty-five percent of the patients initiated symptoms before 6 years of age. Eighty eight patients (74%) had family and/or personal history of atopia. Other associated manifestations were allergic rhinitis in 38 patients (31.9%), asthma and rhinitis in 25 patients (21%) and only asthma in 2 patients (1.7%). In 44 patients, food skin tests were done with a positive result in 25 patients, the most frequent was to egg (68%) and in 64 patients these were positive to aeroallergens being the most frequent Dermatophagoides p teronyssinus (85.1%). **CONCLUSIONS:** The pruritus and eczematous lesions were the most constant manifestations in this group of patients where family and/ or personal history of atopia was frequent.

Meding B. et al. *Incidence of hand eczema-a population-based retrospective study.* J Invest Dermatol. 2004; 122(4) : 873-7.p **Abstract:** When etiological relationship is of interest, the incidence

rate is a preferred measure. The aim of the present retrospective study was to estimate the incidence rate of self-reported hand eczema in a sample from the general population and to study the relation of this to age, sex, and atopy. A questionnaire was mailed to 3000 individuals aged 20-65 y, randomly selected from the population register of Goteborg, Sweden. This gave a response rate of 73.9%. Questions were asked about ever having had hand eczema, time of onset of the disease, history of childhood eczema, and history of asthma/hay fever. The crude incidence rate of self-reported hand eczema was 5.5 cases per 1000 person-years (females 7.1 and males 4.0). There was no difference, however, in incidence rate between women and men above 30 y of age. In a Poisson regression analysis, female sex, childhood eczema, and asthma/hay fever were all significantly associated with hand eczema, but only at ages below 30 y. A moderate influence of recall bias and a probable tendency to underreport imply that the incidence rates presented are to be considered as minimum rates.

Meerwaldt R. et al. *A lower prevalence of atopy symptoms in children with type 1 diabetes mellitus.* Clin Exp Allergy. 2002; 32(2) : 254-5.p **Abstract:** BACKGROUND: The Th1/Th 2 concept is a model to understand the pathophysiology of certain diseases. Atopic diseases (asthma, eczema and hayfever) are characterized by a chronic inflammatory reaction that is dominated by Th 2 cells, and type 1 diabetes mellitus (DM) is Th1 cell dominated. Because it is known that Th1 and Th 2 cells reciprocally counteract each other, it can be speculated that the prevalence of Th 2-mediated disease is lower in patients with Th1-mediated disease. OBJECTIVE: To compare the prevalence of atopic diseases between children with DM and age-matched controls. METHODS: Parents of children with DM were requested by Dutch paediatricians to complete the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire on the prevalence of atopic diseases. A control group was derived from a Dutch cross-sectional survey (the ISAAC2 study). RESULTS: We received 555 completed questionnaires, which is estimated to be 25% of the total number of Dutch children with DM. The control group consisted of 777 children. After age-matching, the questionnaires of 188 DM patients were used. Symptoms of asthma, hayfever and eczema were reported less in the group of children with DM compared with the control group (wheeze last year, OR 0.796, 95% CI 0.408-1.554; hayfever symptoms last year, OR 0.642, 95% CI 0.369-1.118; eczema symptoms last year, OR 0.693, 95% CI 0.430-1.115). CONCLUSION: The lower prevalence of asthma, hayfever and eczema symptoms in DM patients compared with age-matched controls, although not statistically significant, is consistent with the Th1/Th 2 concept.

Melen E. et al. *Haplotypes of G protein-coupled receptor 154 are associated with childhood allergy and asthma.* Am J Respir Crit Care Med. 2005; 171(10) : 1089-95.p **Abstract:** RATIONALE: Allergic diseases are influenced by both genes and environment. A 70-kb haplotype block in the G protein-coupled receptor for asthma susceptibility gene (GPR154; alias GPRA) on chromosome 7p was recently identified to influence susceptibility to asthma and elevated total serum IgE levels in adults. OBJECTIVES: To assess the impact of GPR154 on childhood allergic disease, including allergic sensitization, asthma, and rhinoconjunctivitis, in study populations with diverse environmental backgrounds. METHODS: We studied farm children, Steiner school children, and two reference groups from five Western European countries in the cross-sectional PARSIFAL (Prevention of Allergy Risk factors for Sensitization In children related to Farming and Anthroposophic Lifestyle) study and a sample of children from the Swedish birth cohort study BAMSE. DNA samples from 3,113 PARSIFAL and 800 BAMSE children were genotyped for 7 GPR154 polymorphisms and haplotypes were inferred. The proportions of alleles and haplotypes (H1-H7) were compared in affected children with their healthy counterparts. RESULTS: Data indicate a global association of the haplotype block to sensitization (allergen-specific serum IgE > or = 0.35 kU/L, p =

0.022), with significant haplotype-specific associations for H1, H5, and H6. Haplotypes H1 and H5 were also significantly associated with childhood allergic asthma (p = 0.045 and p = 0.023, respectively), and H5 to asthma regardless of sensitization. A broader involvement of GPR154 in allergic diseases was further supported in allergic rhinoconjunctivitis (H3: p = 0.046). The associated haplotypes could be allocated into risk (H5/H6) and nonrisk (H1/H3) groups, a pattern supported by allelic association of single nucleotide polymorphisms (SNPs) rs324384 and rs324396. CONCLUSIONS: Our results indicate that polymorphisms and haplotypes in the haplotype block of GPR154 are associated with asthma, rhinoconjunctivitis, and sensitization in European children.

Melen E. et al. *Sex specific protective effects of interleukin-9 receptor haplotypes on childhood wheezing and sensitisation.* J Med Genet. 2004; 41(12) : e123.p

Melo R.E. et al. *Exercise-induced bronchoconstriction in children: montelukast attenuates the immediate-phase and late-phase responses.* J Allergy Clin Immunol. 2003; 111(2) : 301-7.p **Abstract:** BACKGROUND: Montelukast, a leukotriene receptor antagonist, attenuates exercise-induced bronchoconstriction. We and others have shown that there is a late-phase response 3 to 8 hours after exercise in a subset of asthmatic patients. OBJECTIVE: We sought to evaluate the protective effect of montelukast on immediate-phase and late-phase responses after exercise challenges. METHODS: Twenty-two atopic asthmatic children aged 7 to 16 years with reproducible exercise-induced bronchoconstriction (minimum of 15% decrease of FEV(1) from baseline) were enrolled in this placebo-controlled crossover study. Exercise challenges were performed while breathing cold dry air, and FEV(1) measurements were taken up to 480 minutes after exercise. Patients underwent exercise challenges on a screening day and 1 week after placebo treatment. Subsequently, after a week with no treatment, pulmonary function was assessed after breathing dry cold air (control day). Finally, an exercise challenge was carried out after a week of treatment with montelukast. RESULTS: Reproducible late-phase reactions occurred in 5 of 22 patients, which correlated with the extent of the immediate response (P <.05). After 1 week of treatment with montelukast, a significant decrease of immediate responses was observed. Montelukast treatment compared with placebo was associated with a lower mean maximum decrease of FEV(1) (mean +/- SEM: 17.3% +/- 2.4% and 35.1% +/- 2.6%, respectively), decrease of the area above the curve (267.8% +/- 42.7%/min and 868.0% +/- 103.8%/min, respectively), and shorter time for recovery (6.9 +/- 1.1 minutes and 30.9 +/- 4.0 minutes, respectively; P <.05). Treatment with montelukast also abolished late-phase responses. CONCLUSION: Once daily treatment with oral montelukast attenuated the immediate-phase response and abolished the late-phase response induced by means of exercise challenge in asthmatic children.

Menezes E.A. et al. *Extracts of Anacardium occidentale (cashew) pollen in patients with allergic bronchial asthma.* J Investig Allergol Clin Immunol. 2002; 12(1) : 25-8.p **Abstract:** Allergic reactions to the pollen of trees is among the most prevalent allergic sensitivities. The cashew tree grows in abundance in the northeast region of the Brazil, mainly in Fortaleza city, in state of the Ceara. It flowers once a year between August and October. This is the first study conducted to establish the possible role of the cashew pollen extract in causing skin test reactivity in patients with allergic asthma. A stock solution of pollen extract was prepared with the standard weight/volume method for intradermal skin tests and for the protein content of the extract, estimated with the use of Folin phenol reagent and a spectrophotometer. Ten nonallergic volunteers and 80 subjects with allergic asthma, as documented by previous positive skin test reactions to various pollens, were studied. All of the 80 patients (100%) had positive test reactions (grade III and grade IV reactions). None of the control subjects (n = 10) had positive responses to the

intradermal tests. This study provided us with knowledge of an additional pollen extract of the *Anacardium occidentale*, which could provoke skin test reactivities in asthmatic individuals from the northeastern area of Brazil. The results suggest a relationship between the period of flowering of the cashew tree and the increased number of allergic asthma cases.

Meng A. et al. *Decision-making in children with asthma and their parents.* J Am Acad Nurse Pract. 2002; 14(8) : 363-71.p **Abstract:** PURPOSE: To learn how children with asthma and their parents make treatment-related decisions. DATA SOURCES: Verbatim transcripts of focus group interviews of 28 school age children with asthma and their parents. Children had attended an educationally based asthma camp program. Questions related to choices parents and children made regarding implementation of their asthma treatment plans both, at home and at school. CONCLUSIONS: Parents and children made many non-adherence decisions especially with respect to preventive aspects of the treatment plan. Symptoms were the driving force for children's decisions. Parents and children had concerns about implementing the management plan at school. Parents and children may not perceive asthma treatment options as true choices, thus affecting motivation for adherence. IMPLICATIONS: Practitioners need to form partnerships with parents and children in developing treatment goals. Goals should focus on achievement of normal daily activities. Asthma education needs to be concrete and include school personnel. Practitioners need to give families positive, informational feedback.

Mermer C. et al. *Omega-3s and childhood asthma.* Thorax. 2002; 57(3) : 281.p

Mertes P.M. et al. *[Anaphylactic and anaphylactoid reactions occurring during anaesthesia in France. Seventh epidemiologic survey (January 2001-December 2002)].* Ann Fr Anesth Reanim. 2004; 23(12) : 1133-43.p **Abstract:** OBJECTIVES: Hypersensitivity reactions IgE-mediated (anaphylaxis) or non-IgE-mediated (anaphylactoid) reactions occurring during anaesthesia remain a major cause of concern for anaesthesiologists, since these reactions remain usually unpredictable, may be potentially life-threatening even when appropriately treated. The authors report the results of the last 2-year survey (2001, 2002) of such reactions conducted in France by the GERAP (groupe d'etude des reactions anaphylactoides peranesthesiques), and compare these results with their previous published surveys. METHODS: Between January 1, 2001 to December 31, 2002, 712 patients who experienced immune-mediated (anaphylaxis) or non-immune-mediated (anaphylactoid) reactions were referred to one of the 40 allergeo-anaesthesia centres members of the GERAP. Anaphylaxis was diagnosed on the basis of clinical history, tryptase measurements during the adverse reaction, and skin tests and/or specific IgE assay. RESULTS: Anaphylactic and anaphylactoid reactions were diagnosed in 491 cases (69%) and 221 cases (31%), respectively. The most common causes of anaphylaxis were neuromuscular blocking agents (NMBA) (n=271, 55%), latex (n=112, 22.3%), and antibiotics (n=74, 14.7%). Succinylcholine (n=102, 37.6%) and rocuronium (n=71, 26.2%) were the most frequently incriminated NMBAs. Cross-reactivity between NMBAs was observed in 63.4 % of cases of anaphylaxis to a NMBA. No difference was observed between anaphylactoid and anaphylactic reactions when the incidences of atopy, food, or drug intolerance were compared. However atopy, asthma and food allergy were significantly more frequent in case of latex allergy, when compared with NMBA allergy. Clinical manifestations were more severe in anaphylaxis. The positive predictive value of tryptase measurement for the diagnosis of anaphylaxis was 95.3%, the negative predictive value 49%. The diagnostic value of specific neuromuscular blocking agent IgE assays was confirmed. CONCLUSION: Our results further corroborate the need for systematic screening in case of immediate hypersensitivity reaction during anaesthesia and for the constitution

of allergeo-anaesthesia centres to provide expert advice to anaesthesiologists and allergologists.

Meuric S. et al. *[Compliance with and acceptability of a new electronic peak flow meter, the PiKo-1].* Rev Mal Respir. 2005; 22(6 Pt 1) : 935-41.p **Abstract:** BACKGROUND: Monitoring airflow obstruction is an essential component of asthma management. We examined home recording of PEFr using a new electronic peak flow meter in terms of compliance and acceptability in a group of children with asthma. METHODS: Twenty three children (3 with intermittent asthma and 20 with persistent asthma) (average age 10.9 +/- 3.8 [5-18] yrs) were asked to assess their PEFr every day during a period of 5.8 +/- 1.2 [4-8] weeks and record it in a diary card. Patients were not aware that their data was also being stored on the PiKo-1. At the end of the study, the written data were compared to the stored data. A multiple choice questionnaire was given to each subject to check the acceptability of the PiKo-1. RESULTS: 2 patients were lost to follow up. The compliance (expressed as a percent of the number of recordings that should have been made) was more than 80% for 14/21(67%) patients and less than 45% for 3/21 (14%). Compliance decreased during the study (96% in the first week, 68% during the fifth). 12% of the values were falsified. The PiKo-1 was considered to be small, attractive and useful. Some children found the mouthpiece too small. CONCLUSION: The good results for compliance that we observed might have been due to the short duration of the study. PiKo-1 was well accepted by the subjects. It will be possible to monitor PEFr and forced expiratory volume in the first second of expiration at home using this new device.

Meyer K.A. et al. *Response to montelukast among subgroups of children aged 2 to 14 years with asthma.* J Allergy Clin Immunol. 2003; 111(4) : 757-62.p **Abstract:** BACKGROUND: Determining who responds to asthma therapies, particularly leukotriene modifiers, continues to be explored. OBJECTIVE: We sought to identify patient characteristics predictive of response to montelukast. METHODS: We used data from 2 clinical trials in which children with asthma received either montelukast or placebo. Symptoms, beta-agonist use, and unanticipated health resource use caused by asthma were recorded in validated daily diaries for children 2 to 5 (n = 689) and 6 to 14 (n = 336) years old. We defined primary end points of days without asthma in 2- to 5-year-old patients (24 hours without symptoms, beta-agonist use, or asthma attack) and change in percent predicted FEV(1) in 6- to 14-year-old children. Asthma attack was defined by the use of rescue oral corticosteroids or by an unscheduled visit to a medical provider. Patients were grouped according to baseline characteristics, such as family history of asthma, personal history of allergy, frequency of asthma symptoms, eosinophilia, and concomitant use of inhaled corticosteroids or cromolyn. We examined the stratum-specific effects of montelukast on the percentage of days without asthma, change in percent predicted FEV(1), asthma attack, and a variety of secondary symptom and FEV(1) end points. RESULTS: We did not identify characteristics that predicted response to montelukast in either preschool or 6- to 14-year-old children. These findings were consistent across all symptom and FEV(1) outcomes. There was also no differential response to montelukast in either age group when asthma attack was the outcome. CONCLUSION: The patient characteristics studied do not appear to provide an indication of who will benefit most from treatment with montelukast.

Meys I. et al. *Exhaled nitric oxide corresponds with office evaluation of asthma control.* Pediatr Pulmonol. 2003; 36(4) : 283-9.p **Abstract:** Exhaled NO (ENO) has been studied as a noninvasive marker of airway inflammation, and has been shown to be elevated in asthma patients. The aim of this study was to investigate whether ENO measurements differ significantly between groups of asthmatic children with different disease control and to compare ENO measurements with the clinical assessment of asthma control.

Seventy-three children between 5-18 years old with a diagnosis of asthma were recruited. ENO was measured online during a slow vital capacity maneuver. The mean of three plateau NO levels was used for analysis. Baseline and postbronchodilator spirometry were performed. The assessment of disease control was based on the frequency of use of beta2-agonists, occurrence of day- and nighttime asthma symptoms, and spirometry results. Twenty-one children (group 1) had good asthma control. In 31 patients (group 2), asthma control was acceptable. In 21 patients (group 3), asthma was insufficiently controlled. ENO levels were (median (quartiles)): group 1, 11 ppb (9-21); group 2, 15 ppb (11-26); and group 3, 28 ppb (19-33). Measurements were significantly different between all three groups ($P = 0.009$, Kruskal-Wallis), between groups 1 and 3 ($P = 0.01$, Mann-Whitney U test), and between groups 2 and 3 ($P = 0.01$, Mann-Whitney-U test). The same was true for reversibility testing. We found significantly different ENO levels between a group of pediatric asthma patients with insufficient and good/sufficient control, as defined by clinical assessment. These results suggest that ENO measurements may be useful for monitoring asthma patients.

Miescier M.J. et al. *Children with asthma admitted to a pediatric observation unit.* *Pediatr Emerg Care.* 2005; 21(10) : 645-9.p **Abstract:** **OBJECTIVE:** Observation units (OUs) serve patients who require more evaluation or treatment than possible during an emergency department visit and who are anticipated to stay in the hospital for a short defined period. Asthma is a common admission diagnosis in a pediatric OU. Our main objective was to identify clinical factors associated with failure to discharge a child with asthma from our OU within 24 hours. **METHODS:** Retrospective chart review at a tertiary care children's hospital. Participants were children 2 years or older with asthma admitted from the emergency department to the OU during August 1999 to August 2001. The OU-discharged group comprised those successfully discharged from the OU within 24 hours. The unplanned inpatient admission group comprised those subsequently admitted from the OU to a traditional inpatient ward or those readmitted to the hospital within 48 hours of OU discharge. **RESULTS:** One hundred sixty-one children aged 2 to 20 years (median 4.0; 63% boys) met inclusion criteria; 40 patients (25%) required unplanned inpatient admission. In a multiple logistic regression model, 3 factors were associated with need for unplanned inpatient admission: female sex (adjusted odds ratio, 2.6; 95% confidence interval, 1.1-6.4; $P = 0.03$), temperature 38.5 degrees C or higher (adjusted odds ratio, 6.1; 95% confidence interval, 1.6-23.5; $P < 0.01$), and need for supplemental oxygen at the end of emergency department management (adjusted odds ratio, 5; 95% confidence interval, 1.7-15.1; $P < 0.01$). **CONCLUSIONS:** Many children with asthma can be admitted to a pediatric OU and discharged safely within 24 hours. Prospective studies are needed to confirm our findings and to identify other factors predictive of unplanned inpatient admission.

Migita O. et al. *ADRB2 polymorphisms and asthma susceptibility: transmission disequilibrium test and meta-analysis.* *Int Arch Allergy Immunol.* 2004; 134(2) : 150-7.p **Abstract:** **BACKGROUND:** The beta(2)-adrenergic receptor (ADRB2) is the most common adrenergic receptor in the lung, and associations between ADRB2 polymorphisms and intermediate phenotypes of asthma have been reported. Four missense polymorphisms (Arg16Gly, Gln27Glu, Val34Met, and Thr164Ile) and one polymorphism in the 5' leader cistron of the ADRB2 messenger RNA has been identified. In vitro studies have shown that these missense polymorphisms can affect ADRB2 function. **METHODS:** To examine possible associations of ADRB2 polymorphisms with asthma susceptibility, we performed transmission disequilibrium tests (TDT) of 137 Japanese families identified through children with atopic asthma. **RESULTS:** We did not find associations between any alleles of the ADRB2 polymorphisms and asthma by TDT ($p > 0.1$). We also performed a meta-analysis of data from all available studies. The random-effects model showed no significant odds ratio for the Arg16Gln (odds ratio

= 1.05, $p = 0.53$) or Gln27Glu (odds ratio = 1.12, $p = 0.22$) polymorphism. **CONCLUSION:** Our data indicate that ADRB2 does not contribute substantially to susceptibility to asthma, but it is possible that these polymorphisms influence disease activity and drug responses in individuals with asthma.

Migliaccio C. et al. *No linkage or association of five polymorphisms in the interleukin-4 receptor alpha gene with atopic asthma in Italian families.* *Eur J Immunogenet.* 2003; 30(5) : 349-53.p **Abstract:** The literature contains conflicting reports on the association of common variants of the interleukin (IL)-4 receptor alpha (IL4RA) gene with atopic asthma. The purpose of the present study was to investigate the linkage and association of several gene polymorphisms with atopic asthma in a large series of well-characterized individuals. Analysis of five polymorphisms (I50V, E375A, C406R, S478P and Q551R) of the IL4RA gene was performed in 823 individuals from 182 families with atopic asthmatic children from north-east Italy. The subjects were tested for clinical asthma, total serum IgE level, skin prick test positivity to common aeroallergens, and bronchial hyperresponsiveness to methacholine. The frequency of the polymorphisms was similar to that reported for other populations. The 375, 406, 478 and 551 polymorphisms were in linkage disequilibrium, as previously reported. No linkage or transmission disequilibrium was observed in the families between any mutation and any of the phenotypes investigated. No multipoint haplotype was associated with any phenotype. In conclusion, the IL4RA gene does not seem to play an important role in genetic predisposition to atopic asthma in the population tested.

Migliaretti G. et al. *Traffic air pollution and hospital admission for asthma: a case-control approach in a Turin (Italy) population.* *Int Arch Occup Environ Health.* 2005; 78(2) : 164-9.p **Abstract:** **OBJECTIVES:** This study investigated the relationship between traffic air pollution and asthma, using a case-control design applied to routinely collected data. **METHODS:** Subjects resident in Turin during the period 1997-1999 and admitted for asthma were defined as cases; patients admitted for causes other than respiratory diseases or heart diseases were defined as controls. Nitrogen dioxide and total suspended particulate were considered as indicators of traffic air pollution. Statistical analysis was performed, separately for young (0-14 years), adult (15-64 years) and elderly (>64 years) patients, with a logistic regression model; results are expressed as percentage of risk modification for a 10 g/m(3) increase in exposure to pollutants. **RESULTS:** The risk of emergency admissions for asthma rose significantly with increased exposure to nitrogen dioxide [2.4%, 95% Confidence Interval: 0.5%; 4.3%], and total suspended particulate [2.3%, 95% Confidence Interval: 1.1%-3.6%]. The significant association was evident, in particular, among young and elderly patients for both pollutants. **CONCLUSION:** Using a case-control design both easy to use and manage, the study confirms the significant association between hospital emergency admissions for asthma and exposure to nitrogen dioxide and total suspended particulate pollutants.

Mihailidou H. et al. *Decreasing morbidity of childhood asthma by regular outpatient follow-up, in Crete.* *Minerva Pediatr.* 2004; 56(2) : 197-206.p **Abstract:** **AIM:** There is evidence that the prevalence and morbidity of childhood asthma are increasing in many countries despite improvement of therapeutic regimens. We aimed to study possible changes in childhood asthma morbidity in Crete, Greece, by evaluating hospital admissions and emergency room visits for childhood asthma before and after 1-year regular follow-up at a special pediatric pulmonary out-patient clinic. **METHODS:** We followed-up 118 asthmatic children, aged 1-14 years, at a special pediatric pulmonary outpatient clinic. We evaluated the total number of hospital admissions due to asthma as well as asthma exacerbations during the 12 months before and 12 months after the regular follow-up care at the special pediatric pulmonary outpatient clinic.

RESULTS: The total annual number of hospital admissions of the 118 children before and after the regular follow-up was 122 and 19, respectively (reduction of 84%). Similarly, the total number of asthma exacerbations was 771 before and 230 after the 1-year follow-up (reduction of 71%). **CONCLUSION:** These findings show that regular follow-up care of asthmatic children at a specialized pediatric pulmonary outpatient clinic considerably reduces the morbidity of childhood asthma, thus reducing hospital costs for asthma and improving the quality of life for asthmatic children and their families.

Mihrshahi S. et al. *Effectiveness of an intervention to reduce house dust mite allergen levels in children's beds.* *Allergy.* 2003; 58(8) : 784-9.p **Abstract:** **BACKGROUND:** In temperate climates, exposure to house dust mite (HDM) allergens is the strongest environmental risk factor for childhood asthma. Environmental modifications to limit exposure have the potential to reduce the prevalence of asthma. The aim of this study was to reduce allergen exposure for children at high risk of developing asthma. **METHODS:** A total of 616 pregnant women were randomized to HDM intervention and control groups. The control group had no special recommendations whereas the intervention group was given allergen impermeable mattress covers and an acaricidal washing detergent for bedding. Children were visited regularly until 18 months of age to have dust collected from their bed. **RESULTS:** Der p 1 concentrations in the control group increased from 5.20 microg/g at 1 month to 22.18 microg/g at 18 months but remained low in the intervention group, ranging from 3.27 microg/g at 1 month to 6.12 microg/g at 18 months. **CONCLUSIONS:** In a high HDM allergen environment, a combined approach using physical barriers and an acaricidal wash, is effective in reducing HDM allergen concentrations in bedding. However, even with these control measures in place, HDM allergen levels remained high by international standards.

Milavec-Puretic V. et al. *Correlation among skin prick test, total and specific IgE UniCAP tests in atopic patients from Zagreb, Croatia.* *Acta Dermatovenerol Croat.* 2004; 12(4) : 257-60.p **Abstract:** The correlation of pollen allergens, Dermatophagoides pteronyssinus and animal dander was assessed during a two-year period. Results of skin prick test, total and specific IgE UniCAP tests were compared in atopic patients (AP) with the following diagnoses: atopic dermatitis, allergic rhinitis, allergic conjunctivitis, allergic bronchitis or asthma, allergic urticaria and angioedema. The study included total and specific IgE (in vitro) tests to allergen mixtures (grass, tree, weed) or to single allergens of Dermatophagoides pteronyssinus (Der p), cat and dog fur, feather, etc. Comparison of skin prick test with total and specific IgE UniCAP immunoassay was done in 173 patients, i.e. 107 female and 66 male atopic patients aged 9-76 years. Allergies were most commonly recorded in the 25-35 age group. Total IgE ranged from 8.63 kU/l to >4000 kU/l, with specific IgE ranging from class 1 to class 5. Skin prick test showed high correlation with specific IgE for grass and weed pollen in patients with respiratory allergy (50.28%). Good correlation among all three tests was quite frequently observed. The results suggest that the study should be continued using these three tests in further cases of atopic dermatitis.

Miles R. *Four pilot projects completed for school-based allergy and asthma screening.* *Ann Allergy Asthma Immunol.* 2003; 90(5) : 461-3.p

Millstein J. et al. *A testing framework for identifying susceptibility genes in the presence of epistasis.* *Am J Hum Genet.* 2006; 78(1) : 15-27.p **Abstract:** An efficient testing strategy called the "focused interaction testing framework" (FITF) was developed to identify susceptibility genes involved in epistatic interactions for case-control studies of candidate genes. In the FITF approach, likelihood-ratio tests are performed in stages that increase in the order of interaction

considered. Joint tests of main effects and interactions are performed conditional on significant lower-order effects. A reduction in the number of tests performed is achieved by prescreening gene combinations with a goodness-of-fit chi2 statistic that depends on association among candidate genes in the pooled case-control group. Multiple testing is accounted for by controlling false-discovery rates. Simulation analysis demonstrated that the FITF approach is more powerful than marginal tests of candidate genes. FITF also outperformed multifactor dimensionality reduction when interactions involved additive, dominant, or recessive genes. In an application to asthma case-control data from the Children's Health Study, FITF identified a significant multilocus effect between the nicotinamide adenine dinucleotide (phosphate) reduced:quinone oxidoreductase gene (NQO1), myeloperoxidase gene (MPO), and catalase gene (CAT) (unadjusted P = .00026), three genes that are involved in the oxidative stress pathway. In an independent data set consisting primarily of African American and Asian American children, these three genes also showed a significant association with asthma status (P = .0008).

Milnes L.J. et al. *The adaptation of written self-management plans for children with asthma.* *J Adv Nurs.* 2003; 41(5) : 444-53.p **Abstract:** **BACKGROUND:** Self-management plans are an important element of asthma care. Although asthma is common in children, there is limited guidance for adaptation of self-management plans for children. **AIMS:** A study was conducted in order to develop a set of criteria for adaptation of asthma self-management plans for school aged children; and to use these criteria to review self-management plans used in United Kingdom (UK) centres. **METHODS:** Self-management plans were obtained by telephone survey (response rate: 81%) of 47 selected UK paediatric, respiratory and community centres during the period between March and October 2001. The content of self-management plans was analysed according to criteria developed from a review of the literature, including objectives, opportunities for individualization, and the implied roles of parent and child in asthma management. Agreement was achieved between the authors and a third independent rater. **RESULTS:** The majority of centres (31 of 47) used or planned to use adapted self-management plans while the remainder used the standard National Asthma Campaign self-management plan. There were wide variations in self-management plans, including variation in the person to whom plans were addressed, criteria for treatment and the objectives stated for self-management. Few opportunities were provided for individualization of self-management. **LIMITATIONS:** The study was limited to the documents used in self-management in selected centres. **CONCLUSION:** The results suggest that many practitioners believe that self-management education requires adaptation for children. There is little consistency in the adaptation of self-management plans for children. Principles for devising adapted self-management plans are proposed.

Mimura T. et al. *Allergens in Japanese patients with allergic conjunctivitis in autumn.* *Eye.* 2005; 19(9) : 995-9.p **Abstract:** **PURPOSE:** The purpose of the current study is to evaluate the relation between various specific class E immunoglobulins (IgE) in the serum and allergic conjunctivitis in autumn. **METHODS:** Total IgE and specific IgE to 12 inhalant allergens were measured using the CAP system in 32 patients with allergic conjunctivitis in spring (spring group), 27 patients with allergic conjunctivitis in autumn (autumn group), and 40 healthy volunteers (control group). **RESULTS:** Specific IgE levels caused by house dust, Dermatophagoides pteronyssinus, and orchard grass were higher in the autumn group than in the spring group. The highest positivity rate for a specific allergen was 51.9% for house dust, followed by D. pteronyssinus(48.1%) in the autumn group, while the highest rate was 68.8 % for cedar pollen, followed by cypress pollen (59.4%) in the spring group. Correlation analysis showed that house dust was significantly correlated with animal epithelia, D. pteronyssinus, acarus, and Alternaria tenuis in the autumn group (P<0.001).

CONCLUSIONS: These results suggest that house dust is the main cause of allergic conjunctivitis during autumn. In spring, cypress pollen is the largest cause of allergic conjunctivitis, while indoor allergens such as house dust, animal epithelia, *D. pteronyssinus*, and *acarus* are not causative allergens in Japan.

Mincewicz G. et al. [*Acarofauna in the apartments of patients with perennial atopic rhinitis and functional tests of the respiratory system*]. *Pol Merkuriusz Lek.* 2003; 14(79) : 17-20.p **Abstract:** Prolonged exposure to house dust mites (HDM) of the Pyroglyphidae family leads to the development of perennial allergic rhinitis (PAR) in sensitized subjects. In PAR patients bronchial hyperreactivity—the clinical manifestation of allergic inflammation in the lower airways is often observed. The aim of the study was to estimate the influence of the exposure to HDM in PAR patients on selected functional parameters of the lower airways. The study was performed on 64 patients with PAR caused by allergy to HDM (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*) without either symptoms of asthma or spirometry abnormalities. The lower airways function was estimated by bronchial histamine provocation test (BHR) and flow-volume spirometry. The house dust mite quantity was measured in dust samples collected in spring and autumn. One sample was assessed by flotation technique with the use of methylene chloride and the mites species were identified (direct method) and the other sample was used to perform the Acarex test (semiquantitative guanidine determination test). Positive result of Acarex test was obtained in spring in 72% houses and in autumn in 63%. The predominance of the Pyroglyphidae family was observed in PAR patients' houses. The study showed that the exposure to the allergenic HDM in the quantity higher than 0.6 mg guanidine/g dust in autumn implies the increased incidence of both bronchial hyperreactivity and decreased airflow in the small bronchi in control spirometry tests. A strict correlation between the quantity of mites in houses in spring and autumn measured by the direct (flotation method) and the indirect (Acarex) tests was observed. Both methods proved to be equivalent in detecting allergens of house dust mites.

Mintegi Raso S. et al. [*Patient demand and management in a hospital pediatric emergency setting*]. *An Pediatr (Barc.)* 2004; 61(2) : 156-61.p **Abstract:** **OBJECTIVE:** To describe patient demand and management in a hospital pediatric emergency setting. **PATIENTS AND METHOD:** We analyzed the number of episodes registered in our pediatric emergency unit between 1995 and 2002 and performed a retrospective, random survey of 540 episodes in children aged less than 14 years admitted between 2001-10-1 and 2002-09-30. Epidemiological details, physical findings, complementary tests, the treatment administered, admissions, and unscheduled return visits were analyzed. **RESULTS:** Between 1995-1-01 and 2002-31-12, a total of 337,842 episodes were registered in our emergency unit, requiring 11,767 (3.48 %) admissions to a ward or the pediatric intensive care unit (PICU). The number of episodes/ year increased from 38,659 in 1995 to 51,933 in 2002 (Delta = 34.3 %). The mean age of the sample (n = 540) was 3.5 6 3.2 years (54.6 % were younger than 3 years) and 306 (56 %) were boys. Nearly one-third of the children presented with processes of recent onset (less than 6 hours). The most frequent chief complaints were fever in 160 children (29.6 %), respiratory distress in 78 (14.4 %) and vomiting-diarrhea in 65 (12 %). Complementary investigations were performed in 176 patients (32.6 %), mainly radiologic tests (115; 21.2 %). One hundred fifty-three (28.3 %) received treatment in our emergency unit, mainly antipyretics and bronchodilators. Sixty-five percent stayed less than 1 hour in the emergency unit. The most frequent diagnoses were fever without source in 66 patients (12.2 %), diarrhea/acute gastroenteritis in 40 (7.4 %), asthma in 35 (6.5 %), and croup in 27 (5 %). Sixteen children (3 %) were admitted to a ward and three (0.6 %) were admitted to the PICU. Home drug treatment was recommended in 359 patients (71.8 %). Unscheduled return visits were registered in 59 patients (10.9 %), and five were admitted. **CONCLUSIONS:** The number of patients attended in our

pediatric emergency unit gradually increased between 1995 and 2002, mostly due to young children with fever or respiratory distress. In nearly half of the patients, a thorough anamnesis and physical examination were sufficient for evaluation. Because many of the processes were of recent onset, continuous observation, whether at home or in hospital, was useful to adequately monitor these children.

Mircetic R.N. et al. *Magnesium concentration in plasma, leukocytes and urine of children with intermittent asthma*. *Clin Chim Acta.* 2001; 312(1-2) : 197-203.p **Abstract:** **BACKGROUND:** Magnesium (Mg) is involved in numerous physiological functions, including protein folding, intracellular signalling and enzyme catalysis. It acts as a smooth muscle relaxant. We decided to test changes of total Mg concentration in plasma, leukocytes and urine of 16 healthy children and 26 patients with intermittent asthma aged 3 to 14 years. **METHODS:** Samples were taken on the first day of broncho-obstruction and five days after the acute attack. During this period, patients were under salbutamol therapy. **RESULTS:** Plasma Mg concentration in patients increased by about 40% (first day 0.58±0.05 mmol Mg/l and five days later 0.64±0.04 mmol Mg/l) compared with healthy children (0.42±0.04 mmol Mg/l). Leukocyte Mg concentrations showed significant changes. On the first day of broncho-obstruction, Mg in leukocytes significantly decreased by about 60% (1.16±0.31 mmol Mg/g protein) compared to healthy children (3.04±0.68 mmol Mg/g protein). Five days later, Mg values significantly increased (3.28±1.09 mmol Mg/g protein) and almost reached the values of the healthy group. Mg concentration in urine statistically decreased by about 30% (0.55±0.06 mmol Mg/mmol creatinine) on the first day of broncho-obstruction compared to healthy children (0.75±0.05 mmol Mg/mmol creatinine). Five days after the acute attack, Mg concentration in patients' urine (0.73±0.07 mmol Mg/mmol creatinine) was close to values of healthy children. **CONCLUSION:** The results obtained indicate that the intracellular measurement of Mg concentration is relevant for estimation of magnesium concentration in the human organism. Hence, determination of Mg concentration in leukocytes may be used in evaluation of asthmatic pathology.

Mo F. et al. *Using Health Utility Index (HUI) for measuring the impact on health-related quality of Life (HRQL) among individuals with chronic diseases*. *ScientificWorldJournal.* 2004; 4 : 746-57.p **Abstract:** Quality of life is an important indicator in assessing the burden of disease, especially for chronic conditions. The Health Utilities Index (HUI) is a recently developed system for measuring the overall health status and health-related quality of life (HRQL) of individuals, clinical groups, and general populations. Using the HUI (constructed based on eight attributes: vision, hearing, speech, mobility, dexterity, cognition, emotion, and pain/discomfort) to measure the HRQL for chronic disease patients and to detect possible associations between HUI system and various chronic conditions, this study provides information to improve the management of chronic diseases. This study is of interest to data analysts, policy makers, and public health practitioners involved in descriptive clinical studies, clinical trials, program evaluation, population health planning, and assessments. Based on the Canadian Community Health Survey (CCHS) for 2000-01, the HUI was used to measure the quality of life for individuals living with various chronic conditions (Alzheimer/other dementia, effects of stroke, urinary incontinence, arthritis/rheumatism, bowel disorder, cataracts, back problems, stomach/intestinal ulcers, emphysema/COPD, chronic bronchitis, epilepsy, heart disease, diabetes, migraine headaches, glaucoma, asthma, fibromyalgia, cancers, high blood pressure, multiple sclerosis, thyroid condition, and other remaining chronic diseases). Logistic Regression Model was employed to estimate the associations between the overall HUI scores and various chronic conditions. The HUI scores ranged from 0.00 (corresponding to a state close to death) to 1.00 (corresponding to perfect health); negative scores reflect health states considered worse than death. The mean HUI score by sex and age group indicated the typical quality of

life for persons with various chronic conditions. Logistic Regression results showed a strong relationship between low HUI scores (< or = 0.5 and 0.06-1.0) and certain chronic conditions. Age- and sex-adjusted Odds Ratio (OR) and p values showed an effect among individuals diagnosed with each chronic disease on the overall HUI score. Results of this study showed that arthritis/rheumatism, heart disease, high blood pressure, cataracts, and diabetes had a severe impact on HRQL. Urinary incontinence, Alzheimer/other dementia, effects of stroke, cancers, thyroid condition, and back problems have a moderate impact. Food allergy, allergy other than food, asthma, migraine headaches, and other remaining chronic diseases have a relatively mild effect. It is concluded that major chronic diseases with significant health burden were associated with poor HRQL. The HUI scores facilitate the measurement and interpretation of results of health burden and the HRQL for individuals with chronic diseases and can be useful for development of strategies for the prevention and control of chronic diseases.

Mo F. et al. *Analysis of prevalence, triggers, risk factors and the related socio-economic effects of childhood asthma in the Student Lung Health Survey (SLHS) database, Canada 1996.* Int J Adolesc Med Health. 2003; 15(4) : 349-58.p Abstract: The purpose of this study was to provide information to improve the management of childhood asthma in Canada. The Student Lung Health Survey (SLHS) was conducted as a stratified and multi-staged cluster survey across Canada in 1996. It included a total of 136 public, private and separate schools in nine health units. The target study population was schoolchildren aged 5 to 19 years. Among all 5-19 years old students, the prevalence of asthma was 13.0%, with the prevalence for males being higher than for females, the adjusted Odds Ratio (OR) was 1.17, (95% CI 1.14-1.19) for males, in comparison with females. The prevalence in the 15-19 age group was higher than that in the 5-9 and 10-14 age group in females, but it was higher in the 5-9 and 10-14 age group than in the 15-19 age group in males. The mean delay from the onset of symptoms to time of first diagnosis was 1, 0.4 and 0.3 years for the 1-4, 5-9 and 10-14 age group respectively. However, there was no delay in the 15-19 group. The prevalence of asthma in Prince Edward Island (17.9%), Halifax (17.1%), and Kingston (16.1%) was higher than that in Saskatoon (10.0%), Sherbrooke (9.7%) and Kelowna (11.9%). The proportion of asthma for students who smoked more than 11 cigarettes per day (OR = 1.41), were exposed to passive smoke in home (OR = 7.29), in car (OR = 4.71), and in school (OR = 4.24) or had a family income less than CAN\$40,000 (OR = 1.19), was significantly higher than groups without those factors. Risk factors and socio-economic status such as living conditions and environment, pets or plants in the home, parental education levels also affected the morbidity of asthma. The results of the SLHS study demonstrated the serious burden of childhood asthma, and asthma triggers, living and environmental conditions and lifestyle influence the prevalence and the effects of childhood asthma diagnosis, treatment, and education in Canada. Asthma is still a serious chronic condition for students and it influences their academic performance and their quality of life. The diagnostic methods and the practice guidelines for asthma control are useful for preventing and controlling asthma. These findings provide indications of interventions are being used for the control of asthma in Canada.

Mo F. et al. *Childhood asthma management and control. Analysis of the Student Lung Health Survey (SLHS) database, Canada 1996.* Int J Adolesc Med Health. 2004; 16(1) : 29-40.p Abstract: The objective of this study was to estimate the severity of childhood asthma in Canada, identify the effects of asthma interventions in different target groups, and to profile asthma management and control practices by geographic area, sex, age, and severity groups. **METHODS:** The SLHS was conducted as a stratified and multi-staged cluster survey across Canada in 1996. It included a total of 136 public, private and separate schools in nine health units (Prince Edward Island, Halifax, Sherbrooke, Kingston, Guelph, Winnipeg,

Saskatoon, Edmonton, and Kelowna). The target study population was schoolchildren aged 5 to 19 years. Descriptive analyses were used to calculate the severity of childhood asthma for the different groups. Logistic regression was then employed to measure the quality of asthma intervention and control. Multivariate logistic regression was also used to compare the severity and treatment of asthma with age, sex and lifestyle, living and housing conditions. Using existing Clinical Practice Guidelines as a reference, the study also evaluated the effectiveness of interventions such as treatment, and asthmatic education. **RESULTS:** Based on the Canadian Consensus Recommendations of definition of asthma control, among all 5-19 years old students, 39.9% were well controlled, 33.8% were acceptably controlled and 26.3% were poor controlled. The rates of intermittent and mild asthma were 44.8% and 11.6% compared with moderate (15.3%) and severe (0.9%). Students with asthma reported receiving more advantaged information from a demonstration of inhaler users (OR = 7.51, 95% CI = 5.65-8.94), during a medical visits (OR = 6.33, 95% CI = 5.11-7.83), from the pamphlet/brochures (OR = 6.22, 95% CI = 5.05-7.76) or from a demonstration of the correct use of medicine (OR = 5.62, 95% CI = 4.62-6.82). More students visited a family doctor (40.3%, OR = 5.52, 95% CI = 4.95-6.64) and medical specialists (31.0%, OR = 3.69, 95% CI = 2.58-4.78) than other specialist when they had respiratory problems. **CONCLUSIONS:** The results of the SLHS study demonstrated variations in the management and control of childhood asthma across Canada. The interventions and the practice guidelines for asthma control are useful for preventing and controlling asthma. These findings provide indications of interventions that are being used for the control of asthma in Canada.

Mochizuki H. et al. *Bronchial sensitivity and bronchial reactivity in children with cough variant asthma.* Chest. 2005; 128(4) : 2427-34.p Abstract: **BACKGROUND:** Cough variant asthma (CVA) is diagnosed in some children with chronic cough who do not have wheezing. However, the precise mechanism of CVA in children is unclear. **OBJECTIVE:** To evaluate the physiologic differences in the airways of children with classic asthma and CVA, the methacholine dose-response curves of respiratory resistance (Rrs) were studied. **PATIENTS AND METHODS:** CVA was diagnosed in 31 children with chronic cough (age range, 5 to 14 years; 19 boys and 12 girls; mean age, 8.5 years) on the basis of methacholine inhalation challenge using an oscillation method. For comparison, the study included 86 age-matched children with classic asthma (age range, 5 to 15 years; 42 boys and 44 girls; mean age, 9.5 years), 25 age-matched children with cough (age range, 5 to 15 years; 17 boys and 8 girls; mean age, 8.8 years), and 23 age-matched control subjects (8 boys and 15 girls; mean age, 9.2 years). Consecutive doses of methacholine were doubled until a 200% increase in Rrs from baseline was reached. The cumulative dose of methacholine at the inflection point of Rrs was considered to represent the bronchial sensitivity to inhaled methacholine (minimum dose of methacholine [Dmin]). The slope of the methacholine dose-response curve (SRrs), which was considered to represent bronchial reactivity, was measured from the increasing Rrs curve. **RESULTS:** The values of Dmin in classic asthma patients and in CVA patients were significantly lower than those for cough patients and control subjects. There was no significant difference in the values of Dmin between the classic asthma and CVA patients. The value of SRrs in CVA patients was significantly lower than that in classic asthma patients, cough patients, and control subjects (p < 0.05, p < 0.01, and p < 0.01, respectively). There was no significant difference in the value of SRrs between classic asthma patients, cough patients, and control subjects. **CONCLUSIONS:** These data show that bronchial reactivity in the children with CVA was significantly lower than that in the children with classic asthma, and this specificity has an effect on prolonged cough without wheezing in children with CVA.

Moffatt M. et al. *Haplotypes and asthma.* Am J Respir Crit Care Med. 2005; 171(10) : 1066-7.p

- Moffatt M.F. et al.** *Atopy, respiratory function and HLA-DR in Aboriginal Australians.* Hum Mol Genet. 2003; 12(6) : 625-30.p **Abstract:** The Class II genes of the MHC represent a major locus with quantified effects on atopic (allergic) phenotypes in many studies of westernized Caucasians. Although asthma is considered a disease of western societies, typical components of the asthma phenotype, such as elevations of the IgE, are seen with parasitic infestation. We have therefore investigated the effects of the HLA-DRB1 locus on asthma and its intermediate phenotypes in Aboriginal people from the Kimberly region of Australia who were suffering from endemic hookworm infection. Recognizable correlates of allergic asthma were present in the subjects, including skin test positivity to house dust mite (HDM), specific IgE responses to HDM, and the total serum IgE. HLA-DRB1 alleles did not predict the presence of asthma, but multi-allelic tests of association showed the locus accounted for approximately 33% of the variance of the total serum IgE concentration and 17% of the variance of the specific IgE titres to HDM. Genetic admixture was excluded as a cause of the results. These effects of the MHC on IgE levels were an order of magnitude greater than that seen in Caucasians, consistent with the hypothesis that the genetic predisposition to allergic disease may be driven by adaptation to helminth infection. The results further suggest that parasitism per se is not protective against asthma.
- Mohammad Y. et al.** *Laryngeal hirudiniasis: an unusual cause of airway obstruction and hemoptysis.* Pediatr Pulmonol. 2002; 33(3) : 224-6.p **Abstract:** Cases of childhood hemoptysis are rare and usually result from foreign body aspiration or congenital heart or lung diseases. However, human hirudiniasis due to the leech still exists, and could involve the upper airways after drinking infested water from quiet streams and pools. We report the case of a 6-year-old child who presented suffocating at the emergency room after having been misdiagnosed and treated for asthma over a 1-month period. His mother reported he had had recurrent hemoptysis, as well. The child inadvertently drank leech-infested water in a rural area of northern Syria. Surgical removal of the leech resulted in prompt resolution of the symptoms. Although laryngeal hirudiniasis is rare in the developed world, it remains a possible cause of childhood airway obstruction, hemoptysis, and anemia which needs to be considered in patients with a suggestive history.
- Mohn A. et al.** *Adrenal suppression from high-dose inhaled fluticasone propionate in children with asthma.* Eur Respir J. 2004; 23(2) : 354-5.p
- Moissidis I. et al.** *Association of IL-13, RANTES, and leukotriene C4 synthase gene promoter polymorphisms with asthma and/or atopy in African Americans.* Genet Med. 2005; 7(6) : 406-10.p **Abstract:** PURPOSE: IL-13, RANTES (Regulated on Activation, Normal T cells Expressed and Secreted), and cysteinyl leukotrienes are asthma and atopy mediators. Two RANTES -403(G to A) and -28(C to G), an -1055 IL-13(C to T), and a -444(A to C) leukotriene C4 synthase (LTC4S) single nucleotide polymorphisms (SNPs) have been shown in Caucasians and Asians as asthma and atopy risk factors. We studied these SNPs in African Americans with asthma and/or atopy. METHODS: We studied 61 patients with asthma and/or atopy and 129 to 157 newborn controls for the -403 RANTES, -28 RANTES, and -1055 IL-13 SNPs, as well as 47 patients and 60 newborn controls for the -444 LTC4S SNP. RESULTS: The two groups did not significantly differ at the genotypes of the -403 and -28 RANTES SNP. On the other hand, the mutant TT genotype for the -1055 IL-13 SNP was detected in 19.7% of patients versus 12.7% in controls ($P < 0.04$, OR 2.9, 95% CI 1.0-8.0), and the mutant T allele in 58.3% versus 36.6% in controls ($P < 0.02$, OR 2.4, 95% CI 1.1-5.2). In a similar fashion, for the -444 LTC4S SNP, the mutant AC genotype was detected in 19.1% versus 10.0% in controls ($P > 0.28$); mutant C allele had an OR of 2.1 (95% CI 0.7-6.3). CONCLUSION: African American asthmatics/atopics had higher frequency of the TT mutant gene for the -1055 IL-13 SNP and of its mutant T allele. Regarding the -444 LTC4S SNP, there was a definite difference, although not statistically significant, with an OR of 2.1 for the mutant AC genotype in patients. If these findings become reproduced by larger studies, it may suggest that IL-13 and LTC4S SNPs can be used as predictive markers for asthma/atopy in African Americans.
- Moller C. et al.** *Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study).* J Allergy Clin Immunol. 2002; 109(2) : 251-6.p **Abstract:** BACKGROUND: Children with allergic rhinitis are likely to develop asthma. OBJECTIVE: The purpose of this investigation was to determine whether specific immunotherapy can prevent the development of asthma and reduce bronchial hyperresponsiveness in children with seasonal allergic rhinoconjunctivitis. METHODS: From 6 pediatric allergy centers, 205 children aged 6 to 14 years (mean age, 10.7 years) with grass and/or birch pollen allergy but without any other clinically important allergy were randomized either to receive specific immunotherapy for 3 years or to an open control group. All subjects had moderate to severe hay fever symptoms, but at inclusion none reported asthma with need of daily treatment. Symptomatic treatment was limited to loratadine, levocabastine, sodium cromoglycate, and nasal budesonide. Asthma was evaluated clinically and by peak flow. Methacholine bronchial provocation tests were carried out during the season(s) and during the winter. RESULTS: Before the start of immunotherapy, 20% of the children had mild asthma symptoms during the pollen season(s). Among those without asthma, the actively treated children had significantly fewer asthma symptoms after 3 years as evaluated by clinical diagnosis (odds ratio, 2.52; $P < .05$). Methacholine bronchial provocation test results improved significant in the active group ($P < .05$). CONCLUSION: Immunotherapy can reduce the development of asthma in children with seasonal rhinoconjunctivitis.
- Moller M. et al.** *Improvement of asthma therapy by a novel budesonide multidose dry powder inhaler.* Arzneimittelforschung. 2003; 53(8) : 562-7.p **Abstract:** The objective of the present post-marketing surveillance (PMS) was the evaluation of efficacy, tolerability and acceptance of the novel budesonide (CAS 51333-22-3) multidose dry powder inhaler (MDPI) Novopulmon 200 Novolizer. A total of 3,057 patients suffering from allergic, non-allergic or mixed bronchial asthma were included in the PMS. The study medication was administered by inhalation at a median dosage of 2 x 200 micrograms budesonide/day. In order to evaluate the efficacy of the novel budesonide MDPI, pulmonary functions (peak expiratory flow rate (PEFR) and FEV1) were measured at the start of the treatment and after 4 weeks of treatment. Severity of the following symptoms was evaluated on a four-score scale: cough, wheezing, diurnal dyspnea, nocturnal dyspnea and dyspnea on physical effort. Furthermore, the patients' satisfaction in dealing with the control mechanisms (optical, acoustic, sensory, dose counter, overdose prevention) of this innovative MDPI was assessed. Patients who already had used another inhalation system assessed the control mechanisms of the novel budesonide MDPI in comparison with their previous inhalation system (e.g. fluticasone premeasured dose MDPI, non-refillable budesonide MDPI). The patients' compliance and any improvement of compliance by the control mechanisms according to physicians' assessments were evaluated. The novel budesonide MDPI was shown to lead to a decrease in the severity of symptoms. The median total symptom score (0 = no symptoms, 15 = all symptoms severe) decreased from 8 before therapy to 2 after therapy. Pulmonary function measurements supported a relief of the patients' symptoms: The median PEFR increased from 5 l/s before therapy to 6.3 l/s at the end of therapy, with a median individual increase of 1 l/s. The median FEV1 increased from 2250 ml before therapy to 2700 ml at the end of therapy, with a median individual increase of 310 ml. The majority of patients were satisfied with the control mechanisms. 97% of the patients were satisfied with the optical control mechanism, 94% with the acoustic, 78% with the sensory mechanism, 92% with the dose counter and 81% with the overdose

prevention. Compliance was assessed by the physicians to be good in 84% of the patients, to be satisfactory in 14% and to be not satisfactory in 2%. An improvement in compliance by the control mechanisms of the inhaler was observed in 80% of the patients. 97% of the patients were satisfied with the control mechanisms, the optical and acoustic mechanisms were confirmed as being the most important ones. The vast majority of patients assessed the control mechanisms of the novel MDPI to be better or much better than those of a previously used inhaler (e.g. 41.2% and 52.1%, respectively, of patients who had previously used a non-refillable budesonide MDPI; 38.7% and 44.7%, respectively, of patients who had previously used a fluticasone premeasured dose MDPI). Overall, the novel budesonide MDPI was shown to be efficient in the relief of asthma symptoms and improvement of lung function. The MDPI's control mechanisms were shown to be well accepted by the patients and considered by the physicians as an important contributor to an improvement of patient compliance.

Monroe K.W. et al. *Comparison of two forms of albuterol for treatment of acute bronchospasm in pediatric patients.* South Med J. 2003; 96(5) : 440-4.p **Abstract:** BACKGROUND: The Circulaire nebulizer (C-Neb) is marketed as superior to low-dose albuterol for acute bronchospasm. METHODS: This clinical trial design compared clinical and fiscal outcomes of patients treated with C-Neb and high-dose albuterol (HDA). Eligibility criteria included reactive airway disease, age >5 years, and asthma score (AS) of 2 to 10. Patients with odd medical record numbers received HDA, and those with even numbers received C-Neb. Treatment was concluded if AS was 0, peak flow was >70% predicted, or after three treatments. RESULTS: One hundred eight patients were enrolled: 48 received HDA, 52 received C-Neb, and 8 were excluded. The two groups were comparable by admission rates ($G2 = 0.90$, $P = 0.34$), return visit rates ($G2 = 0.73$, $P = 0.39$), and final AS ($z = 0.59$, $P = 0.55$). Side effects were similar: change in heart rate ($t = 1.61$, $P = 0.11$) and mean arterial pressure ($t = 1.36$, $P = 0.17$). Charges per treatment, per delivery, and total charges were greater for HDA. CONCLUSION: The C-Neb is equally effective, has similar side effects, and requires less time and charges than HDA.

Montealegre F. et al. *Measuring asthma disparities in Hispanics: adherence to the national guidelines for asthma treatment in emergency departments in Puerto Rico.* Ann Allergy Asthma Immunol. 2004; 93(5) : 472-7.p **Abstract:** BACKGROUND: Puerto Rico has the highest prevalence of asthma in the United States. Currently, there are no data on actual care given to asthmatic patients. OBJECTIVE: To determine the prevalence of documented adherence to the 1997 National Asthma Education Prevention Program guidelines regarding care given in emergency departments (EDs) in Ponce, Puerto Rico. METHODS: A case series was conducted using 6,002 ED records with a physician-based diagnosis of asthma for 1999 through 2001. RESULTS: A history of asthma attack was documented in 82.0% of the cases and in all age groups. In-home beta-agonist use was recorded in only 5.7% of the medical records. Documentation of previous admissions to the ED and the intensive care unit were found in 3.5% and 0.33% of the records, respectively. Nocturnal symptoms before the ED visit were found in only 6.4% of the records, and asthma treatment at home was found in 39.9%. Accessory muscle retraction was documented in 99.1% of the cases, and oxygen saturation was found in 23.2%. Treatment with nebulized beta-agonist was found in 72.1% of the records, and intravenous or oral corticosteroid use was found in 84.1%. Follow-up appointments were detected in 64.8% of the cases, and referrals to specialists were given in only 5.3%. Rate ratios between our data and those of other researchers indicate that there are geographical differences in compliance with the guidelines. CONCLUSION: Of the variables tested, only one had acceptable levels of compliance, as evidenced in the patient's records, indicating that there are alarming differences in ED evaluation and treatment compared with the 1997 National Asthma Education Prevention Program guidelines.

Montefort S. et al. *Allergic conditions in 5-8-year-old Maltese schoolchildren: prevalence, severity, and associated risk factors.* Pediatr Allergy Immunol. 2002; 13(2) : 98-104.p **Abstract:** Allergic conditions, especially asthma, seem to be increasingly common worldwide. The International Study of Asthma and Allergies in Childhood (ISAAC) was the first study carried out worldwide using standardized questionnaires in order to create a reliable global map of childhood allergy. The Maltese Islands were one of the centres that participated in this study and in this article the data obtained from 3,506 5-8-year-old children from 24 state schools (78.5% response rate), and also data obtained from some added 'local' questions addressed to the same children, were analyzed in order to evaluate the problem of allergic conditions in Maltese schoolchildren. Of the participants, 19.1% were wheezers 'ever,' while 8.8% were current wheezers. Of the latter, 15.9% experienced nocturnal wheezing at least once a week and 13.3% had a wheezing episode of sufficient severity to limit speech. Nasal problems were present in 23.4% of these children, and in 20.7% of all respondents these symptoms persisted up to the year of answering the questionnaire. Hay fever had been diagnosed in 14.7% of all the children. Seven per cent of respondents had a recurrent, itchy rash (suggestive of eczema) for at least 6 months of their lives and 5.5% had it currently. The prevalence of wheezing and eczema were slightly lower than the global mean, unlike rhinitis which in Malta was commoner than the world average. Multiple variables, such as gender, breast-feeding, passive smoking, family history of atopy, pets, soft furnishings, and living next to busy roads, were factors that affected the prevalence and severity of the allergic conditions studied. In conclusion, allergic conditions are very common in Maltese schoolchildren and cause great hardship to these same youngsters. The results of this study should serve as a stimulus to try to decrease this suffering through better management of these conditions, measures to control identified detrimental factors (such as passive smoking), and further research on asthma, allergic rhinitis and eczema.

Monteil M.A. *Dust clouds and spread of infection.* Lancet. 2002; 359(9300) : 81.p

Monteiro-Antonio M.A. et al. *[Linear growth evaluation of asthmatic children].* Rev Assoc Med Bras. 2002; 48(2) : 145-50.p **Abstract:** OBJECTIVE: The aim was to assess the effect of atopic asthma on the stature and growth velocity of Brazilian adolescents and children, taking into consideration their socioeconomic conditions, natural disease history and individual growth. METHODS: 66 patients had been seen at the Pneumology, Immunology and Allergy Ambulatory, Unicamp, University Hospital. Their height and weight were measured every 3 months and the bone age was obtained once during this period. The patients were divided into two groups according to their puberal development: prepubertal and puberal. RESULTS: Prepubertal - 40 patients with 0.6 to 1.5 years (1.04+/-0.19) of follow-up. The mean height/age z-score was 0.028 +/- 0.978 and the mean growth velocity z-score was 0.045 +/- 1.11. Puberal - 26 patients with 0.5 to 1.3 years (0.99+/-1.722) of follow-up. The mean height/age z-score was 0.170 +/- 1.209 and the mean growth velocity z-score was 0.042 +/- 2.321. In the prepubertal group the patients who had one or more pneumonia during the follow-up had lower mean growth velocity z-score than the others ($p=0.04$). The high dose of glucocorticoids used by puberal patients was considered a risk factor for growth velocity ($p=0.02$). CONCLUSIONS: The children and adolescents suffering from asthma could grow normally and attain their full genetic potential by treating the disease correctly, controlling infections and having favorable living conditions.

Monti G. et al. *High incidence of adverse reactions to egg challenge on first known exposure in young atopic dermatitis children: predictive*

value of skin prick test and radioallergosorbent test to egg proteins. *Clin Exp Allergy*. 2002; 32(10) : 1515-9.p **Abstract:** BACKGROUND: Egg skin prick test (SPT) and/or radioallergosorbent test (RAST) positivity has been described in infants and children with a food allergy, or in infants at high risk of atopy who have never eaten eggs. Clinical reactions are also observed when some of these children or infants eat eggs for the first time. OBJECTIVE AND METHOD: A prospective study was made of 107 atopic dermatitis (AD) children (66 boys, 41 girls) aged 1-19 months (median 5 months) who had never ingested egg, to compare the outcome of a first oral egg challenge and the results of albumen and yolk SPTs and RASTs. RESULTS: The egg challenge (conducted at age 12-24 months: mean 16 months, median 15 months) was positive in 72/107 children (67.3%). The reactions were immediate or early (first 6 h) in 56/72 (77.8%). The most severe (all within the first 6 h) were one case of anaphylactic shock (1.4%), three cases of laryngeal oedema (4.1%) and one serious attack of asthma (1.4%). The skin weal diameter at and above which reactions always occurred was 5 mm for both albumen and yolk. They were, however, also observed in the complete absence of a weal. The outcome of the challenge was always positive when the specific IgEs (sIgE) for albumen and yolk were > 99 KU/L and > or = 17.5 KU/L, respectively. Here, too, reactions were noted even when sIgE levels were < 0.35 KU/L. CONCLUSION: AD children who have never eaten eggs may be sensitized and display reactions at the first ingestion. The percentage of reactions in this series was by no means negligible. These findings were observed in children with mild as well as moderate-severe AD when first examined. SPT for albumen and yolk diameter > or = 5 mm, and sIgE for albumen > 99 KU/L and for yolk > or = 17.5 KU/L were 100% specific in predicting the outcome of the challenge. It may thus be concluded that children with AD whose SPT and/or RAST for albumen and/or yolk are equal to or higher than these cut-off values should not be subjected to the oral challenge when consideration is given to the introduction of egg in their diet. Even when these cut-offs are not reached, however, clinical reactions to the challenge cannot be ruled out a priori, and it should be preferably performed in a protected environment, such as a hospital.

Montuschi P. et al. *Ion trap liquid chromatography/tandem mass spectrometry analysis of leukotriene B4 in exhaled breath condensate.* *Rapid Commun Mass Spectrom*. 2004; 18(22) : 2723-9.p **Abstract:** The objective of this study is the measurement of leukotriene B7 (LTB4), a potent inflammatory mediator, in exhaled breath condensate by using liquid chromatography/mass spectrometry (LC/MS and LC/MS/MS). Condensation of exhaled breath is a non-invasive method to collect airway secretions. Deuterated (d4)-LTB4 was used as internal standard. The MS and MS/MS behavior of LTB4 and LTB4-d4 was studied by electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI) in both positive and negative ion polarity mode. Preliminary results show that monitoring negative ions in ESI mode has the best sensitivity for both LTB4 and LTB4-d4. Therefore, negative ESI was chosen, and the [M-H]⁻ ions at m/z 335 and 339 were selected for quantification. The lower limit of quantification for LTB4, expressed as the lowest point of the calibration curve, was 100 pg/mL. Using this technique, we measured LTB4 in exhaled breath condensate in two healthy subjects, four asthmatic patients on anti-inflammatory treatment, and four asthmatic patients who were not on anti-inflammatory drugs. Exhaled LTB4 concentrations were detected only in asthmatic patients who were not on anti-inflammatory therapy. This method is potentially useful for non-invasive assessment of airway inflammation, but the sensitivity of the technique needs to be improved.

Moonie S.A. et al. *Community Asthma Program improves appropriate prescribing in moderate to severe asthma.* *J Asthma*. 2005; 42(4) : 281-9.p **Abstract:** Asthma guidelines, established by the National Asthma Education and Prevention Panel (NAEPP), seek to guide

physicians in the appropriate assessment and treatment of asthma. Poor physician adherence to these guidelines has been documented because of a variety of reported barriers. We sought to test the efficacy of the Community Asthma Program (CAP), which was designed to help primary care physicians (PCP) assess asthma severity and to prescribe medications according to NAEPP guidelines. A prospective, observational study was conducted in 723 patients with asthma (aged < 1-85 years) in two primary care clinics. PCPs had access to patient responses to asthma symptom questions at each visit. The correlations between patient self-reported and PCP-classified asthma severity, treatment prescribed, and missed days from work or school were determined. The effect of the intervention on guideline adherence was assessed by asthma severity level and time. An overall moderate measure of agreement was found between patient self-reported and PCP-classified asthma severity (kappa = 0.48; p < 0.001) although this agreement decreased with increasing severity of asthma. Patient self-reported (r = 0.14; p < 0.001) and PCP-classified (r = 0.17; p < 0.001) asthma severity was weakly correlated with missed days from work or school. Those with severe persistent asthma were 89% less likely to be appropriately treated than the mild intermittent group (OR = 0.11; 95% CI-0.1-0.2). This relationship was not influenced by the different clinics or providers nor by the age of the patient. Over time, the CAP-trained PCPs were more likely to appropriately prescribe asthma medications for those with moderate to severe asthma (Mantel-Haenszel chi2 = 5.11; p = 0.02). Despite appropriate assessment of asthma severity, physicians are undertreating patients with severe asthma, the group with the highest health care use. Use of the CAP over time aided PCPs in appropriately medicating patients with moderate to severe asthma in accordance with guidelines.

Moore S.J. et al. *Clinical and genetic epidemiology of Bardet-Biedl syndrome in Newfoundland: a 22-year prospective, population-based, cohort study.* *Am J Med Genet A*. 2005; 132(4) : 352-60.p **Abstract:** Bardet-Biedl syndrome (BBS) and Laurence-Moon syndrome (LMS) have a similar phenotype, which includes retinal dystrophy, obesity, and hypogenitalism. They are differentiated by the presence of spasticity and the absence of polydactyly in LMS. The aims of this study were to describe the epidemiology of BBS and LMS, further define the phenotype, and examine genotype-phenotype correlation. The study involved 46 patients (26 males, 20 females) from 26 families, with a median age of 44 years (range 1-68 years). Assessments were performed in 1986, 1993, and 2001 and included neurological assessments, anthropometric measurements, and clinical photographs to assess dysmorphic features. The phenotype was highly variable within and between families. Impaired co-ordination and ataxia occurred in 86% (18/21). Thirty percent (14/46) met criteria for psychiatric illness; other medical problems included cholecystectomy in 37% (17/46) and asthma in 28% (13/46). Dysmorphic features included brachycephaly, large ears, and short, narrow palpebral fissures. There was no apparent correlation of clinical or dysmorphic features with genotype. Two patients were diagnosed clinically as LMS but both had mutations in a BBS gene. The features in this population do not support the notion that BBS and LMS are distinct. The lack of a genotype-phenotype correlation implies that BBS proteins interact and are necessary for the development of many organs.

Moral Gil L. et al. *[Choice of oral corticosteroids for asthma exacerbations].* *An Pediatr (Barc)*. 2005; 62(3) : 294.p

Moral Gil L. et al. *Nonallergic childhood asthma: a common diagnosis for transient and nonatopic wheezers?* *J Allergy Clin Immunol*. 2003; 112(5) : 1013; author reply 1014.p

Morales Suarez-Varela M.M. et al. *[Study of the obesity and overweight as a risk factor for asthma and severity of the asthma in children of Valencia (Spain)].* *Nutr Hosp*. 2005; 20(6) : 386-92.p **Abstract:**

BACKGROUND: Obesity and overweight have been described as factors associated with asthma. Our aim was to evaluate the role obesity plays on asthma in children. **SCOPE AND SUBJECTS:** A study carried out on children and teenagers between 8 and 15 years of age, chosen for a cluster-type random sampling from children who studied in 80 schools, which represents 30% of the schools in the city of Valencia. **MATERIAL AND METHODS:** The analysed data was organized into two groups, obese (from the Body Mass Index (Kg/m²)), showing children with a percentile over 85% of the measuring reference for the Spanish population) and non obese, when they did not fulfil this condition. The prevalence of the different parameters studied was calculated by an Interval of Confidence of 95%. The risk was calculated (Relative Risk) from those symptoms compatible with asthma among obese children compared to non obese children. **RESULTS:** No significant relative risk (RR) was seen for obesity with regards to asthma in those percentiles of obesity over 85. Otherwise, an increase in the relative risk (RR) regarding the severity of asthma was seen in relation to obesity, mainly in the 85th percentile (RR = 1.51 of suffering between 4-12 wheezing attacks and RR = 1.86 of suffering more than 12 attacks in obese children as opposed to non obese children). **CONCLUSIONS:** In this study, we did not identify a higher risk of asthma among obese children than among non obese children, although we did find there was a higher risk of severity of asthmatic symptoms. As far as the severity of the asthma is concerned, we saw a higher risk of wheezing and whistling attacks among obese children with the 85th and the 95th percentiles according to the Body Mass Index.

Morden N.E. et al. *Clinical inquiries. How effective are leukotriene inhibitors for asthma in children?* J Fam Pract. 2004; 53(4) : 325-6.p

Moreno-Ancillo A. et al. *Lupine inhalation induced asthma in a child.* *Pediatr Allergy Immunol.* 2005; 16(6) : 542-4.p **Abstract:** The ingestion of lupine seed flour has been reported as a cause of allergic reactions. There is some evidence of its allergenic potential after inhalation. An 8-year-old asthmatic child, who was allergic to peanut, was studied in our clinic with the suspicion of an adverse drug reaction due to salbutamol. He suffered an asthma attack while playing with his brother, who had been eating lupine seed as snack; surprisingly, the asthma attack worsened with salbutamol. The skin tests showed a positive result with *Lupinus albus* extract, peanut, garbanzo bean, navy bean, pea, green bean, lentil, soy, *Olea europea* pollen, grass pollen and *Plantago lanceolata* pollen. The prick-by-prick tests both from dried seeds and those preserved in salt and water were strongly positive. Serum specific IgE antibodies were positive to *Lupinus albus* (1.43 kU/l), peanut (4.32 kU/l), soy (2.15 kU/l), lentil (3.12 kU/l) and garbanzo (0.7 kU/l). After informed consent salbutamol was well tolerated but the patient had asthma in 5 min of manipulation of the lupine seeds. In our case, reactivity with other legumes was also demonstrated, but only peanut allergy was relevant because boiled legumes were tolerated. It is also notorious that anamnesis is so important to assess the true etiological agents of asthma.

Moreno C. et al. *Immunotherapy safety: a prospective multi-centric monitoring study of biologically standardized therapeutic vaccines for allergic diseases.* *Clin Exp Allergy.* 2004; 34(4) : 527-31.p **Abstract:** **BACKGROUND:** The fear of side-effects has led to strict regulations preventing a more widespread use of specific immunotherapy (SIT) in some countries, in spite of the low risk of systemic reactions (SRs) reported in well-controlled studies. The goal of the study was to carry out a prospective and multi-centric trial to evaluate the safety, risk factors and compliance degree of commercially available SIT. **MATERIALS AND METHODS:** The study was carried out in 14 allergy departments from Spain. Four-hundred and eighty-eight patients with rhinitis and/or asthma were submitted to treatment with biologically standardized allergen

extracts commercially available. They were administered following the European Academy of Allergy and Clinical Immunology guidelines. **RESULTS:** Four hundred and twenty-three patients (86.7%) completed the treatment and remained under control at the end of the trial. Out of 17,526 administered doses, 17,368 doses (99.1%) were not associated with a reaction. Eighteen patients (3.7%) experienced 53 (0.3% of the doses) SRs. All immediate SRs were mild or moderate and responded well to ordinary treatment measures. There were no fatal reactions, anaphylactic shock or life-threatening reactions. A higher ratio of SRs was found among asthmatic and dust mite allergic patients, although multi-variable logistic analysis did not demonstrate any risk factor associated with SRs. There was also a subgroup of patients at risk for recurrent reactions, and therefore 40% of SRs had been avoided if the maximal number of SRs had been previously limited to only three SRs. **CONCLUSIONS:** This multi-centric study showed that SIT was a safe treatment with a very good compliance. Future guidelines of SIT should limit the maximal number of SRs.

Morgan W.J. et al. *Outcome of asthma and wheezing in the first 6 years of life: follow-up through adolescence.* *Am J Respir Crit Care Med.* 2005; 172(10) : 1253-8.p **Abstract:** **RATIONALE:** The effect of early life wheezing on respiratory function and continued symptoms through adolescence has not been fully described. Using data from a population-based birth cohort in Tucson, Arizona, we previously described four phenotypes based on the occurrence of wheezing lower respiratory illnesses before age 3 yr and active wheeze at age 6 yr: never wheezers (n = 425), transient early wheezers (n = 164), persistent wheezers (n = 113), and late-onset wheezers (n = 124). **OBJECTIVE:** We sought to determine the prognosis for these phenotypes, with reference to lung function and symptoms, through adolescence. **METHODS:** Current wheeze was assessed by questionnaire, lung function was measured by conventional spirometry, and atopy was determined by skin prick tests. **RESULTS:** The prevalence of atopy and wheeze by age 16 yr was similar for never and transient wheezers and for persistent and late-onset wheezers. Both transient early, and persistent wheezers had significantly lower FEF(25-75) (-259 ml/s, p < 0.001, and -260 ml/s, p = 0.001, respectively), FEV1 (-75 ml, p = 0.02, and -87 ml, p = 0.03, respectively), and FEV1:FVC ratio (-1.9%, p = 0.002, and -2.5%, p = 0.001, respectively) through age 16 yr compared with never wheezers. Late-onset wheezers had levels of lung function similar to those of never wheezers through age 16 yr. There was no significant change in lung function among subjects with any of the four phenotypes, relative to their peers, from age 6 to 16 yr. **CONCLUSION:** Patterns of wheezing prevalence and levels of lung function are established by age 6 yr and do not appear to change significantly by age 16 yr in children who start having asthma-like symptoms during the preschool years.

Morgans A. et al. *Barriers to accessing ambulance services in rural Victoria for acute asthma: patients' and medical professionals' perspectives.* *Aust J Rural Health.* 2005; 13(2) : 116-20.p **Abstract:** **OBJECTIVE:** To study the attitudes and perceptions of rural asthma patients and medical health professionals towards accessing ambulance services for acute asthma. **DESIGN:** Health professional and patient based focus groups, audit of ambulance patient care records and self administered survey. **SETTING:** Asthma patients and medical professionals from rural south-western Victoria. **RESULTS:** The audit of patient care records included 69 asthma case records, and identified short response times (mean, 7 min; SD, 5 min), and documented patient improvement in clinical status in response to ambulance treatment. The focus group analysis identified patient perceptions which act as barriers to accessing ambulance services in acute asthma. These included the perception of response time delays, '000' call centre delays and misunderstanding of the role of paramedics, and when it is appropriate to call an ambulance for acute asthma. These perceptions were expressed by both patients and medical professionals, and both groups had poor knowledge of how

and when to access ambulance services for acute asthma. CONCLUSIONS: The misperceptions expressed are of particular concern in a rural population where distance can cause prolonged response times to treatment, and patients who are acutely ill need to contact emergency services promptly and appropriately to improve patient health outcomes.

Mortimer K.M. et al. *Evaluating the use of a portable spirometer in a study of pediatric asthma.* Chest. 2003; 123(6) : 1899-907.p
Abstract: STUDY OBJECTIVES: Laboratory-based spirometry is the "gold standard" for the assessment of lung function, both in clinical and research protocols. These spirometers, however, are neither practical nor affordable for home-based monitoring or studies that collect data in multiple locations. Traditionally, peak flowmeters have been used, but they have important limitations. DESIGN: Based on data from a cohort of 92 children with asthma, we evaluated the agreement between a portable spirometer and an office-based spirometer, using an in-line technique to evaluate measures from the same effort. We compared a range of pulmonary function parameters collected during office-based tests, and also evaluated whether adequate adherence and data quality could be achieved in a home-based study of children with asthma. RESULTS: The agreement between the devices for the actual values of peak expiratory flow, FEV(1), and forced expiratory flow at 25% of FVC was excellent. The portable device was programmed with customized software to grade each curve using revised American Thoracic Society acceptability and reproducibility criteria. For 74% of the curves, quality grade agreed with a grade assigned by physician review of the curve from the office-based spirometer. During 2 weeks of twice-daily monitoring at home, children completed an average of 23 of 28 possible sessions (83%). Of these, 84% had at least two acceptable and two reproducible curves. Although children ≥ 8 years old were not more adherent, they were significantly more likely to achieve acceptable and reproducible curves. CONCLUSIONS: Portable spirometers can provide measurements that are highly comparable to those obtained from "gold standard" laboratory spirometers, and high-quality tracings can be achieved both at home and in the office setting. Visual inspection of the curves by experienced reviewers identified unacceptable curves that were not rejected by the quality control software. Portable spirometers are an important contribution to epidemiologic and clinical studies that require frequent measures of a more broad range of pulmonary function parameters than can be provided by peak flowmeters.

Mortimer K.M. et al. *The effect of air pollution on inner-city children with asthma.* Eur Respir J. 2002; 19(4) : 699-705.p
Abstract: 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.

Mortimer K.M. et al. *An application of model-fitting procedures for marginal structural models.* Am J Epidemiol. 2005; 162(4) : 382-8.p
Abstract: Marginal structural models (MSMs) are being used more frequently to obtain causal effect estimates in observational studies. Although the principal estimator of MSM coefficients has been the inverse probability of treatment weight (IPTW) estimator, there are few published examples that illustrate how to apply IPTW or discuss the impact of model selection on effect estimates. The authors applied IPTW estimation of an MSM to observational data from the Fresno Asthmatic Children's Environment Study (2000-2002) to evaluate the effect of asthma rescue medication use on pulmonary function and compared their results with those obtained through traditional regression methods. Akaike's Information Criterion and cross-validation methods were used to fit the MSM. In this paper, the influence of model selection and evaluation of key assumptions such as the experimental treatment assignment assumption are discussed in detail. Traditional analyses suggested that medication use was not associated with an improvement in pulmonary function--a finding that is counterintuitive and probably due to confounding by symptoms and asthma severity. The final MSM estimated that medication use was causally related to a 7% improvement in pulmonary function. The authors present examples that should encourage investigators who use IPTW estimation to undertake and discuss the impact of model-fitting procedures to justify the choice of the final weights.

Moshhammer H. *Indoor- and outdoor-generated particles and children with asthma.* Environ Health Perspect. 2005; 113(9) : A581; author reply A581.p

Moshhammer H. et al. *Parental smoking and lung function in children: an international study.* Am J Respir Crit Care Med. 2006; 173(11) : 1255-63.p
Abstract: RATIONALE: Both prenatal and postnatal passive smoking have been linked with respiratory symptoms and asthma in childhood. Their differential contributions to lung function growth in the general children's population are less clear. OBJECTIVE: To study the relative impact of pre- and postnatal exposure on respiratory functions of primary school children in a wide range of geographic settings, we analyzed flow and volume data of more than 20,000 children (aged 6-12 yr) from nine countries in Europe and North America. METHODS: Exposure information had been obtained by comparable questionnaires, and spirometry followed a protocol of the American Thoracic Society/European Respiratory Society. Linear and logistic regressions were used, controlling for individual risk factors and study area. Heterogeneity between study-specific results and mean effects were estimated using meta-analytic tools. MAIN RESULTS: Smoking during pregnancy was associated with decreases in lung function parameters between -1% (FEV1) and -6% maximal expiratory flow at 25% of vital capacity left (MEF25). A 4% lower maximal midexpiratory flow (MMEF) corresponded to a 40% increase in the risk of poor lung function (MMEF < 75% of expected). Associations with current passive smoking were weaker though still measurable, with effects ranging from -0.5% (FEV1) to -2% maximal expiratory flow (MEF50). CONCLUSIONS: Considering the high number of children exposed to maternal smoking in utero and the even higher number exposed to passive smoking after birth, this risk factor for reduced lung function growth remains a serious pediatric and public health issue.

Moudiou T. et al. *Growth of asthmatic children before long-term treatment with inhaled corticosteroids.* J Asthma. 2003; 40(6) : 667-71.p
Abstract: The aim of this study was to examine the growth of asthmatic children before any long-term inhaled corticosteroid

treatment. We studied 436 asthmatic children (254 boys and 182 girls), age range 3.9-15.4 years, that had not been treated with long-term inhaled corticosteroids. In each child height and weight were measured, and the height standard deviation score (HSDS) and the weight for height ratio (%WFH) were calculated. We also estimated asthma severity and tested atopic status by skin testing. Children were grouped into three age groups: prepuberty (3.9-7.9 years), peripuberty (8-11.9 years), and puberty (12-15.5 years). HSDS was correlated to asthma severity and duration, atopic status, and other coexisting allergic diseases. Seven hundred ten healthy children (345 boys, 365 girls) ages 4.1-15.5 years were used as controls for height and weight. There was no statistically significant difference in HSDS and %WFH between patients and controls, except for HSDS of pubertal female patients that was significantly less than that of controls, $x: 0.06 (0.80)$ vs. $x: 0.40 (0.90)$, respectively, $p < 0.02$. There was also no significant correlation between HSDS or %WFH and severity or duration of the disease, allergy status and other coexisting allergic diseases. However, there was significant difference in menarcheal age between asthmatic girls $x: 12.49 (0.12)$ and controls $x: 12.00 (0.10)$, $p < 0.001$. In conclusion, our data show that the growth of asthmatic children before any long-term treatment with inhaled corticosteroids is not different from the control population, except for the asthmatic girls of pubertal age who are shorter than control girls probably because of delay in pubertal maturation.

Munoz-Lopez F. *Rhinitis as a precursor for asthma.* Allergol Immunopathol (Madr). 2003; 31(6): 297-302.p

Munzenberger P.J. et al. *Impact of an asthma program on the quality of life of children in an urban setting.* Pharmacotherapy. 2002; 22(8): 1055-62.p **Abstract:** A comprehensive asthma program involving a pharmacist and physician evaluated quality of life (QOL) for children with asthma and the relationship between changes in QOL and traditional outcomes. The program consisted of aggressive medical management and a comprehensive education program. Children were from an inner-city population who had been referred to a specialist. Twenty of the 29 children enrolled in the program were available for 1-year follow-up. Significant improvements were seen in overall QOL scores and in each domain in the instrument, which exceeded the minimal important difference. A strong relationship was not found between changes in QOL total score and changes in asthma questionnaire score, frequency of nocturnal asthma, symptomatic days, and exercise tolerance. Further research is necessary to support these findings.

Murphy J.C. *Telemedicine offers new way to manage asthma.* Am J Health Syst Pharm. 2001; 58(18): 1693, 1696.p

Murphy K.R. et al. *Effects of budesonide inhalation suspension compared with cromolyn sodium nebulizer solution on health status and caregiver quality of life in childhood asthma.* Pediatrics. 2003; 112(3 Pt 1): e212-9.p **Abstract:** **OBJECTIVE:** To compare the effects of 2 nebulizable controller asthma medications on caregiver and pediatric quality of life. **METHODS:** In this 52-week, randomized trial, children aged 2 to 6 years with mild to moderate persistent asthma received budesonide inhalation suspension 0.5 mg (total daily dose) once or twice daily ($n = 168$) or cromolyn sodium nebulizer solution 20 mg 4 times daily ($n = 167$) for 8 weeks, with dosage adjustment thereafter at the investigators' discretion. The Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ), Compliance/Caregiver Satisfaction Questionnaire (CCSQ), Modified Child Health Questionnaire-Parent Form 50 (CHQ-PF50), and Functional Status-II(R) (FS-II[R]) Questionnaire were administered at baseline and weeks 8, 28, and 52. Global assessments of ease of asthma management and child health status were obtained from caregivers and physicians at the end of the study. **RESULTS:** Improvements from baseline in domain-specific

(activities and emotional function) and total PACQLQ scores were greater at each time point (weeks 8, 28, and 52) for caregivers of patients treated with budesonide compared with caregivers of patients receiving cromolyn sodium. Only the budesonide group met the criterion for a clinically important improvement ($>or=0.5$ unit change) in all PACQLQ domains by week 8, which was maintained at weeks 28 and 52. Moreover, improvements surpassed the criterion for moderate clinical importance (1.0 unit change) in all PACQLQ domains for the budesonide group, but this level of improvement was only achieved in the activities domain (at week 28) for the cromolyn sodium group. Based on the CCSQ, budesonide resulted in greater caregiver satisfaction, treatment convenience, ease of use, and compliance compared with cromolyn sodium. Thus, 90.7% of caregivers in the budesonide group were "completely or very satisfied" compared with 53.4% in the cromolyn sodium group. Over half (54.6%) of caregivers in the budesonide group rated budesonide "highly or very convenient" compared with 23% for cromolyn sodium; 77% rated budesonide "extremely or very easy" to use compared with 47% for cromolyn. Adherence with daily medication regimens was reported for 76% of children in the budesonide group compared with 57% in the cromolyn sodium group. Child health status, as indicated by mean FS-II(R) scores, showed improvements from baseline in both groups at weeks 8, 28, and 52. There was a trend for these improvements to be superior in the budesonide group. Additionally, budesonide was superior to cromolyn sodium in caregiver and physician global assessments. At the end of the study, 76% of caregivers of children receiving budesonide reported asthma management to be "a great deal easier" compared with the start of the study, and 74% rated the overall health status of their child as "much better now than 1 year ago." In contrast, only 29% and 37% of caregivers whose children received cromolyn sodium provided these respective ratings. **CONCLUSIONS:** Budesonide inhalation suspension improved the quality of life for caregivers of children with asthma. Caregivers of children treated with budesonide had significantly fewer limitations in daily activities and emotional functioning compared with caregivers of children treated with cromolyn sodium nebulizer solution. The improvements in caregiver quality of life occurred earlier with budesonide compared with cromolyn sodium. Only caregivers in the budesonide group had a clinically important mean change from baseline in all PACQLQ domains by week 8. These benefits were maintained at week 52. Children treated with budesonide inhalation suspension and cromolyn sodium experienced improvements in health status, assessed using the FS-II(R). The greatest differences between treatments were seen in the disease-specific portion of the FS-II(R), which relates impairments in functional status to the child's illness. Caregiver and physician global assessment indicated significantly better overall child health after 1 year of treatment with budesonide, supporting an improvement in health status. Clinical trials in children 4 to 16 years of age with asthma have demonstrated greater effectiveness of inhaled corticosteroids versus cromolyn sodium on several clinical measures of efficacy. Measures of asthma control in this study, reported in detail elsewhere [Leflein et al. Pediatrics 2002;109:866-872], also have shown greater improvements with budesonide therapy. Treatment with budesonide inhalation suspension resulted in a significantly lower mean rate of asthma exacerbations, significantly longer times to first asthma exacerbation, significantly longer times to first additional use of chronic asthma therapy, and significant improvements in asthma symptom scores and breakthrough medication use compared with cromolyn sodium therapy. Additionally, children receiving budesonide inhalation suspension experienced more symptom-free days and episode-free days compared with children receiving cromolyn sodium. Safety profiles were similar between the 2 treatment groups. Budesonide inhalation suspension was associated with significantly greater caregiver satisfaction, convenience, ease of use, and compliance compared with cromolyn sodium nebulizer solution. This greater caregiver satisfaction and quality of life may be related to the greater asthma control achieved in children treated with budesonide therapy compared with cromolyn sodium. In addition, the convenience of once- or twice-daily dosing with budesonide inhalation suspension, compared with 3- or 4-times-daily dosing of cromolyn sodium, may

decrease caregiver burden and enhance the willingness of caregivers to adhere to treatment regimens prescribed for their young children with asthma. This effect on caregiver adherence could further improve treatment effectiveness. This is the first clinical trial comparing the effects of a nebulized corticosteroid with that of an alternative nebulized therapy on quality of life in young children with asthma and their families. Compared with nebulized cromolyn sodium, budesonide inhalation suspension not only provides better overall child health status and asthma management, but greater caregiver quality of life and greater caregiver satisfaction, convenience, ease of use, and compliance.

Murray E. *Breastfeeding, atopy, and asthma.* Lancet. 2003; 361(9352) : 174; author reply 175-6.p

Musken H. et al. *In vivo and in vitro sensitization to domestic mites in German urban and rural allergic patients.* J Investig Allergol Clin Immunol. 2002; 12(3) : 177-81.p **Abstract:** Sensitization to domestic mites is common in Germany. The main objectives of this study were (1) to establish the rate of skin test sensitivity to Dermatophagoides pteronyssinus, Acarus siro, Lepidoglyphus destructor, and Tyrophagus putrescentiae in 512 consecutive patients evaluated for upper and/or lower respiratory complaints; (2) to verify how many of the patients with a positive skin test to at least one of the three storage mites were also skin test positive to D. pteronyssinus; and (3) to verify how many of the patients with at least one positive skin test to one of the storage mites previously mentioned were also sensitized, in vitro, to other mite species. A total of 512 consecutive patients with rhinitis and/or asthma, living in urban or rural areas of central Germany were skin tested with extracts of D. pteronyssinus, A. siro, L. destructor, and T. putrescentiae. In addition, specific IgE determinations to Euroglyphus maynei, Blomia tropicalis, Blomia tjobodas, Blomia kulagini, and Gohieria fusca were conducted in those individuals with a positive skin test to at least one of the storage mites used in skin testing. Of the 512 patients, 103 (20.1%; 77 urban dwellers and 26 farmers) reacted to at least one of the storage mites. From this latter group, 88 individuals (85.4%) also skin tested positive to D. pteronyssinus. In vitro specific IgE determinations revealed a high rate of sensitization to the other mite species studied. We conclude that sensitization to storage mites in Germany is frequently associated with sensitivity to D. pteronyssinus. Overall, skin test sensitivity to storage mites was greater in rural than in city dwellers. In vitro sensitization to B. tjobodas was also significantly greater in rural than in city dwellers.

Musken H. et al. *Sensitization to different mite species in German farmers: clinical aspects.* J Investig Allergol Clin Immunol. 2000; 10(6) : 346-51.p **Abstract:** Various mite species referred to collectively as house dust and storage mites are recognized worldwide as a cause of allergic airway disease. Our study aimed to investigate the frequency of sensitization and potential importance of mite species in farmers using a broad mite spectrum. A total of 86 German farmers with rhinitis and/or asthma were studied by skin prick testing and/or enzyme allergosorbent test (EAST) with the following mites: Blomia tjobodas, Blomia tropicalis, Blomia kulagini, Glycyphagus domesticus, Thyreophagus entomophagus, Euroglyphus maynei, Chortoglyphus arcuatus, Dermatophagoides pteronyssinus, Dermatophagoides farinae, Acarus siro, Lepidoglyphus destructor, Tyrophagus putrescentiae, Acarus farris and Cheyletus eruditus. Sensitization to at least one mite species was detected in 51 patients (59%) by skin prick testing, and in 31 patients (36%) by EAST. The most frequent sensitizations determined by skin tests were found for the three Blomia species, E. maynei and G. domesticus. Twelve patients (14%) gave a positive EAST with the predator mite C. eruditus. A total of 22 patients gave positive EAST results with the Dermatophagoides species. We were able to document sensitization to C. arcuatus, E. maynei and T. entomophagus for the first time in Germany. A considerable

proportion of the German farmers tested were sensitized to storage mites. The allergological potential of various mite species has been recognized, some for the first time. It was concluded that B. tjobodas, G. domesticus, C. arcuatus and C. eruditus in particular should be included in an allergy diagnosis. Further investigations into the clinical relevance of the sensitizations and possible cross-reactivity between the mite species are necessary.

Musken H. et al. *Sensitization to different mite species in German farmers: in vitro analyses.* J Investig Allergol Clin Immunol. 2003; 13(1) : 26-35.p **Abstract:** Allergic airway diseases are often caused by house dust mites (HDM) and storage mites (SM), respectively, and we were recently able to demonstrate that symptomatic German farmers are frequently sensitized to different mite species. The present study aimed to obtain information on the protein and immunobiochemical characteristics of the extracts of the following mites: Dermatophagoides pteronyssinus, Dermatophagoides farinae, Acarus siro, Acarus farris, Lepidoglyphus destructor, Tyrophagus putrescentiae, Blomia tjobodas, Blomia tropicalis, Blomia kulagini, Glycyphagus domesticus, Thyreophagus entomophagus, and Cheyletus eruditus. Specific IgE determinations were performed with EAST. The protein patterns of the mite extracts were studied by SDS-PAGE estimating the weighted-average molecular weights of the proteins. Using the Western blot technique, we determined the allergen pattern in several mite extracts. The allergens in each extract were classified in terms of the frequency of sensitization as major, intermediate, and minor allergens using allergograms. As already reported, a positive EAST to at least one mite was measured in 31/86 patients, and most sera were positive with several mite species. The majority of the mite extracts exhibited a very complex protein pattern according to SDS-PAGE. An allergen was found in Western blots of nearly all species equivalent to a molecular weight of 14 to 15 kD. This was, in our opinion, the first time that this particular allergen was detected in Blomia tjobodas and Glycyphagus domesticus. In conclusion, using EAST we were able to show that 36% of the German farmers tested were sensitized to SM. All mite extracts showed a complex protein pattern in the molecular weight range -95 kD to -10 kD. A common allergen band in the region of -14 to -15 kD was found in the majority of the mites studied, and it can be assumed that this corresponds with the group 2 allergen.

Mutti A. et al. *Reporting data on exhaled breath condensate.* Am J Respir Crit Care Med. 2003; 168(6) : 719; author reply 719.p

Myers S.N. et al. *Lead poisoning and asthma: an examination of comorbidity.* Arch Pediatr Adolesc Med. 2002; 156(9) : 863-6.p **Abstract:** OBJECTIVES: To determine the comorbidity of lead poisoning and asthma in urban children, and to examine associated clinical factors. METHODS: One-hundred-one patients at an inner-city clinic with blood lead levels (BLLs) of 25 microg/dL or higher (> or =1.2 micromol/L) (BLL25 group) were randomly selected from a tracking lead database and matched on age, sex, and primary language to 101 randomly selected patients with a first BLL recorded in the database of lower than 5 microg/dL (<0.2 micromol/L) (BLL5 group) and no subsequent BLLs of 10 microg/dL or higher (> or =0.5 micromol/L). Medical records were reviewed to determine diagnosis or symptoms of asthma or wheezing at any visit, immunization status, and number of visits. Analyses for matched pairs were conducted. RESULTS: The BLL25 and BLL5 groups did not differ on age at diagnostic BLL (26.6 months vs 24.2 months), sex (54% male), or language (12% Spanish). The BLL25 and BLL5 groups had a similar number of subjects with a diagnosis of asthma (6% vs 11%; odds ratio, 0.5; 95% confidence interval, 0.2-1.6); 26% of BLL25 and 34% of BLL5 subjects had either a diagnosis or symptoms of asthma or wheezing (odds ratio, 0.7; 95% confidence interval, 0.4-1.3). Subjects with BLL25 were more likely to have delayed immunization and a first clinic visit when older than subjects with BLL5. CONCLUSIONS: There was no increased likelihood of asthma diagnosis or symptoms among young children with lead

poisoning. Children with lead poisoning also had delayed medical care. These data may help guide interventions aimed at preventing or reducing the impact of lead poisoning and asthma.

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Naberan Tona K. et al. *[Mortality due to asthma in the city of Barcelona (1983-1993)]*. Aten Primaria. 2004; 33(1) : 13-9.p Abstract: OBJECTIVE: To find asthma mortality in the city of Barcelona. DESIGN: Descriptive study of mortality. SETTING: City of Barcelona. MAIN MEASUREMENTS: Deaths due to asthma in the city of Barcelona in the period 1983-1993 were studied through the register of mortality at Barcelona's Municipal Institute of Health, which in turn is supplied by the Statistical Gazette of Deaths. Rates of mortality per 100,000 inhabitants were calculated, overall and broken down by sex and by age. The ratio of mortality comparing city districts and the place and season of decease was also worked out. RESULTS: There were 716 deaths due to asthma (overall rate of 3.82/100,000 inhabitants; 3.3 in men and 4.33 in women). Almost two-thirds of deaths occurred in people over 65. Mortality was stable in the entire period except in the over-65s, in which a downwards trend was discerned ($\beta = -0.63$; $P = 0.037$). For the 5-34 year old group, the rate oscillated between 0.1 and 0.6/100,000 inhabitants. The number of deaths in the over-65s was greater in winter (31.7%; 95% CI, 27.8-35.7). 56.2% of deaths occurred at home. Hospital deaths were more common among women ($P < .001$) and the under-65s, and their trend is upwards ($P = .004$). CONCLUSIONS: Asthma mortality in the city of Barcelona was stable during the period studied. Its rate for the 5-34 year-old age group was higher than for Spain and slightly greater than in similar nearby countries.

Nafstad P. et al. *Day care center characteristics and children's respiratory health*. Indoor Air. 2005; 15(2) : 69-75.p Abstract: Day care centers provide an important exposure arena with potential harmful health effects for children. This study has linked health effect data from a survey among 942 3-5-year-old Oslo children with information on day care center characteristics collected during inspection of the 175 day care centers these children attended. The aim of the study was to estimate associations between dampness problems and other building characteristics and several respiratory health outcomes. Dampness problems (sign of molds, water leakage, damage to floor/wall) were observed in 51% of the day care centers. In multiple logistic regression analyses none of the studied symptoms and diseases (nightly cough, blocked or runny nose without common cold, wheeze, heavy breathing or chest tightness, the common cold, tonsillitis/pharyngitis, otitis media, bronchitis, pneumonia, asthma, and allergic rhinitis) were systematically associated with dampness problems or type of ventilation in day care centers. None of the studied indicators of day care center exposures were found to have a clear effect on day care children's respiratory health. Even so this study does not rule out negative health effects of day care center exposures. The study demonstrates that population-based studies of these relations are demanding with regard to assessment of exposure and health outcomes. PRACTICAL IMPLICATIONS: Simple and easy-to-register indicators of exposures like dampness problems and type of ventilation assessed in 175 day care centers were not related to respiratory health among 3-5-year-old Norwegian children attending the day care centers. The study does not rule out negative health effects of day care center exposures, but demonstrates methodological challenges needed to be addressed in studies of health effects of the day care environment.

Nafstad P. et al. *The use of a feather quilt, childhood asthma and allergic rhinitis: a prospective cohort study*. Clin Exp Allergy. 2002; 32(8) : 1150-4.p Abstract: BACKGROUND: Feather bedding has long

been considered as a potential source of allergen exposure and thus a potential risk factor for allergic diseases. However, recent cross-sectional studies have reported a higher risk of allergic diseases among users of synthetic bedding compared with feather-bedding users. OBJECTIVE: To explore associations between early life exposure to feather bedding and the risk of developing asthma allergic rhinitis in childhood. METHODS: We assessed the association between early life exposure to feather quilts and the risk of bronchial obstruction during the first 2 years of life and asthma and allergic rhinitis in a prospective 4-year cohort study of 2531 Norwegian children. RESULTS: At the age of 6 months, 24% of the children had a quilt with feathers, decreasing to 20% at the age of 2 years. The adjusted odds ratio for bronchial obstruction 0 to 2 years by exposure to a feather quilt at the age of 6 months was 0.59, 95% confidence interval 0.41 to 0.86, for asthma at the age of 4 years 0.38, 0.23 to 0.64 and for allergic rhinitis at the age of 4 years 0.73, 0.43 to 1.18. CONCLUSION: The use of a feather quilt in early life does not seem to increase the risk of asthma and allergic rhinitis later in childhood.

Nagayama Y. et al. *Analysis of sputum taken from wheezy and asthmatic infants and children, with special reference to respiratory infections*. Pediatr Allergy Immunol. 2001; 12(6) : 318-26.p Abstract: Children who are destined to develop asthma are considered to be susceptible to a variety of respiratory pathogens. To elucidate respiratory inflammation among these children, we measured the levels of eosinophil cationic protein (ECP) and tryptase in sputum taken from three different groups of wheezy infants and young children: those with a first wheeze ($n = 15$); those with recurrent wheeze ($n = 27$); and those with recurrent wheeze with respiratory distress, namely asthma ($n = 56$). The numbers of eosinophils or metachromatic cells determined by microscopic analysis of sputum samples were also evaluated in combination with the ECP and tryptase levels. Although neither sputum ECP nor tryptase was a clear discriminative marker that differentiated the three different types of wheezy disease, ECP levels in sputum from the asthma group were significantly higher (2,269.2 \pm 6,216.8 ng/g) than those in the recurrent wheezy group (440.3 \pm 1,199.8 ng/g) or in the first-wheeze group (209.0 \pm 172.9 ng/g). A similar trend was observed with tryptase levels in sputum, but there were no significant differences among the three groups. Sputum taken from asthmatic children showed a marked accumulation of eosinophils. However, an accumulation of eosinophils in sputum (even in the presence of an elevated level of sputum ECP) was not identified in the asthmatic infants < 1 year of age. An accumulation of eosinophils in sputum was not evident until children became > 1 year old and thereafter the eosinophils rapidly increased in number until the children reached 5 years of age. It was noteworthy that sputa positive for pathogenic bacteria, taken from the 1- and 2-year-old asthmatic infants, had a tendency to show high levels of ECP but a reduced number of eosinophils. Along with the wheezy episodes induced by viral infection, primarily and occasionally in combination with secondary bacterial infection, eosinophil activation and infiltration may develop. These predestined immune reactions to various pathogens might be associated with triggering the onset of asthma.

Nagy A. et al. *No association between asthma or allergy and the CCR5Delta 32 mutation*. Arch Dis Child. 2002; 86(6) : 426.p Abstract: AIMS: To investigate whether the presence of the CCR5Delta32 allele was associated with atopy or asthma. METHODS: A total of 118 children with asthma, 145 children with non-asthmatic, but allergic phenotype, and 303 children without allergic or asthmatic disorders were studied. RESULTS: There were no significant differences in the frequency of CCR5Delta32, or in the distributions of genotypes between the groups. The relative eosinophil blood count was slightly lower in patients with heterozygous genotype, than in patients with wild type genotype. CONCLUSION: No association was found between the

susceptibility of allergy or asthma and the functional deficient CCR5Delta32 allele.

Nair S.J. et al. *The influence of pulmonary function testing on the management of asthma in children.* J Pediatr. 2005; 147(6) : 797-801.p **Abstract:** OBJECTIVE: To assess how often in a single encounter that pulmonary function tests (PFTs) influenced management decisions in children with asthma, beyond what was obtained from history and physical examination alone. STUDY DESIGN: Children with asthma (n = 367, age 4 to 18 years) performed spirometry before clinical evaluation. Physicians and nurse practitioners in the outpatient pulmonary office evaluated the children and made initial treatment recommendations before reviewing the spirometry results. Any changes based on the test results were documented. RESULTS: Spirometry was abnormal in 45% of the visits, related to underlying asthma severity but not to clinical findings. PFT results changed management decisions in 15% of visits. This frequency was not affected by the patient's age, disease severity, symptom control, or exam findings. When spirometry did not change treatment decisions, the provider was more likely to maintain therapy (58%) than to increase (17%) or decrease (24%) therapy. In contrast, when spirometry did change treatment decisions, the provider was more likely to increase therapy (75%) than to maintain (20%) or decrease (5%) therapy. CONCLUSION: Without PFTs, providers often overestimated the degree of asthma control. This incorrect assessment could have resulted in suboptimal therapy.

Najafi N. et al. *Differential cytology of bronchoalveolar lavage fluid in asthmatic children.* Pediatr Pulmonol. 2003; 35(4) : 302-8.p **Abstract:** Although asthma usually begins in childhood, limited information is available as to the inflammatory reaction of asthmatic children compared to adults and the influence of age. We investigated the cytology of bronchoalveolar lavage fluid (BALF) in 39 newly diagnosed wheezy children (minimum of 3 wheezing episodes during last 6 months): 21 allergic and 18 nonallergic subjects. None had received antiinflammatory treatment. Bronchoalveolar lavage (BAL) was performed, instilling 0.5 ml.kg(-1) body weight of warmed saline in 4 successive fractions. The first 2 aliquots (BALF 1) were pooled for microbiology and cytology, and the last 2 (BALF 2) for cytology only. Recovery correlated inversely with age, the most significant being for BALF 2 (r = -0.52, P = 0.001). Children under 2 years of age had larger amounts of ciliated columnar and goblet cells (P = 0.0074). Other cell types did not show age dependency. Differential cytology was characterized by a high number of creola bodies, bronchial epithelial cells (M = 68 x 10(3).ml(-1), R = 5-349), and neutrophils (M = 92 x 10(3).ml(-1), R = 0-1,257). Eosinophils were the only cells distinguishing allergic from nonallergic subjects (P = 0.003). The 16 children with positive microbiology had more neutrophils than the noninfected (P = 0.008), the latter still having more neutrophils than found in adults. These data suggest a limited age dependency in BALF cytology. Differential cytology in BALF might be helpful in differentiating asthma in children. Neutrophil inflammation might be more important than in adults.

Najam F.I. et al. *Complement components (C3, C4) in childhood asthma.* Indian J Pediatr. 2005; 72(9) : 745-9.p **Abstract:** OBJECTIVE: To assess the involvement of complements (C3, C4) in the pathophysiology of bronchial asthma. METHODS: Selection of patients (n = 64) were made according to the recommended international criteria for diagnosis and classification of asthma. Serum levels of complement components (C3, C4) were measured by radial immunodiffusion technique in 64 Libyan children (age: 1-12 years, sex: 39 males, 25 females) with mild to moderately severe asthma (Group A). Among these patients, 35 had active disease (AA) and 29 had inactive disease (NA). According to age range, 20, 21 and 23 patients were between 1-3 years (A1), > 3-5 years (A2) and > 5-12 years (A3) respectively. A1 had 9 and 11 patients with active

(AA1) and inactive (NA1) disease; A2 had 10 and 11 patients with active (AA2) and inactive (NA2) disease; A3 had 16 and 7 patients with active (AA3) and inactive (NA3) disease respectively. Age matched comparisons were made with 57 healthy children (age: 1-12 years; sex: 30 males, 27 females) (Group B). Among the controls, 15, 19 and 23 children were between 1-3 years (B1), > 3-5 years (B2) and > 5-12 years (B3) respectively. RESULTS: Mean C3 level was significantly elevated in patients, while C4 level was normal (A vs B --> C3: P < 0.2, C4: P > 0.2). Serum C3 level was significantly higher in patients with active disease only, while it was normal in patients with inactive disease (AA, NA, B --> P = 0.045); AA vs NA --> P < 0.05, AA vs B --> P < 0.02, NA vs B --> P > 0.05) and C4 levels were normal in both the groups (AA, NA, B --> P = 0.354). Further, C3 levels were significantly elevated in all the age groups, but in patients with active disease only (AA1, NA1, B1 --> P = 0.0024; AA2, NA2, B2 --> P = 0.0411; AA3, NA3, B3 --> P = 0.0102). CONCLUSION: The elevated C3 level was possibly due to induction by pro-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-alpha) and interleukin-1 (IL-1). The probable mechanisms of C3 involvement in the pathophysiology of bronchial asthma were discussed.

Nakade S. et al. *Population pharmacokinetics of pranlukast hydrate dry syrup in children with allergic rhinitis and bronchial asthma.* Drug Metab Pharmacokinet. 2006; 21(2) : 133-9.p **Abstract:** This study aimed to assess the steady-state pharmacokinetics of pranlukast, a leukotriene receptor antagonist, in children with allergic rhinitis and bronchial asthma, and to clarify factors affecting apparent clearance (CL/F). A total of 192 plasma samples were obtained from 98 children (rhinitis 64, asthma 13, complications 21), aged 3-14 years in 2 clinical trials. Plasma concentration of pranlukast was determined by liquid chromatography connected with a tandem mass spectrometer and analyzed by a population approach using NONMEM program. The plasma concentration-time course of pranlukast was described by using a one-compartment model with the first-order absorption and lag time. The robustness of the population pharmacokinetic model was evaluated by using 200 bootstrap samples. The results of population pharmacokinetic analysis showed that only age was a factor affecting the CL/F per body weight, with CL/F decreasing with increasing age. No significant variation was seen in the CL/F between rhinitis and asthma. The interindividual variability in the CL/F and the residual variability were 19.7% and 48.4%, respectively. All the parameters fell within 10% of the bootstrapped mean. In conclusion, the results show that age is the most influential factor for explaining interindividual variability in CL/F, and the difference in diseases does not affect CL/F.

Nakashima K. et al. *An association study of asthma and related phenotypes with polymorphisms in negative regulator molecules of the TLR signaling pathway.* J Hum Genet. 2006; 51(4) : 284-91.p **Abstract:** Although associations between endotoxin exposure or respiratory infection and asthma have been recognized, the genetic effects in these conditions are unclear. Toll-like receptors (TLRs) play an essential role in innate host defense and in the control of adaptive immune responses. IL-1R-associated kinase-M (IRAK-M) and single immunoglobulin IL-1R-related molecule (SIGIRR) negatively regulate TLR-signaling pathways. To investigate whether polymorphisms in these genes were associated with asthma or asthma-related phenotypes, we screened these genes for polymorphisms by direct sequencing of 24 asthmatics and identified 19 variants in IRAK-M and 12 variants in SIGIRR. We next conducted linkage disequilibrium mapping of the genes, and examined the association of polymorphisms and haplotypes using 391 child patients with asthma, 462 adult patients with asthma, and 639 controls. None of the alleles or haplotypes of IRAK-M and SIGIRR were associated with asthma susceptibility or asthma-related phenotype. Our results indicate that polymorphisms in IRAK-M and

SIGIRR are not likely to be associated with the development of asthma in the Japanese population.

Nambu M. et al. *Rice allergy*. *Pediatrics*. 2006; 117(6) : 2331-2.p

Nandi-Lozano E. et al. [*Acute respiratory infections in children attending a child day care center*]. *Salud Publica Mex.* 2002; 44(3) : 201-6.p
Abstract: **OBJECTIVE:** To assess the incidence of acute respiratory infections and bacterial colonization in children attending a daycare center. **MATERIAL AND METHODS:** A cohort study was conducted from April to October 1999, among 85 children aged under four years, who attended the daycare center at Hospital Infantil de Mexico (Mexico City's Children's Hospital) "Federico Gomez". Acute respiratory infection incidence rates and quarterly point prevalence figures of nasopharyngeal colonization were obtained. Data were analyzed using descriptive statistics. **RESULTS:** A total of 85 children were studied (40 girls and 45 boys) during 9,090 children-days of follow-up. Three children had a history of atopia (3.5%), six a history of asthma (7%), and 39 (46%) were exposed to passive smoking. There were 258 events of respiratory tract infection for an incidence rate of 10.3 infections per person-year (95% CI 8.7-12.0). The main clinical syndromes were pharyngitis (95%), acute otitis media (3.5%), and bronchiolitis (1%). The incidence rates of otitis and bronchiolitis were 0.36 and 0.12 per child-year of observation, respectively. The prevalence figures of nasopharyngeal colonization for the three main bacteria were: *S. pneumoniae* 20.4%; nontypable *H. influenzae* 13%; and *Moraxella catarrhalis* 8%. **CONCLUSIONS:** Study results show a high prevalence of colonization due to invasive strains, as well as a two-fold incidence rate of acute respiratory infection, higher than those reported in community surveys. These results add to the description of this poorly documented infectious disease in Mexico. The English version of this paper is available at: <http://www.insp.mx/salud/index.html>.

Narang I. et al. *Nitric oxide in chronic airway inflammation in children: diagnostic use and pathophysiological significance*. *Thorax*. 2002; 57(7) : 586-9.p
Abstract: **BACKGROUND:** The levels of exhaled and nasal nitric oxide (eNO and nNO) in groups of patients with inflammatory lung diseases are well documented but the diagnostic use of these measurements in an individual is unknown. **METHODS:** The levels of nNO and eNO were compared in 31 children with primary ciliary dyskinesia (PCD), 21 with non-CF bronchiectasis (Bx), 17 with cystic fibrosis (CF), 35 with asthma (A), and 53 healthy controls (C) using a chemiluminescence NO analyser. A diagnostic receiver-operator characteristic (ROC) curve for PCD using NO was constructed. **RESULTS:** The median (range) levels of nNO in parts per billion (ppb) in PCD, Bx, CF, and C were 60.3 (3.3-920), 533.6 (80-2053), 491.3 (31-1140), and 716 (398-1437), respectively; nNO levels were significantly lower in PCD than in all other groups ($p < 0.05$). The median (range) levels of eNO in ppb in PCD, Bx, CF, A, and C were 2.0 (0.2-5.2), 5.4 (1.0-22.1), 2.6 (0.8-12.9), 10.7 (1.6-46.7), and 4.85 (2.5-18.3), respectively. The difference in eNO levels in PCD reached significance ($p < 0.05$) when compared with those in Bx, A and C but not when compared with CF. Using the ROC curve, nNO of 250 ppb showed a sensitivity of 97% and a specificity of 90% for the diagnosis of PCD. **CONCLUSIONS:** eNO and nNO cannot be used diagnostically to distinguish between most respiratory diseases. However, nNO in particular is a quick and useful diagnostic marker which may be used to screen patients with a clinical suspicion of PCD.

Narayanan S. et al. *Asthma control and patient satisfaction among early pediatric users of montelukast*. *J Asthma*. 2002; 39(8) : 757-65.p
Abstract: **OBJECTIVE:** To assess asthma control and patient satisfaction among pediatric users of montelukast in a clinical practice setting. **STUDY DESIGN:** A prospective study of 175

children with persistent asthma, 6 to 14 years of age, who initiated treatment with montelukast between Feb-1998 and Aug-1998, in primary care and pediatric offices across the United States. Data on asthma control and satisfaction with treatment was collected in physicians' offices after enrollment and by survey to the patients' homes at 1 month of treatment. **RESULTS:** Across the study population, improvements in mean scores for asthma control and parent satisfaction were observed at the 1-month follow-up compared with baseline. At 1 month, 57.7% of patients had none or four issues indicative of poor asthma control, compared with 19.4% at baseline. Similarly, after 1 month of treatment with montelukast, 2.7 times as many parents reported being very satisfied with asthma therapy (using montelukast) compared with the previous controller therapy regimen at baseline. During the 1-month follow-up period, montelukast was used as the only controller medication by 18.3% of patients, and in combination with another controller medication by 81.7%. **CONCLUSIONS:** Observations from this study over one month suggest that a significant percentage of pediatric patients successfully managed their asthma with montelukast and their parents were satisfied with their medication, compared to baseline.

Narhi U. et al. *Do asthma patients receive sufficient information to monitor their disease--a nationwide survey in Finland*. *Pharm World Sci*. 2001; 23(6) : 242-5.p
Abstract: **OBJECTIVES:** The aim of this study was to assess to what extent the principles of asthma monitoring are implemented among Finnish asthma patients and if the patients have received sufficient information to adjust their medication according to asthma symptoms. **SETTING:** All Finnish asthma patients receiving asthma medication from Finnish community pharmacies during two days in June 1998. **MAIN OUTCOME MEASURES:** The proportions of asthma patients who monitor their asthma status according to the national guidelines and have received specific instructions on how and when to adjust their asthma medication. **RESULTS:** Eighty-six per cent of the respondents (86%) monitored their asthma status on a method recommended by the national guidelines. They made Peak Expiratory Flow (PEF) measurements (39% of the respondents), they monitored their symptoms (34%) or both (13%). A smaller proportion of the respondents (58%) were instructed on adjusting their medication according to symptoms. The lowest rates for monitoring the asthma status was found among the elderly (65 years or more) and among those who reported that they had been on medication for longer than 5 years (17% and 13% of the subgroup populations, respectively). The lowest rates for having received specific instructions on adjusting their asthma medication according to symptoms were found among the elderly (36%), among those who reported that they had been on asthma medication less than one year (44%), and among males (54%). **CONCLUSIONS:** Pharmacists and other health care professionals need to enhance their education activities and their co-operation in training asthma patients to monitor their disease, especially principles of adjusting medication according to symptoms. In this process, especially the training needs of the elderly patients and those who have been using asthma medicines for a long time need to be taken into account.

Nascimento Silva M.T. et al. [*Asthma and ascariasis in children aged two to ten living in a low income suburb*]. *J Pediatr (Rio J)*. 2003; 79(3) : 227-32.p
Abstract: **OBJECTIVE:** To assess the relation between children with asthma and ascariasis in the low income neighborhood of Pedregal, in Campina Grande (Paraiba, Brazil). **MATERIAL AND METHOD:** The International Study of Asthma and Allergies in Childhood (ISSAC) standard questionnaire was distributed to 1,095 children but only 742 of them answered it and provided stool samples for parasite examination. The cross-sectional study included those 742 children, whose age ranged from 2 to 10 years. The association between asthma and ascariasis was studied through Kappa rating. Demographic and clinic variants comparing the two groups were analyzed by chi-square test (χ^2) or t Student test. **RESULTS:** Among the 742 children analyzed, 51.9% (385) were

males and 48.1% (357) females. The prevalence of asthma was 59.7% (443) and that of ascariasis was 56.3% (418). The frequency of asthma in the ascariasis group (60.5%) was similar ($\chi^2(2) = 0.27$, $p > 0.06$) to the frequency of asthma in the non-infected group (58.6%). **CONCLUSION:** Despite the high prevalence of the diseases studied, there is no apparent relation between asthma and ascariasis in the population studied.

Naumann P.L. et al. *A+ Asthma Rural Partnership coloring for health: an innovative rural asthma teaching strategy.* *Pediatr Nurs.* 2004; 30(6) : 490-4.p **Abstract:** Asthma is the leading chronic illness in children, affecting about 4.8 million children in the United States. Recent reports indicate a lack of asthma educational resources for rural school health nurses to use in their practice. This article describes the development of the My Asthma Coloring Book educational tool for children and their families living in rural communities. My Asthma Coloring Book was developed to provide asthma information in a short-story format for children with asthma. The coloring book content is described, including its utilization as part of the A+ Asthma Rural Partnership research project funded by the National Institute of Nursing Research (R01NR05062-01).

Navaie-Waliser M. et al. *Evaluating the needs of children with asthma in home care: the vital role of nurses as caregivers and educators.* *Public Health Nurs.* 2004; 21(4) : 306-15.p **Abstract:** To date, few evaluations have examined issues specific to children's asthma management in their homes. This study examined the characteristics, risk factors, and needs of children with asthma, and the impact of home health nurses on improving parents'/family caregivers' knowledge about asthma triggers and management. The medical records of children, ≤ 19 years, residing in New York City, who were admitted to home care with asthma in 1999 ($n = 1,007$) were reviewed retrospectively to collect a wide range of data. The majority of children with asthma in home care were ≤ 5 years, male, racial/ethnic minorities, and hospital referred. Approximately one in four children with asthma suffered from additional comorbidities. Home environmental triggers included dust/dust mites, animal dander, mold, perfumes/detergents, and cigarette smoke. Notable psychosocial triggers were family tensions, physical activity, anxiety/stress, and friends/peer pressure. Most parents/family caregivers had inadequate knowledge about recognition of asthma attacks and its triggers and management. Discharge assessments suggested that home health nurses can help improve caregivers' knowledge about asthma management. Children with asthma in home care have diverse needs, receive few nurse home visits, and have parents/family caregivers in need of more intensive education on asthma symptom recognition and management.

Nayak A. et al. *Efficacy and safety of beclomethasone dipropionate extrafine aerosol in childhood asthma: a 12-week, randomized, double-blind, placebo-controlled study.* *Chest.* 2002; 122(6) : 1956-65.p **Abstract:** **BACKGROUND:** Beclomethasone dipropionate (BDP) has been formulated as an extrafine aerosol (hydrofluoroalkane-134a [HFA]-BDP) [QVAR; 3M Pharmaceuticals; St Paul, MN], which gives improved lung deposition compared with chlorofluorocarbon (CFC)-BDP. The clinical efficacy of HFA-BDP has been established in adult asthma at a required dose below that of CFC-BDP, but has not been evaluated in children. **OBJECTIVE:** To examine the efficacy and safety of HFA-BDP in childhood asthma. **DESIGN:** A 12-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study involving 353 children aged 5 to 12 years with moderate, symptomatic asthma. After a 2-week run-in period, patients were randomized to HFA-BDP, 80 micro g/d ($n = 120$); HFA-BDP, 160 micro g/d ($n = 117$); or HFA-placebo ($n = 116$) administered twice daily. **SETTING:** Hospital outpatient. **RESULTS:** HFA-BDP, 80 micro g/d and 160 micro g/d, produced a significant, dose-related increase from baseline in FEV(1) percent predicted compared with

placebo. At week 12, mean changes from baseline in FEV(1) percent predicted were 9.2% ($p < \text{or} = 0.01$ vs placebo), 10% ($p < \text{or} = 0.01$ vs placebo), and 3.9% for the HFA-BDP 80 micro g/d, HFA-BDP 160 micro g/d, and placebo groups, respectively. There was also a significant decrease in daily beta-agonist use, improvement in peak expiratory flow, and increase [correction] in the percentage of days free from asthma symptoms ($p < \text{or} = 0.05$ for HFA-BDP, 160 micro g/d, vs placebo at weeks 11 to 12). HFA-BDP was well tolerated, with no significant differences in the incidence or nature of adverse events between HFA-BDP and placebo groups. Neither were there significant differences between groups in mean percentage change from baseline in the morning plasma cortisol level at week 12 or in the percentage of patients with morning plasma cortisol levels below the reference range at baseline and week 12. In a subgroup tested, the percentage of patients with an abnormal response to low-dose adrenocorticotropic hormone stimulation at week 12 was low and similar among all groups. **CONCLUSIONS:** HFA-BDP, 80 to 160 micro g/d, is effective and safe in childhood asthma.

Neffen H. et al. *Asthma control in Latin America: the Asthma Insights and Reality in Latin America (AIRLA) survey.* *Rev Panam Salud Publica.* 2005; 17(3) : 191-7.p **Abstract:** **OBJECTIVES:** The aims of this survey were (1) to assess the quality of asthma treatment and control in Latin America, (2) to determine how closely asthma management guidelines are being followed, and (3) to assess perception, knowledge and attitudes related to asthma in Latin America. **METHODS:** We surveyed a household sample of 2,184 adults or parents of children with asthma in 2003 in 11 countries in Latin America. Respondents were asked about healthcare utilization, symptom severity, activity limitations and medication use. **RESULTS:** Daytime asthma symptoms were reported by 56% of the respondents, and 51% reported being awakened by their asthma at night. More than half of those surveyed had been hospitalized, attended a hospital emergency service or made unscheduled emergency visits to other healthcare facilities for asthma during the previous year. Patient perception of asthma control did not match symptom severity, even in patients with severe persistent asthma, 44.7% of whom regarded their disease as being well or completely controlled. Only 2.4% (2.3% adults and 2.6% children) met all criteria for asthma control. Although 37% reported treatment with prescription medications, only 6% were using inhaled corticosteroids. Most adults (79%) and children (68%) in this survey reported that asthma symptoms limited their activities. Absence from school and work was reported by 58% of the children and 31% of adults, respectively. **CONCLUSIONS:** Asthma control in Latin America falls short of goals in international guidelines, and in many aspects asthma care and control in Latin America suffer from the same shortcomings as in other areas of the world.

Negro Alvarez J.M. et al. *Pressurised metered-dose inhalers (MDIs) versus dry powder inhalers devices (DPIs) to rapid-acting inhaled b2-agonists for asthma in children.* *Allergol Immunopathol (Madr).* 2002; 30(4) : 245-9.p **Abstract:** **OBJECTIVE:** To compare the clinical effectiveness of pressurized metered-dose inhalers (MDIs) with that of dry powder inhalers (DPIs) in delivering short-acting b2-agonists in children with asthma. **METHODS:** Searches were performed in Medline (1997-March 2002), the Cochrane Library Database and the Embase reference lists of review articles and clinical trials. In addition, the international headquarters of b2-agonist manufacturers were contacted. We performed a review of randomized controlled trials. **RESULTS:** Ten randomized controlled trials were included. No differences in clinical effectiveness were found between MDIs and PDIs. Two studies reported that fewer adverse events occurred when the Turbuhaler was used. Two long-term studies in children found that children preferred the MDI to the Rotohaler. **CONCLUSIONS:** 1) In stable asthma, short-acting b2 bronchodilators in standard MDIs are as effective as dry powder inhalers. 2) Pooling of results was limited by the small number of studies and therefore no overall conclusions could be drawn. 3) From

the limited data available, we found little or no evidence for an additional clinical benefit of DPI devices over standard MDIs in children with asthma.

Negro R.D. et al. *Evidence of adequacy of the performance of the Pulvinal by measuring through-device peak inspiratory flow rate in severe airways obstruction in adults and children.* J Aerosol Med. 2001; 14(3) : 343-9.p **Abstract:** Pulvinal is a novel DPI designed to deliver inhaled drugs to the airways. Previous in vitro and in vivo data has suggested that the peak inspiratory flow rate (PIFR), measured through Pulvinal, does not depend on the severity of expiratory airflow obstruction and that the lowest PIFR values seem sufficient to deliver an effective bronchodilator dose. To study this further, we have investigated through-Pulvinal PIFR in categories of patients who are likely to generate low inspiratory flow rates. Three different patients' groups were selected (severe asthmatics, n = 52, including elderly) patients with severe chronic obstructive pulmonary disease (COPD, n = 21) and children with asthma (n = 16). This study aimed to measure the through-device PIFR and also to assess whether this correlated with measures of expiratory flow rate. Inspiratory flow measurements were made with a Pulvinal inhaler inserted into the adapted mouthpiece of a pneumotachograph. No significant correlations were seen between through-device PIFR and expiratory volumes or flow rates when expressed as percent predicted normal (forced expiratory volume in 1 sec [FEV1] and peak expiratory flow rate [PEFR]) in any of the three studied populations. A significant correlation was present for FEV1 (when expressed in liters) and through-device PIFR in the adult asthmatic and COPD study groups. In spite of the disease severity in adult populations and the age of children, the lowest generated PIFR values were within the range producing adequate performance of Pulvinal DPI (>20 L/min). We conclude that inspiratory flow rates generated through the Pulvinal inhaler can be adequate in asthma and COPD, including patients at the extremes of severity and age, who may theoretically have a limitation in their inspiratory flow.

Nelson H.S. et al. *Efficacy and safety of fluticasone propionate 44 microg/salmeterol 21 microg administered in a hydrofluoroalkane metered-dose inhaler as an initial asthma maintenance treatment.* Ann Allergy Asthma Immunol. 2003; 91(3) : 263-9.p **Abstract:** **BACKGROUND:** We wanted to evaluate whether treatment with an inhaled corticosteroid and an inhaled long-acting beta2-agonist is more effective than an inhaled corticosteroid alone for patients using as-needed albuterol who are initiating maintenance treatment. **OBJECTIVE:** To compare the efficacy and safety of twice-daily fluticasone propionate (FP) 88 microg and salmeterol 42 microg combined in a chlorofluorocarbon (CFC)-free (hydrofluoroalkane 134a) metered-dose inhaler (MDI) with the individual agents alone, each delivered through an MDI containing CFC propellants, in patient with persistent asthma previously uncontrolled with as-needed short-acting beta2-agonists alone. **METHODS:** Patients with asthma (n = 283) were randomized to twice-daily treatment for 12 weeks with FP 88 microg combined with salmeterol 42 microg (FSC) in a CFC-free MDI or the individual components alone from CFC-containing MDIs. **RESULTS:** At endpoint, mean change from baseline in morning predose forced expiratory volume in 1 second was significantly (P < or = 0.016) greater with FSC (0.69 L) compared with FP (0.51 L) or salmeterol (0.47 L). Fewer patients treated with FSC withdrew due to worsening asthma (1%) compared with FP (3%) or salmeterol (8%; P = 0.024). FSC significantly increased (P < or = 0.002) morning and evening peak expiratory flow rate at endpoint (66.5 and 51.5 L/min, respectively) compared with FP (43.0 and 29.9 L/min, respectively) and salmeterol (29.2 and 21.6 L/min, respectively). In addition, asthma symptom scores were reduced, and percentages of days with no asthma symptoms increased in all treatment groups. **CONCLUSIONS:** Treatment with FSC in a CFC-free MDI is more effective than FP or salmeterol alone in asthma patients who are symptomatic taking short-acting beta2-agonists alone.

Neto A.S. et al. *Risk factors for the nasopharyngeal carriage of respiratory pathogens by Portuguese children: phenotype and antimicrobial susceptibility of Haemophilus influenzae and Streptococcus pneumoniae.* Microb Drug Resist. 2003; 9(1) : 99-108.p **Abstract:** Between 1997 and 2000 nasopharyngeal specimens were obtained from 466 children < or = 12 years old attending the Pediatric Emergency Department at S. Francisco Xavier Hospital, Lisbon, to evaluate risk factors for nasopharyngeal carriage of Haemophilus influenzae and Streptococcus pneumoniae and to characterize their phenotype and antimicrobial susceptibility. The attending pediatrician completed written questionnaires about the children's demographic and clinical histories. Over half the children (52.8%) carried H. influenzae and/or S. pneumoniae. Forty-one percent of these children had H. influenzae, 22.8% had S. pneumoniae and 36.2% had both. Risk factors identified for carriage of respiratory pathogens were: age below 3 years (p < 0.05), black race (p < 0.01), attending a daycare center (p < 0.05), and having a lower respiratory infection (p < 0.05). Asthmatic children were less likely to be carriers (p = 0.004). About two-thirds of H. influenzae isolates were susceptible to all antibiotics tested, 7.9% were beta-lactamase producers, 16.4% were nonsusceptible to trimethoprim, and 6.9% were intermediately resistant to clarithromycin. Over half (57.1%) of S. pneumoniae isolates were susceptible to all antibiotics tested, 21.1% were multiresistant, 23.3% were nonsusceptible to penicillin, and about 20% were resistant to macrolides. Low-level resistance to third-generation cephalosporins was detected in 2.3%. The data reflect the controversy surrounding risk factors of nasopharyngeal colonization. These may have significant implications on clinical practice and on antimicrobial strategies to prevent the appearance of further resistant strains. Our findings highlight the importance to investigate the relationship between asthma and carriage.

Neuharth-Pritchett S. et al. *Asthma and the school teacher: the status of teacher preparedness and training.* J Sch Nurs. 2001; 17(6) : 323-8.p **Abstract:** The increasing number of children with asthma in the nation's schools necessitates an examination of the preparedness of teachers in the care and management of children with asthma. This article reports the findings of a random sample of 291 public elementary school teachers regarding the knowledge and perception of the training they have received on asthma and its management. Data from this study suggest that teachers are not adequately prepared to assist children with the management of asthma in the classroom. Implications for school nurses on assisting teachers with asthma management are provided.

Newhouse C.P. et al. *Correlation of environmental factors with asthma and rhinitis symptoms in Tulsa, OK.* Ann Allergy Asthma Immunol. 2004; 92(3) : 356-66.p **Abstract:** **BACKGROUND:** Airborne allergens, pollutants, and climatic changes are known to influence the symptoms of asthma patients. **OBJECTIVE:** To correlate airborne fungal spore and pollen concentrations, meteorological data, and airborne pollutants with asthma and rhinitis symptoms to develop predictive models for asthma severity. **METHODS:** Patients from the Tulsa community participated in this study from September 1 to October 31, 2000, by filling out daily symptom diaries and measuring morning and evening peak expiratory flow rates. Air samples were collected using a volumetric spore trap. Meteorological variables and maximum and average pollutants were also included in the analysis. Linear regression analyses were performed for all environmental variables and symptom scores. Forward stepwise multiple regression analyses were performed to determine sets of variables that could be used to predict the conditions of increased symptom severity. **RESULTS:** Twenty-four patients participated in this study. The predominant spore types included Cladosporium, ascospores, and basidiospores. The predominant pollen type was Ambrosia. September was unusually hot and dry in Tulsa, but 161

mm of precipitation fell in October, primarily during the last 11 days. Two periods of peak symptoms occurred during the study, the first during the peak week of Ambrosia and the second after a 22 degrees C drop in temperature over 6 days. Numerous environmental variables showed significant correlations with symptom scores; however, there was no single predictive model for all symptoms. CONCLUSIONS: Ambrosia pollen and other environmental variables, including ozone levels, were significantly correlated with asthma and rhinitis symptoms.

Ng Man Kwong G. et al. *Diagnostic and treatment behaviour in children with chronic respiratory symptoms: relationship with socioeconomic factors.* Thorax. 2002; 57(8) : 701-4.p **Abstract:** BACKGROUND: The prevalence and severity of asthma is believed to increase with increasing socioeconomic deprivation. The relationship between asthma diagnosis, symptoms, diagnostic accuracy, and socioeconomic deprivation as determined by Townsend scores was determined in Sheffield schoolchildren. METHODS: All 6021 schoolchildren aged 8-9 years in one school year in Sheffield were given a parent respondent survey based on International Survey of Asthma and Allergies in Childhood (ISAAC) questions. RESULTS: 5011/6021 (83.2%) questionnaires were returned. Postcode data were available in 4131 replies (82.4%) and were used to assign a composite deprivation score (Townsend score). Scores were divided into five quintiles, with group 1 being least and group 5 being most deprived. A positive trend was observed from group 1 to group 5 for the prevalence of wheeze in the previous 12 months, wheeze attacks ≥ 4 /year, nocturnal wheeze and cough (all $p < 0.001$), cough and/or wheeze "most times" with exertion ($p < 0.03$), current asthma ($p < 0.001$), and significant asthma symptoms ($p < 0.001$). No significant trend was observed for lifetime wheeze or attacks of speech limiting wheeze. There were no significant trends in the prevalence of current asthmatic children without significant symptoms (overdiagnosis) or children with significant asthma symptoms but no current asthma diagnosis (underdiagnosis) across the social groups. There was a significant negative trend in the ratio of asthma medication to asthma diagnosis from least to most deprived groups ($p < 0.001$). CONCLUSIONS: Asthma morbidity and severity increase according to the level of socioeconomic deprivation. This may be due to differences in environment, asthma management, and/or symptom reporting. Diagnostic accuracy does not vary significantly across deprivation groups but children living in areas of least deprivation and taking asthma medication are less likely to be labelled as having asthma, suggesting diagnostic labelling bias.

Ng T.P. et al. *Trends and ethnic differences in asthma hospitalization rates in Singapore, 1991 to 1998.* Ann Allergy Asthma Immunol. 2003; 90(1) : 51-5.p **Abstract:** BACKGROUND: A few reports have indicated that asthma hospitalization rates in several countries have stopped rising or started falling in the 1990s. AIM: To describe recent trends and ethnic differences in asthma hospitalization rates in Singapore from 1991 to 1998. METHODS: Asthma hospitalization rates in all hospitals were analyzed by age groups, sex, ethnicity, and individual years, using aggregated data for asthma (ICD-9 493 and ICD-10 J45, J46) from 1991 to 1998, when nationwide data from the Central Claims Processing System were available. RESULTS: Between 1991 and 1998 there were a total of 37,615 hospital admissions for asthma, giving an annual average rate of 17.1 hospital admissions per 10,000 persons. Overall, the rates of asthma hospitalization fell by 28% from 21.7 per 10,000 in 1991 to 15.4 per 10,000 in 1998 (3.5% annually). The trends were broadly based across all age, sex, and ethnic groups. Hospitalizations were more common in boys than in girls aged 0 to 4 (male/female ratio 1.69), but less common in men than women aged 35 to 64 (male/female ratio 0.81). Rates of asthma hospital admissions were higher in Malays (32.8 per 10,000) and Indians (40.8 per 10,000) than Chinese (11.9 per 10,000). CONCLUSIONS: In line with findings from several countries, there have been recent declines in rates of hospital

admissions for asthma in Singapore in the 1990s. The declines were broadly based across all population subgroups and parallel previously observed declines in mortality in adults. However, considerable ethnic differences in levels of asthma hospitalization still exist.

Nguyen L.H. et al. *Similar allergic inflammation in the middle ear and the upper airway: evidence linking otitis media with effusion to the united airways concept.* J Allergy Clin Immunol. 2004; 114(5) : 1110-5.p **Abstract:** BACKGROUND: Otitis media with effusion (OME) is a chronic inflammatory disease of the middle ear space characterized by the accumulation of fluid. Previous investigations have suggested that the immunopathologic mechanism underlying the development of middle ear effusion in patients with allergy is largely due to the effects of T(H)2 mediators. The composition of the inflammatory substrate in the effusions of allergic otitis media is similar to the late-phase allergic response seen elsewhere in the respiratory tract, such as in asthma and in allergic rhinitis. OBJECTIVE: To determine whether the middle ear compartment may be a component of the united airways in allergic disease by comparing the inflammatory profiles of the middle ear to the upper airway. METHODS: Middle ear effusions, torus tubaris (Eustachian tube mucosa at the nasopharyngeal orifice), and adenoidal tissue biopsies were obtained from 45 patients undergoing simultaneous tympanostomy tube placement for OME and adenoidectomy for adenoid hypertrophy. The cellular and cytokine profiles of each site were investigated by using immunocytochemistry (elastase, CD3, major basic protein) and in situ hybridization (IL-4, IL-5, IFN-gamma mRNA). Atopic status was determined for each patient by using skin prick testing. RESULTS: Eleven of the 45 patients with OME (24%) were atopic. The middle ear effusions of atopic patients had significantly higher levels of eosinophils, T lymphocytes, and IL-4 mRNA + cells ($P < .01$) and significantly lower levels of neutrophils and IFN-gamma mRNA + cells ($P < .01$) compared with nonatopic patients. The nasopharyngeal tissue biopsies revealed similar cellular and cytokine profiles. CONCLUSION: In atopic patients with OME, the allergic inflammation occurs on both sides of the Eustachian tube, both in the middle ear and in the nasopharynx. The results of this study support the concept that the middle ear may be part of the united airway in atopic individuals.

Nickel R. et al. *Association study of Glutathione S-transferase P1 (GSTP1) with asthma and bronchial hyper-responsiveness in two German pediatric populations.* Pediatr Allergy Immunol. 2005; 16(6) : 539-41.p **Abstract:** Glutathione S-Transferase P1 (GSTP1) is an important enzyme in the detoxification of products of oxidative stress. Several studies have shown an association of the amino acid variant Ile105Val with bronchial asthma and the reaction of the lung to inhalant pollutants. The aim of this study was to test the two known amino acid variants in GSTP1 for association with bronchial asthma and airway hyper-responsiveness in two German pediatric populations. We genotyped Ile105Val and Ala114Val in the Multicenter Allergy Study cohort (85 children with asthma, 123 controls) and asthmatic children from Freiburg ($n = 178$). We did not find association of either polymorphisms with bronchial asthma or airway hyper-responsiveness. We conclude from our data that polymorphisms within GSTP1 do not play a major role in the development of bronchial asthma in German children.

Nicolae D. et al. *Fine mapping and positional candidate studies identify HLA-G as an asthma susceptibility gene on chromosome 6p21.* Am J Hum Genet. 2005; 76(2) : 349-57.p **Abstract:** Asthma affects nearly 14 million people worldwide and has been steadily increasing in frequency for the past 50 years. Although environmental factors clearly influence the onset, progression, and severity of this disease, family and twin studies indicate that genetic variation also influences susceptibility. Linkage of asthma and related phenotypes to chromosome 6p21 has been reported in seven genome screens, making it the most replicated region of the genome. However,

because many genes with individually small effects are likely to contribute to risk, identification of asthma susceptibility loci has been challenging. In this study, we present evidence from four independent samples in support of HLA-G as a novel asthma and bronchial hyperresponsiveness susceptibility gene in the human leukocyte antigen region on chromosome 6p21, and we speculate that this gene might contribute to risk for other inflammatory diseases that show linkage to this region.

Nicolai T. et al. *Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children.* Eur Respir J. 2003; 21(6) : 956-63.p **Abstract:** Conflicting results have been reported for the relationship between traffic exposure and inception of atopy. The effect of traffic on the prevalence of asthma and atopy at school age was investigated in a representative population. Random samples of schoolchildren (n=7,509, response rate 83.7%) were studied using the International Study of Asthma and Allergies in Childhood phase-II protocol with skin-prick tests, measurements of specific immunoglobulin E and lung function. Traffic exposure was assessed via traffic counts and by an emission model which predicted soot, benzene and nitrogen dioxide (NO₂). Traffic counts were associated with current asthma, wheeze and cough. In children with tobacco-smoke exposure, traffic volume was additionally associated with a positive skin-prick test. Cough was associated with soot, benzene and NO₂, current asthma with soot and benzene, and current wheeze with benzene and NO₂. No pollutant was associated with allergic sensitisation. High vehicle traffic was associated with asthma, cough and wheeze, and in children additionally exposed to environmental tobacco smoke, with allergic sensitisation. However, effects of socioeconomic factors associated with living close to busy roads cannot be ruled out.

Nicolai T. et al. *Longitudinal follow-up of the changing gender ratio in asthma from childhood to adulthood: role of delayed manifestation in girls.* Pediatr Allergy Immunol. 2003; 14(4) : 280-3.p **Abstract:** Boys suffer more often from asthma than girls, while in adults the gender ratio is reversed. It is not clear when exactly this change occurs and by what mechanism. From a cohort of all 5030 German 4th grade pupils (age 10 years) in Munich, 274 children with current asthma were identified (164 males, 110 females) through a questionnaire, and skin prick tests were performed. These subjects were re-evaluated at ages 14 and 20 years with a questionnaire. A random sample (n = 1000) of all 3538 German children without current asthma at age 10 was also re-evaluated at age 20 (controls). At age 20, only 24.5% (21 males, eight females) of the initial asthma group still had symptoms, and their gender ratio remained male dominated. In the controls, 4.8% (48/1000) had current asthma at age 20 and these were predominantly female: 6.4% (31/485) of control girls vs. 3.3% (17/515) of boys (p = 0.022). Half of the new asthma cases had had no symptoms or diagnoses until age 10, and atopy at age 10 was not associated with subsequent asthma in these. Asthma at age 10 has no better prognosis in boys than in girls, and the mechanism of the changing gender ratio appears to be late incidence of asthma among girls. Because the latter constitute a considerable part of adult asthma cases, it appears important to further explore this asthma phenotype and the risk factors associated with it.

Nielsen K.G. et al. *Bronchodilation and bronchoprotection in asthmatic preschool children from formoterol administered by mechanically actuated dry-powder inhaler and spacer.* Am J Respir Crit Care Med. 2001; 164(2) : 256-9.p **Abstract:** We evaluated the bronchodilatory and the bronchoprotective effect of the long-acting beta(2)-agonist formoterol administered as dry powder from a mechanically actuated dry-powder inhaler (DPI) using spacer in 12 asthmatic children 2 to 5 yr of age. Lung function was measured as the specific airway resistance (sRaw) in a whole body plethysmograph. Hyperventilation of cold, dry air was used as bronchial challenge, and the responsiveness was estimated as change

in sRaw. The bronchoprotective effect of formoterol Turbohaler 9 microg was compared with salbutamol 200 microg and placebo at 15 min, 4 and 8 h postdose in a randomized, double-blind, placebo-controlled, crossover study. All treatments were administered from DPI (Turbohaler) actuated mechanically into a spacer. Formoterol and salbutamol caused similar and significant bronchodilation at the first measurement 3 min postdose. Formoterol offered a sustained and stable bronchodilation for at least 8 h. Salbutamol provided significant bronchodilation for less than 4 h. Formoterol caused significant bronchoprotection of 80% for at least 8 h compared with placebo, and from 4 h onward compared with salbutamol. Bronchoprotection from salbutamol lasted less than 4 h. In conclusion, formoterol administered as dry powder in a single dose provided rapid and sustained bronchodilation and clinically significant bronchoprotection for at least 8 h in 2- to 5-yr-old asthmatic children. Furthermore, this study suggests that mechanical actuation of DPI using a spacer is effective for aerosol treatment of young asthmatic children.

Nielsen K.G. et al. *Hyperventilation with cold versus dry air in 2- to 5-year-old children with asthma.* Am J Respir Crit Care Med. 2005; 171(3) : 238-41.p **Abstract:** Cold air challenge (CACH) has been shown to discriminate between children with asthma and healthy young children. Hyperventilation with dry room-temperature air is a simplified alternative. We compared responsiveness in young children with asthma between two standardized, single-step protocols: dry air challenge (DACH) performed as 6 minutes of eucapnic hyperventilation with dry room-temperature air and CACH as 4 minutes of hyperventilation. Response was measured as specific airway resistance by whole-body plethysmography and expressed as change from baseline in numbers of within-subject SDs (SDw). The challenge sequence was randomly assigned. A comparator challenge was performed 1 hour later if the first challenge gave a change of 3 SDw or more. Forty 2- to 5-year-old children with asthma were included. Responsiveness to cold versus dry air showed significant, but weak, correlation (r(2) = 0.34, p < 0.0001), but responsiveness to CACH exceeded DACH (7.6 vs. 5.4 SDw, p < 0.02). CACH seemed to induce reduction in response to the following DACH (p < 0.01), whereas no such reduction was seen after DACH. Conclusion: Responsiveness to CACH exceeded responsiveness to DACH, and CACH seemed to induce refractoriness in contrast to DACH, probably because of the additional stimulus from airway cooling. This finding suggests CACH as the preferred method of challenge.

Nies M.A. et al. *Model for community health nursing care: application to an integrated asthma intervention program.* J Sch Nurs. 2002; 18(2) : 74-8.p **Abstract:** The article describes the use of a model for community health nursing care applied to an integrated asthma intervention program in an inner-city context. Asthma is a chronic childhood disease with broad physical, social, and economic impact on children, families, and communities. Despite recent advances in asthma understanding and treatment, morbidity and mortality continue to rise. This model suggests ways to combine individual, family, school, and community interventions to enhance coordination and increase the impact of services. It outlines needs and opportunities for collegial collaboration between professional nurses in varied practice settings. Application of the model to the management of asthma in the urban setting demonstrates the potential to produce significant improvement in the management of conditions such as asthma and highlights the key role that school nurses play.

Nijevitch A.A. et al. *Helicobacter pylori infection and reflux esophagitis in children with chronic asthma.* J Clin Gastroenterol. 2004; 38(1) : 14-8.p **Abstract:** BACKGROUND: Reflux esophagitis is uncommon in countries in which most people are colonized by H. pylori infection and is extremely rare in persons with reflux esophagitis, although esophagitis is detected in almost 50% of

children with recurrent lower respiratory tract symptoms. **HYPOTHESIS:** Failure to acquire *H. pylori* can enhance esophagitis risk in children with chronic asthma. **PATIENTS AND METHODS:** Forty-two pediatric out-patients with chronic asthma (mean age 13.2 +/- 1.18 years, range 12-15 years, 23 boys and 19 girls) were included in the study. They had undergone endoscopy with gastric and esophageal biopsies for upper dyspeptic complaints. *H. pylori* positivity was confirmed by positive Giemsa staining. Esophagitis was diagnosed by standard histologic procedure (presence of intraepithelial leukocytes or basal cell hyperplasia). **RESULTS:** *H. pylori* colonization was detected histologically in 22 of 42 patients (52.4%) enrolled in the study. Histology demonstrated that in asthmatic children with evidence of *H. pylori* infection esophagitis was a dramatically rare finding than in the patients without the infection ($P < 0.001$). It was an unexpected finding, that lung function parameters (FEF50, FEF75) were significantly lower in asthmatics infected with *H. pylori* ($P < 0.05$). **CONCLUSION:** The present findings suggest inverse association between esophagitis and *H. pylori* in course of asthma in pediatric patients.

Nilsson L. et al. *Allergic disease at the age of 7 years after pertussis vaccination in infancy: results from the follow-up of a randomized controlled trial of 3 vaccines.* Arch Pediatr Adolesc Med. 2003; 157(12) : 1184-9.p **Abstract:** **OBJECTIVE:** To prospectively assess sensitization rates and the development of allergic diseases in a follow-up of a randomized controlled pertussis vaccine trial. **SETTING:** Two-month-old infants were the subject of this double-blind study in 1992 in a collaboration between the Pediatric Clinic and the Primary Care Centers in Linköping. **PATIENTS AND INTERVENTION:** Allergic diseases were evaluated in 667 children, who were randomized to 1 of 4 vaccine groups: a 2-component, a 5-component, or a whole cell pertussis vaccine (all of which were administered with the diphtheria and tetanus toxoids vaccine) and the diphtheria and tetanus toxoids vaccine alone. Allergy development was assessed by questionnaires ($n = 667$) and skin prick tests ($n = 538$) at the age of 7 years. **MAIN OUTCOME MEASURES:** Allergic diseases and skin prick test results at the age of 7 years. **RESULTS:** The cumulative incidence of allergic diseases was 34.9%, and was similar in the 4 groups (33.3%-37.3%, $P = .89$), even after adjusting for family history, sex, pets, dampness, environmental smoking at home, and other living conditions. Positive skin prick test results were more prevalent, however, after vaccination with the 2-component acellular vaccine (19.4%) than in the other 3 groups (11.1%-13.5%, adjusted for confounding factors, $P = .01$). Furthermore, allergic rhinoconjunctivitis was more common in children who were initially immunized with the 2-component pertussis vaccine and received a booster dose with an acellular vaccine compared with those who received no booster vaccination (relative risk, 3.6; 95% confidence interval, 1.1-12.0). **CONCLUSION:** Pertussis vaccination in infancy with any of these vaccines was not associated with allergic manifestations at the age of 7 years, apart from a higher prevalence of positive skin prick test results after an experimental 2-component vaccine, which is no longer in use.

Nishi N. et al. *Squamous cell carcinoma-related antigen in children with acute asthma.* Ann Allergy Asthma Immunol. 2005; 94(3) : 391-7.p **Abstract:** **BACKGROUND:** Increased serum levels of squamous cell carcinoma-related antigen (SCCA) have been observed in patients with allergic disorders, such as atopic dermatitis and bronchial asthma. T(H)2 cytokines, which are known to be involved in the pathogenesis of allergic disorders, stimulate new synthesis of SCCA in cultured human airway epithelial cells. **OBJECTIVE:** To investigate whether SCCA levels increase during acute exacerbations of asthma in children and whether the T(H)2 cytokines, interleukin 4 (IL-4) and IL-13, are associated with SCCA levels. **METHODS:** Serum levels of SCCA, IL-4, and IL-13 were measured by enzyme immunoassay during the acute phase of an asthma exacerbation (on hospital admission) and in the recovery phase (after symptoms had

subsided). **RESULTS:** In the 35 children who participated in this study, serum levels of SCCA were significantly elevated in the acute phase (mean +/- SD, 3.09 +/- 2.03 ng/mL) compared with the recovery phase (mean +/- SD, 1.47 +/- 0.64 ng/mL) of an asthma exacerbation ($P < .001$). In 12 children, the IL-13 levels were observed to correlate with SCCA levels during the recovery phase ($r = 0.68$, $P = .02$) but not during the acute phase of an asthma exacerbation. **CONCLUSIONS:** Serum SCCA levels increase during the acute phase of an asthma exacerbation. During this phase, the increased synthesis of SCCA is not associated with IL-13 but rather mediated by other undefined stimuli. IL-13 may contribute to the basal production of SCCA in asthmatic children.

Niti M. et al. *Temporal trends and ethnic variations in amenable mortality in Singapore 1965-1994: the impact of health care in transition.* Int J Epidemiol. 2001; 30(5) : 966-73.p **Abstract:** **BACKGROUND:** Amenable mortality is used to assess the effects of health care services on gains in mortality outcomes. Possibly differing patterns of trends in amenable mortality may be expected in economically less developed countries, which have undergone rapid epidemiological transition and recent reforms in health care systems, but such studies are scarce. This study was set up to examine the trends in amenable mortality in Singapore from 1965 to 1994; to estimate the relative impact of medical care and primary preventive policy measures in terms of gains in mortality outcomes; to examine ethnic differences in amenable mortality among Chinese, Malays and Indians. **METHODS:** Age-standardized mortality rates were calculated for 16 amenable causes of death in Singapore for six 5-year periods (1965-1969, ..., 1990-1994), and for each of the three main ethnic groups for three periods (1989-1991, 1992-1994, 1995-1997). Amenable mortality rates were divided into those which can be reduced by timely therapeutic care for 'treatable' conditions (e.g. asthma and appendicitis), or by primary preventive measures for 'preventable' conditions (e.g. lung cancer and motor vehicle injury). **RESULTS:** Amenable mortality was higher in males (age-standardized rate 109.7 per 100 000 population) than in females (age-standardized rate 60.7 per 100 000 population). Amenable mortality declined by 1.77% a year in males and 1.72% a year in females. By comparison, the average yearly decline in non-amenable mortality was 0.91% in males and 1.17% in females. The decline in amenable mortality was largely due to 'treatable' causes rather than a decline in mortality due to 'preventable' causes of death. Amenable mortality was lowest for Chinese and highest for Malays. Over the recent 9-year period from 1989 to 1997, amenable mortality declined more in Chinese than in Malays and Indians. However, Indian females showed by far the sharpest decline, whereas Indian males, by contrast, showed an increase in amenable mortality, due to both treatable and preventable causes. **CONCLUSIONS:** In line with findings from European countries, amenable mortality in Singapore declined more than non-amenable mortality. There were more significant gains in mortality outcomes from medical care interventions than from primary preventive policy measures. Gender and ethnic differences in amenable mortality were also observed, highlighting issues of socioeconomic equities to be addressed in the financing and delivery of health care.

Niven R. *The endotoxin paradigm: a note of caution.* Clin Exp Allergy. 2003; 33(3) : 273-6.p

Nizet T.A. et al. *Tremor side effects of salbutamol, quantified by a laser pointer technique.* Respir Med. 2004; 98(9) : 844-50.p **Abstract:** **OBJECTIVE:** To study tremor side effects of salbutamol an easily applicable, quick and low-priced method is needed. A new method using a commercially available, pen-shaped laser pointer was developed. Aim of the study was to determine sensitivity, reproducibility, reference values and the agreement with a questionnaire. **METHODS:** Tremor was measured using a laser pointer technique. To determine sensitivity we assessed tremor in 44 patients with obstructive lung disease after administration of

cumulative doses of salbutamol. Subjects were asked to aim at the centre of a target, subdivided in concentric circles, from 5 m distance. The circle in which the participant succeeded to aim was recorded in millimetres radius. In another series of measurements, reproducibility and reference values of the tremor was assessed in 65 healthy subjects in three sessions, at 9 a.m., 4 p.m. and 9 a.m., respectively, 1 week later. Postural tremor was measured with the arm horizontally outstretched rest tremor with the arm supported by an armrest and finally tremor was measured after holding a 2-kg weight until exhaustion. Inter-observer variability was measured in a series of 10 healthy subjects. Tremor was measured simultaneously by two independent observers. RESULTS: Salbutamol significantly increased tremor severity in patients in a dose-dependent way. Within healthy adults no age-dependency could be found ($b = 0.262$ mm/year; $P = 0.72$). There was no agreement between the questionnaire and tremor severity ($r = 0.093$; $P = 0.53$). Postural tremor showed no significant difference between the first and third session ($P = 0.07$). Support of the arm decreased tremor severity, exhaustion increased tremor severity significantly. A good agreement was found between two independent observers (interclass correlation coefficient 0.72). DISCUSSION: Quantifying tremor by using an inexpensive laser pointer is, with the exception of children (<12 years) a sensitive and reproducible method.

Noah T.L. et al. *Repeated measurement of nasal lavage fluid chemokines in school-age children with asthma.* Ann Allergy Asthma Immunol. 2006; 96(2) : 304-10.p **Abstract:** BACKGROUND: Inflammatory processes at the mucosal surface may play a role in maintenance of asthma pathophysiology. Cross-sectional studies in asthmatic patients suggest that chemokines such as interleukin 8 (IL-8) are overproduced by respiratory epithelium. OBJECTIVE: To test the hypothesis that chemokine levels are persistently elevated in the respiratory secretions of asthmatic children at a stable baseline. METHODS: We measured nasal lavage fluid (NLF) levels of chemokines and other mediators at 3- to 4-month intervals in a longitudinal study of asthmatic children, with nonasthmatic siblings as controls. RESULTS: In a linear mixed-model analysis, both family and day of visit had significant effects on nasal mediators. Thus, data for 12 asthmatic-nonasthmatic sibling pairs who had 3 or more same-day visits were analyzed separately. For sibling pairs, median eosinophil cationic protein levels derived from serial measurements in NLF were elevated in asthmatic patients compared with nonasthmatic patients, with a near-significant tendency for elevation of total protein and eotaxin levels as well. However, no significant differences were found for IL-8 or several other chemokines. Ratios of IL-13 or IL-5 to interferon-gamma released by house dust mite antigen-stimulated peripheral blood mononuclear cells, tested on a single occasion, were significantly increased for asthmatic patients. CONCLUSIONS: Substantial temporal and family-related variability exists in nasal inflammation in asthmatic children. Although higher levels of eosinophil cationic protein are usually present in NLF of patients with stable asthma compared with patients without asthma, chemokines other than eotaxin are not consistently increased. Eosinophil activation at the mucosal surface is a more consistent predictor of asthmatic symptoms than nonspecific elevation of epithelium-derived inflammatory chemokine levels.

Noguchi E. et al. *An association study of asthma and total serum immunoglobulin E levels for Toll-like receptor polymorphisms in a Japanese population.* Clin Exp Allergy. 2004; 34(2) : 177-83.p **Abstract:** BACKGROUND: The prevalence of atopic diseases has been increasing in developed countries. This could be explained by the hygiene hypothesis, which states that exposure to specific infections or endotoxins during infancy drives the maturing immune system towards a Th1 phenotype and away from the Th2 phenotype, which is associated with allergic diseases. Toll-like receptors (TLRs) play important roles in the signalling of many pathogen-related molecules and endogenous proteins associated with immune

activation. OBJECTIVE: The aim of the present study was to investigate whether polymorphisms in genes encoding TLRs are associated with asthma or total serum IgE levels. METHODS: We screened the 5' flanking and coding regions of the TLR2, TLR3, TLR4, and TLR9 genes for polymorphisms by direct sequencing of DNA from 32 asthmatics, and analysed the effect of the polymorphisms on the development of atopic asthma and on total serum IgE levels. RESULTS: We identified 16 variants in TLRs. The transmission disequilibrium test of the families revealed that none of the alleles or haplotypes were associated with asthma or total IgE levels ($P > 0.05$). However, we found an insertion/deletion polymorphism in the 5' untranslated region of TLR2, and an expression construct containing the deletion allele showed lower luciferase activity than the wild-type alleles, suggesting that the deletion allele has reduced transcriptional activity. CONCLUSION: Our results indicate that polymorphisms in TLRs are not likely to be associated with the development of atopy-related phenotypes in a Japanese population.

Noguchi E. et al. *Association between a new polymorphism in the activation-induced cytidine deaminase gene and atopic asthma and the regulation of total serum IgE levels.* J Allergy Clin Immunol. 2001; 108(3) : 382-6.p **Abstract:** BACKGROUND: Activation-induced cytidine deaminase (AICDA) is a recently identified RNA-editing deaminase that plays an important role in class-switching. Defects in AICDA result in a hyper-IgM phenotype and lack of IgG, IgA, and IgE in both human beings and mice. OBJECTIVE: The aim of this study was to determine whether the AICDA gene is related to regulation of total serum IgE and development of atopic asthma. METHODS: We screened for polymorphisms in the 5'-flanking and coding regions of the AICDA gene in subjects with atopic asthma and analyzed the effect of these polymorphisms on the development of atopic asthma and on total serum IgE levels in Japanese asthmatic families. RESULTS: We identified 3 novel polymorphisms (5923A/G, 7888C/T, and 8578A/C) and 1 rare variant (Arg25Cys) in the AICDA gene. Transmission disequilibrium testing showed that the 7888C allele was transmitted preferentially to asthma-affected children ($P = .007$). Mean log [total serum IgE] levels of parents with the 7888C/7888C, 7888C/7888T, and 7888T/7888T genotypes were 2.12, 1.99, and 1.77, respectively, and a significant association was observed between the genotypes ($P = .02$). In RT-PCR experiments, we found 2 novel splice variants of AICDA, one lacking all of exon 4 (variant 1; 367 base pairs) and the other lacking the first 30 base pairs of exon 4 (variant 2; 453 base pairs). These variants were not associated with the 7888C/T polymorphism. CONCLUSION: The 7888C/T polymorphism might be associated with the pathogenesis of atopic asthma and the regulation of total serum IgE levels.

Noguchi E. et al. *New polymorphisms of haematopoietic prostaglandin D synthase and human prostanoid DP receptor genes.* Clin Exp Allergy. 2002; 32(1) : 93-6.p **Abstract:** BACKGROUND: Prostaglandin D₂ (PGD₂), a major cyclo-oxygenase metabolite of arachidonic acid in mast cells, induces bronchoconstriction in the human lung. It has been reported that mice lacking PGD receptor fail to develop the bronchial hyper-responsiveness upon ovalbumin challenge, suggesting that PGD₂ functions as a mediator of allergic asthma. OBJECTIVE: To determine if there are any mutations associated with the development of asthma in the haematopoietic prostaglandin D synthase (H-PGDS) gene and the human prostanoid DP receptor (PTGDR) gene. METHODS AND RESULTS: We screened the 5'flanking and coding regions of the H-PGDS gene and the PTGDR gene by direct sequence. We identified one variant in intron 2 (IVS2 + 11 A > C) and one variant in intron 3 (IVS3 + 13T > C) of the H-PGDS gene, and two variants in the 5'flanking region of the PTGDR gene (-197T > C and -2C > T). The IVS3 + 13T > C and -197T > C variants were rare, appearing only once in 48 subjects. transmission disequilibrium test (TDT) analysis of 144 asthmatic families revealed that the IVS2 + 11 A allele of the H-PGDS gene was significantly transmitted preferentially to asthma-affected

children ($P = 0.0056$), but no association was observed between -2C/T polymorphism of the PTGDR gene and asthma ($P > 0.05$). **CONCLUSION:** Our results suggest that the IVS2 + 11A/C allele may be involved in the development of asthma in the Japanese population.

Noguchi E. et al. *Association between TNFA polymorphism and the development of asthma in the Japanese population.* Am J Respir Crit Care Med. 2002; 166(1) : 43-6.p **Abstract:** Tumor necrosis factor (TNF) is a proinflammatory cytokine that participates in the inflammatory reaction in patients with asthma. The TNFA and TNFB genes, which encode TNF-alpha and TNF-beta, respectively, are located within the region encoding the human major histocompatibility complex on chromosome 6p21.3, which showed linkage to atopic asthma in our genome-wide search. To determine whether polymorphisms in the 5' flanking region of the TNFA gene (-1031C/T, -863C/A, and -857C/T) and an NcoI polymorphism in the TNFB gene (LTA NcoI) are associated with the development of asthma, we performed transmission disequilibrium tests of families identified through children with atopic asthma. Genotypes of families were determined by polymerase chain reaction-based restriction fragment length polymorphism or SNaPshot analysis. Transmission disequilibrium tests of 144 asthmatic families revealed that transmission of the -857C allele and the -1031T-863C-857C haplotype in the TNFA gene to asthma-affected offspring occurred more frequently than expected (-857C allele, $p = 0.0055$; -1031T-863C-857C haplotype, $p = 0.0002$). Our results suggest that TNFA or nearby genes, including those in the major histocompatibility complex region, may contribute to the development of asthma in the Japanese population.

Noguchi E. et al. *Positional identification of an asthma susceptibility gene on human chromosome 5q33.* Am J Respir Crit Care Med. 2005; 172(2) : 183-8.p **Abstract:** **RATIONALE:** Asthma is a common respiratory disease with complex genetic components. We previously reported strong evidence for linkage between mite-sensitive asthma and markers on chromosome 5q33. This area of linkage includes a region homologous to a mouse area that contains a locus involved in regulation of airway hyperreactivity. **OBJECTIVE:** The aim of the present study is to identify asthma susceptibility genes on chromosome 5q33. **METHODS AND RESULTS:** We performed mutation screening and association analyses of genes in the 9.4-Mb human linkage region. Transmission disequilibrium test analysis of 105 polymorphisms in 155 families with asthma revealed that six polymorphisms in cytoplasmic fragile X mental retardation protein (FMRP)-interacting protein 2 gene were associated significantly with the development of asthma ($p = 0.000075$; odds ratio, 5.9). These six polymorphisms were in complete linkage disequilibrium. In real-time quantitative polymerase chain reaction analysis, subjects homozygous for the haplotype overtransmitted to asthma-affected offspring showed significantly increased level of cytoplasmic FMRP interacting protein 2 gene expression in lymphocytes compared with ones heterozygous for the haplotype ($p = 0.038$). **CONCLUSIONS:** Our data suggest that cytoplasmic FMRP interacting protein 2 are associated with the development of atopic asthma in humans, and that targeting cytoplasmic FMRP interacting protein 2 could be a novel strategy for treating atopic asthma.

Noma T. et al. *Induction of peripheral mononuclear cell apoptosis in asthmatic patients in remission.* J Asthma. 2002; 39(7) : 591-601.p **Abstract:** Apoptosis regulates inflammatory cell survival in allergic inflammation, and decreased apoptosis contributes to the chronicity of inflammation. To investigate the mechanisms of onset and remission of mite-sensitive childhood asthma, we evaluated peripheral blood mononuclear cell apoptosis in patients with asthma and in remission. There was a similar percentage of hypodiploid cells in unstimulated mononuclear cell cultures from patients with active asthma (29.5+/-5.0%) and normal individuals (25.9+/-4.9%). In

contrast, the percentage increased in patients in remission (44.5+/-3.2%). In Dermatophagoides farinae (Df) antigen-stimulated mononuclear cell, the stimulation index was lower in patients with active asthma (0.95+/-0.06%) than in normal individuals (1.31+/-0.16%). In contrast to active patients, the proportion of hypodiploid cells stimulated with Df in patients with remission was equivalent to that of normal controls. After phytohemagglutinin (PHA) stimulation, the percentage of hypodiploid cells in patients with active asthma (35.1+/-3.2%) was also lower than in normal individuals (48.5+/-4.3%) or patients in remission (49.5+/-5.7%). Apoptosis occurred predominantly in CD8+, but not CD4+, cells in patients in remission. Interleukin IL-2 inhibited apoptosis in Df-activated cells in normal individuals, whereas IL-2 did not inhibit apoptosis in cells from patients in remission as well as with active asthma. The expression of Fas receptors on resting mononuclear cells was similar in the three groups. However, Fas receptor expression in Df-stimulated mononuclear cells was greater in patients with active asthma than in healthy individuals. In patients with remission that was equivalent to healthy controls. The PHA increased Fas expression to a similar degree in the three groups. With regard to Fas ligand, the expression was lower in unstimulated cultured mononuclear cells from patients than in normal individuals. In patients in remission that was comparable to normal individuals. The Df stimulation upregulated the Fas ligand in patients with active asthma, and downregulated it in patients in remission. In conclusion, apoptosis in Df-stimulated mononuclear cells is impaired in patients with active asthma, while spontaneous apoptosis of CD8+ cells in vivo is augmented in patients in remission, and may be involved in the onset and remission of mite-sensitive asthma.

Noma T. et al. *Functional human IgE specific for Dermatophagoides farinae antigen is produced in SCID mice reconstituted with peripheral mononuclear cells derived from healthy persons and patients with asthma.* Allergy. 2001; 56(12) : 1137-43.p **Abstract:** **BACKGROUND:** Whether normal peripheral blood mononuclear cells (PBMCs) transferred to severe combined immunodeficient (SCID) mice produce specific IgE remains unclear. **METHODS:** Mice received injections of Dermatophagoides farinae antigen (Df)-stimulated PBMCs from healthy persons (IgE RAST score of 0). **RESULTS:** High titers of Df-specific IgE were detected. The Df-specific IgE activity produced was comparable to or higher than that produced by cells from patients with asthma although the time to maximal production was longer. IgE derived from PBMCs of healthy persons or patients with asthma induced histamine release from cultured human basophils that had been stimulated with Df antigen or an anti-IgE antibody. Treatment of Df-stimulated PBMCs with a high dose, but not a low dose, of interleukin-4 stimulated production of Df-specific IgE by PBMCs from healthy persons or patients with asthma. In contrast, intravenous injection of IFN-gamma into reconstituted SCID mice decreased Df-specific IgE production by PBMCs from patients with asthma. In PBMCs from healthy persons, IgE class-switching may occur later and block the effects of treatment with IFN-gamma. **CONCLUSIONS:** PBMCs from healthy persons and persons with asthma have clones reactive to allergen and produce functional IgE specific for relevant antigens in mite-sensitive bronchial asthma.

Nowak-Wegrzyn A. et al. *Contamination of dry powder inhalers for asthma with milk proteins containing lactose.* J Allergy Clin Immunol. 2004; 113(3) : 558-60.p

Nuhoglu Y. et al. *The association between delayed type hypersensitivity reaction to Mycobacterium tuberculosis and atopy in asthmatic children.* Allergol Immunopathol (Madr). 2003; 31(1) : 14-7.p **Abstract:** **BACKGROUND:** It has been postulated that there is an inverse association between mycobacterium tuberculosis infection and atopy. We aimed to investigate if there is a similar relation in our study group, consisting 252 asthmatic children. **METHODS:** In tuberculin testing indurations greater than or equal to 5 mm were

accepted as positive. The most common aeroallergens were used in skin prick testing and reactions ≥ 3 mm were accepted as positive. RESULTS: In 139 patients PPD was negative, whereas in 113 patients PPD was positive. Among the PPD (-) patients skin prick test was positive in 64 % (n = 89). Among the PPD (+) patients skin prick test was positive in 71 % (n = 80). As the two groups were compared for having positive skin prick test reactions no statistically significant difference was detected between them (p = 0.283). CONCLUSIONS: Tuberculin reactivity is not inversely associated with atopy in asthmatic children.

Nunes C. et al. *Asthma, from childhood to adulthood: a prospective 20-year longitudinal study of a cohort of asthmatics.* J Investig Allergol Clin Immunol. 2002; 12(4) : 242-9.p Abstract: This study analyzes the evolution of a group of children under 10 years of age with asthma over a period of 20 years. We selected a random group of 32 children with asthma and compared it with a control group composed of 33 children without asthma, similar in age, sex, and socio-economic characteristics. Throughout the 20 years we analyzed the number of ambulatory visits, morbidity, environmental tobacco smoke (ETS) as well as social and economic characteristics. The results after 20 years of evaluation showed that inflammatory and infectious processes in the airways (upper and lower) were more frequent among asthmatics than in the control group. ENT infections were more predominant in the group with inadequate sanitary conditions. There were no significant differences for the other pathologies. We studied the frequency of asthmatic crises requiring emergency care according to age and sex. Clinical ambulatory visits in asthmatic children were 2.8 times more frequent than in the control group. We found no differences between males and females, either in terms of global morbidity or the worsening of their asthmatic disease e.g., crises, going to emergency services and hospitalization. In the asthmatic group, the frequency of asthma crises, visits to emergency services and hospitalization were analyzed, with no differences being found between the sexes. We measured the PEFr, FEV1, and FEF25-75 in both groups for 20 years and compared those values to age, weight, height, and sex. We found that the parameters of lung function were lower in the asthmatic group than in the control group. We used as statistical method the chi 2 test, and regression analyses were made to relate the PEFr, FEV1, and FEF25-75 values to age and gender. A paired t-test was used to compare ambulatory visits, morbidity, emergency care, ETS, and sanitary housing conditions to age and sex in both groups. A p value ≤ 0.05 was taken as indicating statistical significance.

Nystad W. et al. *The effect of respiratory tract infections on reported asthma symptoms.* Scand J Public Health. 2002; 30(1) : 70-5.p Abstract: BACKGROUND: Wheezing and chest tightness is associated with respiratory tract infections. Thus the occurrence of respiratory tract infections may influence the prevalence of asthma. AIMS: To assess the strength of relation between two main symptoms of asthma and the prevalence of respiratory tract infections in children with and without asthma. METHODS: The study population was 3,796 children, four years of age, whose parents had answered a questionnaire on respiratory symptoms and asthma. The prevalence of wheezing and chest tightness in the last 12 months and four weeks was estimated according to the occurrence of respiratory tract infections during the corresponding time periods; 95% confidence intervals of the prevalence and the statistical significance of the differences in the prevalence by using chi-square test were calculated. RESULTS: The prevalence of wheezing and chest tightness was higher in children who had experienced respiratory tract infections than in those who had not. The prevalence of wheezing was 17.5% among children who had experienced bronchitis and 3.0% among children who had not (p<0.001). The prevalence of chest tightness in the last 12 months was 3.7% (95% CI 3.1-4.1) among children without asthma and 59.3% (95% CI 53.4-65.2) among children with asthma (p<0.001). The prevalence of wheezing and chest tightness increased with increasing number of

different types of respiratory tract infections among children without asthma (p<0.001) and tended to be so among children with asthma. CONCLUSIONS: These findings have implications for the interpretation of results from epidemiological studies using respiratory symptoms as a health-related outcome of asthma.

Nystad W. et al. *Baby swimming increases the risk of recurrent respiratory tract infections and otitis media.* Acta Paediatr. 2003; 92(8) : 905-9.p Abstract: AIM: To estimate the association between baby swimming and recurrent respiratory tract infections and otitis media in the first year of life in children of parents without and with atopy. METHODS: Norwegian schoolchildren (n = 2862) was enrolled in a cross-sectional study of asthma and allergy using the questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC). The outcomes were parental retrospective report of recurrent respiratory tract infections and otitis media diagnosed by a physician in the first year of life. The exposure was baby swimming during the same period. Parental atopy reflects a history of maternal or paternal asthma, hayfever or eczema. RESULTS: The prevalence of recurrent respiratory tract infections was higher (12.3%) among children who took part in baby swimming than among those who did not (7.5%). The prevalence of recurrent respiratory tract infections during the first year of life was 5.6% and 10.5%, respectively, in children of parents without and with atopy, whereas the prevalence of baby swimming was 5.6% and 5.1%, respectively, in the two groups. Stratified analysis using parental atopy as strata showed that the increased risk of recurrent respiratory tract infections was only present among children of parents with atopy [adjusted odds ratio (aOR) 2.08, 95% confidence interval (95% CI) 1.08-4.031. A similar trend was present for otitis media (aOR 1.77, 95% CI 0.96-3.25). CONCLUSION: The results of this study suggest that baby swimming and infant respiratory health may be linked. The findings need to be examined in a longitudinal study.

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O'Byrne P.M. et al. *Budesonide/formoterol combination therapy as both maintenance and reliever medication in asthma.* Am J Respir Crit Care Med. 2005; 171(2) : 129-36.p Abstract: Asthma control is improved by combining inhaled corticosteroids with long-acting beta2-agonists. However, fluctuating asthma control still occurs. We hypothesized that in patients receiving low maintenance dose budesonide/formoterol (bud/form), replacing short-acting beta2-agonist (SABA) reliever with as-needed bud/form would provide rapid symptom relief and simultaneous adjustment in antiinflammatory therapy, thereby reducing exacerbations. In this double-blind, randomized, parallel-group study, 2,760 patients with asthma aged 4-80 years (FEV1 60-100% predicted) received either terbutaline 0.4 mg as SABA with bud/form 80/4.5 microg twice a day (bud/form + SABA) or bud 320 microg twice a day (bud + SABA) or bud/form 80/4.5 microg twice a day with 80/4.5 microg as-needed (bud/form maintenance + relief). Children used a once-nightly maintenance dose. Bud/form maintenance + relief prolonged time to first severe exacerbation (p < 0.001; primary endpoint), resulting in a 45-47% lower exacerbation risk versus bud/form + SABA (hazard ratio, 0.55; 95% confidence interval, 0.44, 0.67) or bud + SABA (hazard ratio, 0.53; 95% confidence interval 0.43, 0.65). Bud/form maintenance + relief also prolonged the time to the first, second, and third exacerbation requiring medical intervention (p < 0.001), reduced severe exacerbation rate, and improved symptoms, awakenings, and lung function compared with both fixed dosing regimens.

- O'Callaghan C. et al.** *Salbutamol dry powder inhaler: efficacy, tolerability, and acceptability study.* *Pediatr Pulmonol.* 2002; 33(3) : 189-93.p **Abstract:** Dry powder inhaler (DPI) devices are frequently used in children over 5 years of age in order to avoid coordination difficulties often seen with the use of pressurized metered dose inhalers (pMDI). This study assessed the efficacy, tolerability, and acceptability of salbutamol delivered via two delivery systems, in a population of pediatric patients. The primary aim of the study was to investigate the bronchodilator efficacy of a single dose (100 microg) of salbutamol administered via a dry powder inhaler (Clickhaler) compared to a similar dose administered by a pressurized metered dose inhaler via a large-valved holding chamber (VHC) to children with asthma. The study comprised two phases: the first comparator phase, followed by an open 4-week treatment period. Sixty-one children with a mean (SD) age of 11.3 years (2.9) (range, 6-17) and mild or moderate asthma completed the study. The primary efficacy endpoint, forced expiratory volume in 1 sec (FEV1), indicated that there was no clinically or statistically significant difference between the bronchodilator effects of salbutamol delivered via either device, with a maximum posttreatment percentage change in FEV1 (SD) of 12.4% (10.0) and 14.15 (9.3) for Clickhaler and pMDI plus VHC, respectively. Most patients rated the Clickhaler as easy to use (97%) and liked the device (84%). Both treatments were well-tolerated. These results support the suitability of salbutamol Clickhaler as an acceptable, well-tolerated, and effective alternative to a pMDI plus VHC in mild to moderate asthmatic children over age 6 years.
- O'Connell E.J.** *Review of the unique properties of budesonide.* *Clin Ther.* 2003; 25 Suppl C : C42-60.p **Abstract:** BACKGROUND: The aim of inhaled corticosteroid (ICS) therapy for asthma is to attain high therapeutic activity in the airways while keeping the risk of systemic adverse effects relatively low. However, the physicochemical and pharmacokinetic properties of various ICSs affect this ratio, thereby influencing their ability to fulfill the requirements of an ideal agent. OBJECTIVE: This article reviews the physical and pharmacokinetic properties of budesonide, outlining how they, safety data, and use of different inhalation devices enable budesonide to meet many of the clinical requirements of an ideal ICS for the treatment of asthma. RESULTS: ICS efficacy is influenced by lipophilicity, lung deposition, and retention in airway tissue, whereas the rate of elimination determines systemic activity. Budesonide is retained in the airways to a greater extent than other ICSs because of an esterification process that increases its lipophilicity. The prolonged retention of budesonide in the airways may contribute to its efficacy when administered QD. In addition to a pressurized metered-dose inhaler, budesonide is available as a dry-powder inhaler and in nebulized form, which can be used by asthma patients aged > or =6 months. CONCLUSIONS: When combined with delivery devices suitable for a spectrum of patient groups, the physical and pharmacokinetic properties of budesonide lend it many of the characteristics of an ideal ICS, including favorable efficacy and tolerability profiles.
- O'connor G.T. et al.** *Airborne fungi in the homes of children with asthma in low-income urban communities: The Inner-City Asthma Study.* *J Allergy Clin Immunol.* 2004; 114(3) : 599-606.p **Abstract:** BACKGROUND: Despite growing evidence of the importance of exposure to fungi as an environmental risk factor for asthma, few data have been reported on the exposure to airborne fungi of asthmatic children living in US inner cities. OBJECTIVE: We sought to examine the spectrum and concentration of fungi in the air inside and outside of the homes of mold-sensitive children with asthma living in US cities. We also analyzed the relationship of the concentration of fungi in indoor air to home characteristics. METHODS: We performed a home environmental survey and measured the concentrations of culturable airborne fungi inside and outside the homes of 414 mold-sensitive children with asthma in 7 urban communities. RESULTS: The airborne fungi encountered indoors generally paralleled those found outdoors, and the similarities between communities were more striking than the differences. Indoor fungal concentrations were correlated with outdoor concentrations measured on the same day, suggesting the need to adjust for the outdoor concentration in analyses by using the indoor concentration as an indicator of the relative moldiness of a home. The concentration of fungi in indoor air in excess of outdoor air—that is, the indoor-outdoor difference—was significantly related to home characteristics, including dampness, having a cat, and cockroach infestation. CONCLUSION: Mold-sensitive children with asthma living in urban communities across the US are exposed to airborne fungi in indoor and outdoor air. The concentrations of fungi are higher in homes with dampness problems, cockroach infestation, and cats. The indoor-outdoor difference in the concentration of airborne fungi may provide a valuable metric for investigations of the role of fungal exposure as a risk factor for asthma.
- O'Connor S.L. et al.** *Measuring adherence with the Doser CT in children with asthma.* *J Asthma.* 2004; 41(6) : 663-70.p **Abstract:** Non-adherence with prescribed asthma treatment causes compromised treatment effectiveness, including greater morbidity, mortality, and health care utilization costs. As a result, there is an increasing interest in measuring patient adherence behaviors. Electronic monitoring devices offer a promising method for assessing patient adherence behavior patterns. The reliability of the Doser Clinical Trials (CT) (Meditrack Products, Hudson, MA), an inexpensive, pressure-actuated device that monitors metered-dose inhaler (MDI) usage, was evaluated in a field study of outpatient pediatric asthmatics. Canister weight and various Doser CT measures of patient medication use were compared to determine the reliability and usefulness of the device. Doser CTs were dispensed to 16 research subjects for use on corticosteroid MDIs over a period of several months. One Doser CT per month was dispensed to each subject. Doser CTs were collected at 30-60 day intervals, with a total of 61 months of Doser CT data obtained across the subjects. MDI canister weights were monitored for a subset of 6 subjects. Usable Doser CT data were summarized and average adherence estimates were computed. Adherence estimates differed from one another and the adherence estimate, as measured by canister weight, was significantly higher than each Doser CT estimate. However, overall, the Doser CT showed adequate reliability as evidenced by high correlations among the Doser CT estimates of adherence and the existing gold standard of canister weight. The Doser CT is likely to be useful for monitoring MDI use in clinical care and research, potentially providing greater accuracy than the standard of canister weight.
- Oberle D. et al.** *Childhood asthma and continuous exposure to cats since the first year of life with cats allowed in the child's bedroom.* *Allergy.* 2003; 58(10) : 1033-6.p **Abstract:** BACKGROUND: There are controversial data as to interdependencies of exposure to furred pets in infancy and the prevalence of asthma and hay fever in children. Does the timing, intensity and type of pet exposure matter? METHODS: Cross-sectional questionnaire data on 8216 German schoolchildren aged 5-7 years not living on a farm in ten rural districts in Bavaria in 1997 were analysed. The diagnosis of asthma and hay fever was ascertained with the International Study of Asthma and Allergies in Childhood (ISAAC) core questions. Wheeze and asthma were classified as 'atopic' in children who also had hay fever or atopic dermatitis. Prevalence and intensity of exposure to pets in the first year of life and at present were assessed via questionnaire. RESULTS: Although the study was of considerable size we found no convincing association between atopic disease and pet exposure in general. Exposure to cats from the first year of life to school entry, however, was associated with a reduced prevalence of atopic asthma, if cats were allowed to be in the child's bedroom: no case of atopic asthma in 296 children exposed and an aOR 0.11 (95% CI:0.01-0.52) for atopic wheeze in the last 12 months. CONCLUSIONS: Allowing cats to be in the child's bedroom from the first year of life onwards

may be an indicator of intensive exposure to cats and appears to prevent the development of childhood asthma.

Obihara C.C. et al. *The association of prolonged breastfeeding and allergic disease in poor urban children.* Eur Respir J. 2005; 25(6) : 970-7.p **Abstract:** The fact that breastfeeding may protect against allergic disease remains controversial, with hardly any reports from developing countries. This study investigated the association between allergic disease in children and prolonged breastfeeding. Data were collected from a 15% random sample of households from two poor suburbs of Cape Town, South Africa. Parents completed a validated International Study on Asthma and Allergies in Childhood questionnaire on allergic diseases for children aged 6-14 yrs. Other questions included breastfeeding duration, maternal smoking and parental allergy. Results were adjusted for possible confounders and for possible clustering within the household. Out of the 861 children included in the study, allergic disease in general, and hay fever in particular, were significantly less frequent in those with prolonged (> or =6 months) breastfeeding. There was a significant linear inverse association between breastfeeding duration and allergic disease in children without allergic parents, but not in children with an allergic predisposition. In conclusion, these results from a developing country suggest a protective effect of prolonged breastfeeding on the development of allergic disease, particularly hay fever, in children born to nonallergic parents. This protective effect was not found in children with an allergic predisposition.

Ochsner A.K. et al. *Increasing awareness of asthma and asthma resources in communities on the southwest border.* J Am Acad Nurse Pract. 2002; 14(5) : 225-30, 232, 234.p **Abstract:** PURPOSE: To provide outpatient asthma education for children and families along the southwest border of the U.S. and to study the effectiveness of a southwest border hospital's in-house asthma educational program. DATA SOURCES: (1) "Increasing the Knowledge Base of Asthmatics and Their Families through Asthma Clubs along the Southwest Border." (2) American Lung Association. (3) National Institutes of Health, National Heart, Lung and Blood Institute. (4) Referrals from a southwest border hospital. CONCLUSIONS: Only two of 23 patients referred for asthma follow-up were readmitted to hospital and/or emergency care during the following year. Large group teaching pretest-posttest score means for 3,429 fourth and fifth grade students revealed a 23% increase in asthma knowledge. Small follow-up groups of students received in-depth asthma education. IMPLICATIONS FOR PRACTICE: Effectiveness of hospital inpatient asthma education combined with outpatient family follow-up was supported. An additional finding was that southwest border families are more receptive to visits arranged with a school nurse in their children's school than to home visits from primary care clinic nurses.

Oddy W.H. et al. *Ratio of omega-6 to omega-3 fatty acids and childhood asthma.* J Asthma. 2004; 41(3) : 319-26.p **Abstract:** Asthma is a leading cause of morbidity for children and is a major public health problem in Australia. Ecological and temporal data suggest that dietary factors may have a role in recent increases in the prevalence of asthma. AIM: The aim of conducting this study was to investigate whether childhood asthma was associated with the ratio of omega 6 (n-6) to omega 3 (n-3) fatty acids in the diet (n-6:n-3). METHOD: The Western Australian Pregnancy Cohort Study is a prospective birth cohort of 2602 children. Using a nested case-control cross-sectional study design within this cohort, a group of children were identified as cases with current asthma at 6 or at 8 years of age or as controls with no asthma at 6 or at 8 years. Dietary details including n-6 and n-3 fatty acid intake data were collected by parent response to a questionnaire when the children were 8 years old. Logistical regression was used to compare quartiles of n-6:n-3 intake in cases and controls. Adjustment was made for covariates: gender, gestational age, breastfeeding, older siblings, maternal smoking

during pregnancy, maternal age, maternal asthma, child's current age in months, body mass index, total energy intake, and antioxidant intake (vitamins A, C, E, and zinc). RESULTS: A response rate of 83% was achieved by providing complete data from 335 children [49% cases with current asthma (n = 166), 51% controls (n = 169)]. Following adjustment for covariates the association between the ratio of n-6:n-3 fatty acids and risk for current asthma was statistically significant (p = 0.022). CONCLUSION: We found evidence for a modulatory effect of the dietary n-6:n-3 fatty acid ratio on the presence of asthma in children. Our results provide evidence that promotion of a diet with increased n-3 fatty acids and reduced n-6 fatty acids to protect children against symptoms of asthma is warranted.

Oddy W.H. et al. *The effects of respiratory infections, atopy, and breastfeeding on childhood asthma.* Eur Respir J. 2002; 19(5) : 899-905.p **Abstract:** 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< or =0.0005) and atopic children (OR 9.00, p< or =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.

Oddy W.H. et al. *Maternal asthma, infant feeding, and the risk of asthma in childhood.* J Allergy Clin Immunol. 2002; 110(1) : 65-7.p **Abstract:** 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.

Oddy W.H. et al. *Breastfeeding, body mass index, and asthma and atopy in children.* *Adv Exp Med Biol.* 2004; 554 : 387-90.p

Oddy W.H. et al. *The relation of breastfeeding and body mass index to asthma and atopy in children: a prospective cohort study to age 6 years.* *Am J Public Health.* 2004; 94(9) : 1531-7.p **Abstract:** **OBJECTIVES:** We investigated the relationship between breastfeeding, asthma and atopy, and child body mass index (BMI). **METHODS:** From a prospective birth cohort (n = 2860) in Perth, Western Australia, 2195 children were followed up to age 6 years. Asthma was defined as doctor-diagnosed asthma and wheeze in the last year, and atopy was determined by skin prick test of 1596 children. Breastfeeding, BMI, asthma, and atopy were regressed allowing for confounders and the propensity score for overweight. **RESULTS:** Using fractional polynomials, we found no association between breastfeeding and overweight. Less exclusive breastfeeding was associated with increased asthma and atopy, and BMI increased with asthma. **CONCLUSIONS:** Less exclusive breastfeeding leads to increases in child asthma and atopy and a higher BMI is a risk factor for asthma.

Oermann M.H. et al. *Evaluation of asthma websites for patient and parent education.* *J Pediatr Nurs.* 2003; 18(6) : 389-96.p **Abstract:** The purpose of this study was to evaluate the quality of websites on asthma for patient and parent education. Seventy websites were evaluated based on the Health Information Technology Institute (HITI) criteria; eight core content criteria from the National Heart, Lung, and Blood Institute guidelines; and readability. The ten best websites for asthma education were identified for patient teaching and educating parents about asthma.

Oh J.W. et al. *Urine leukotriene E and eosinophil cationic protein in nasopharyngeal aspiration from young wheezy children.* *Pediatr Allergy Immunol.* 2005; 16(5) : 416-21.p **Abstract:** Respiratory syncytial virus (RSV) infection is a risk factor for the development of asthma. It is very hard to distinguish bronchiolitis with respiratory virus infection from allergic asthma at first wheezing attack in early childhood. To distinguish wheezing children with RSV bronchiolitis from asthmatic children, we measured leukotriene E(4)(LTE(4)) in urine and ECP in nasopharyngeal aspiration (NPA) at first day of admission with wheezing attack. Thirty-two non-atopic children younger than the age of 3 yr with RSV induced bronchiolitis, 35 atopic asthmatic children with/without respiratory viral infection, and 23 children who exhibited no evidence of atopy, asthma, or virus infections as controls were selected in this study. We measured urinary LTE(4) and ECP level in NPA from subjects. Urinary LTE(4) concentrations in children with asthma were significantly higher than urinary LTE(4) in bronchiolitis and in controls (240.8 +/- 129.8 vs. 162.8 +/- 73.9 vs. 85.1 +/- 31.6 pg/ml). Children with RSV infection demonstrated higher urinary LTE(4) levels compared to children without RSV infection among asthmatic children. ECP in NPA was significantly correlated with urinary LTE(4) (r = 0.57, p < 0.01) in children entered this study who had detectable levels for both LTE(4) and ECP. In summary, Urinary LTE(4) concentrations may be suggested to useful mediators for differential diagnosis of wheezy diseases in early childhood. RSV infection also is associated with synergizing LT biosynthesis and this study demonstrated ECP in NPA was significantly correlated with urinary LTE(4) and may suggest that cysteinyl leukotriene initiate the production of ECP in early childhood, which could contribute to the development of wheeze.

Ones U. et al. *Prevalence of mycoplasma pneumoniae infections in asthmatic children in Istanbul, Turkey.* *J Trop Pediatr.* 2003; 49(3) : 186.p

Ordenez M.P. et al. *[Congenital malformations and chronic diseases of the mother. Latin American Collaborative Study of Congenital Malformations (ECLAMC) 1971-1999].* *Rev Med Chil.* 2003; 131(4) : 404-11.p **Abstract:** **BACKGROUND:** Several maternal diseases, such as diabetes mellitus or high blood pressure, are associated with a higher risk for fetal or neonatal problems. **AIM:** To study the association between chronic diseases of the mother and congenital malformations. **MATERIAL AND METHODS:** Review of the records of the Latin American Collaborative Study of Congenital Malformations (ECLAMC) at the University of Chile Clinical Hospital. A sample of 383 mothers with a chronic disease was compared with 297 healthy mothers. The presence of congenital malformations in the newborns was studied. The odds ratio (OR) of a mother to have a child with a congenital malformation was calculated. **RESULTS:** Mothers with bronchial asthma, diabetes mellitus, hypertension and hypothyroidism had an OR over 1 of having a child with a congenital malformation. No association between maternal obesity and offspring malformations was observed. Offspring of diabetic mothers had 8.95 times more probabilities of having a major malformation and 4.95 times more probabilities of having a minor defect. **CONCLUSIONS:** Offspring of mothers with diabetes mellitus, bronchial asthma, hypertension or hypothyroidism have a higher risk of presenting a congenital malformation, when compared with offspring of healthy mothers.

Ortega A.N. et al. *Impact of site of care, race, and Hispanic ethnicity on medication use for childhood asthma.* *Pediatrics.* 2002; 109(1) : E1.p **Abstract:** **OBJECTIVE:** To understand the importance of source of care and other factors that influence differences in asthma medication use by race and Hispanic ethnicity. **METHODS:** The Childhood Asthma Severity Study provided 12-month, retrospective, parent-reported questionnaire data on a monthly basis for children ages <=12 years in a community sample of 1002 children and their families from Connecticut and Massachusetts. Medications considered included cromolyn, beta2-agonist, inhaled steroids, anticholinergics, theophylline, and systemic steroids. Information was available on demographics, insurance status, symptom severity, primary care contact, and provider practice types. **RESULTS:** Black and Hispanic children received fewer beta2-agonists, and Hispanic children received fewer inhaled steroids than white children after adjusting for patients' race, age, gender, insurance status, symptom severity, number of primary care visits for asthma, number of urgent visits to the regular provider, family income, maternal education, and site of care. When multivariate analyses were restricted to patients in private practice, the significant association between Hispanic ethnicity and low inhaled steroid use persisted, whereas differences in beta2-agonist use by race and ethnicity changed little but became nonsignificant. **CONCLUSION:** Even within private practices, patients' race and ethnicity are associated with clinician nonadherence to national guidelines. Programs to eliminate these disparities will need both to focus on site of care and to intervene at the provider and patient levels to be successful.

Ortega A.N. et al. *Parental mental health, childhood psychiatric disorders, and asthma attacks in island Puerto Rican youth.* *Ambul Pediatr.* 2004; 4(4) : 308-15.p **Abstract:** **OBJECTIVE:** Previous research documents an association of poor parental mental health with asthma in children. This study aims to determine whether the associations between parental mental health problems and childhood asthma attacks persist after controlling for childhood anxiety and depression and other confounding factors. **DESIGN/METHODS:** A community household sample of youth ages 4 to 17 years and their primary caregivers from the US Commonwealth of Puerto Rico was studied to determine the associations between parental mental health and childhood asthma attacks. Regression models that predicted asthma attacks in youth controlled for parental mental health problems, childhood anxiety and depression, zone of residence, and parents' age, education, and perception of poverty. **RESULTS:** After adjusting for children's depressive and anxiety disorders as well as

other important confounders, associations between parental depression, suicide attempts, ataque de nervios, and history of mental health treatment and asthma attacks in offspring, by parental report, persisted. Additionally, the frequency of parental mental health problems was associated with children's asthma attacks. **CONCLUSION:** Parents with mental health problems were more likely to report histories of asthma attacks in their children compared with parents without mental health problems in Puerto Rico. These associations were not attributable to internalizing disorders in youth but persisted independent of childhood psychopathology and other confounding factors. Clinicians and researchers should recognize the relations between poor parental mental health and childhood asthma and explore the potential role of family psychosocial and behavioral factors related to the manifestation of the disease.

Ortega A.N. et al. *Association of psychiatric disorders and different indicators of asthma in island Puerto Rican children.* Soc Psychiatr Epidemiol. 2003; 38(4) : 220-6.p **Abstract:** **BACKGROUND:** We examined the relationship between three different indicators of childhood asthma (asthma diagnosis, ever had an asthma attack, and asthma hospitalization) and having any psychiatric disorder, comorbid disorders, or specific disorders. Three study hypotheses were examined: 1) there will be subject variability in responses to the asthma indicators; 2) there will be different observed associations between the three asthma indicators and psychiatric disorders; and 3) maternal mental health, family income, and maternal education will confound the associations between childhood asthma and psychiatric disorders. **METHOD:** Data were drawn from a community-based, random sample of 1,891 island Puerto Rican children aged 4-17 years. Information was collected through direct interview with children and adolescents and their primary caretakers. The Diagnostic Interview Schedule for Children (DISC) was used to determine DSM-IV diagnoses. **RESULTS:** Thirty-two percent of the children had been diagnosed with asthma but only 22 % had ever experienced an asthma attack. Seventeen percent of the children had been hospitalized for asthma. Having been hospitalized for asthma was not associated with any of the psychiatric disorders, having a diagnosis was associated with some of the disorders, and having experienced an asthma attack was associated with almost all the disorders, after controlling for family income and maternal education and mental health. **CONCLUSIONS:** Determining and measuring asthma may be difficult because of confusion and differing perceptions of what constitutes asthma or an asthma attack. Future studies should consider the problems in capturing perceptions of asthma and severity in Puerto Rican children and should continue to explore the relationship between asthma and mental illness.

Ortiz G. et al. *The effects of inhaled albuterol and salmeterol in 2- to 5-year-old asthmatic children as measured by impulse oscillometry.* J Asthma. 2002; 39(6) : 531-6.p **Abstract:** The functional assessment of the response to bronchodilators in 2- to 5-year-old asthmatic children is technically difficult. For this reason, there have been no reports on the effects of long-acting bronchodilators, such as salmeterol, in this age group. Of the several techniques available for measuring resistance to airflow, forced oscillation remains the most adaptable to young children and the most practical for research and clinical use. In this study we used the Jaeger MasterScreen Impulse Oscillometry System to assess the response of 2 to 5 year-old asthmatic children to an inhaled long-acting bronchodilator, salmeterol, by comparing it to the effect of a standard dose of the short-acting bronchodilator, albuterol. We performed a placebo-controlled, randomized, crossover study in 10 children aged 2 to 5 years who had a history of physician-diagnosed asthma and who were not on regular controller therapy. At weekly intervals after baseline measurements of reversibility, each child received two inhalations from an albuterol metered-dose inhaler (MDI) with a spacer (200 microg), or placebo MDI with spacer, or two inhalations from a salmeterol MDI (50 microg), or 50 microg from a salmeterol

Diskus. Measurements were obtained at 5, 30, 60, 360, and 540 min, the last time interval only on the salmeterol days. Based on previous studies, total respiratory system reactance at 5 Hz (X5), calculated by the MasterScreen computer from mouth pressure and flow data, was used as the primary efficacy variable. The mean intra-individual variability in X5 was 10.5% (range 3.6% to 17.9%). The mean (SE) changes from baseline X5 at each time point were as follows: for placebo, 9.6 (3.0), 10.1 (2.6), 5.1 (2.9), 6.1 (3.5), $p=0.36$ vs. baseline; after treatment with albuterol, 32.7 (3.8), 53.9 (1.2), 47.3 (5.4), 18.1 (5.8), $p<0.01$ vs. baseline at all time points; after salmeterol MDI, 16 (6.4), 28.9 (5.2), 32.7 (3.9), 34.6 (4.4), 31.2 (4.8), $p<0.05$ at 60, 360, and 540 min; and after salmeterol Diskus, 16.4 (4.0), 16.9 (6.6), 27.8 (5.9), 28.6 (5.6), 33.8 (4.0), $p<0.05$ at 540 min. No significant adverse events or electrocardiographic changes were noted at any time. Impulse oscillometry is an acceptable method of assessing airway responses to bronchoactive drugs in this age group. Compared to albuterol and to its effect in older children and adults, the response to salmeterol Diskus appears to be somewhat blunted in this age group. The MasterScreen system is well suited for pharmacodynamic studies and clinical investigations in pre-school-aged children.

Oruwariye T. et al. *Do school-based health centers provide adequate asthma care?* J Sch Health. 2003; 73(5) : 186-90.p **Abstract:** School-based health centers (SBHCs) are increasingly charged with providing primary care services including asthma care. This study assessed SBHC provider adherence to the National Heart, Lung, and Blood Institute (NHLBI) asthma care guidelines and the association among provider adherence, patient characteristics, and asthma outcomes. A cross-sectional study design was used to assess SBHC chart data from 415 children with asthma attending four inner-city elementary schools (K-5) in the Bronx, NY. Asthma symptoms, peak flow use, follow-up visits, and referrals to asthma specialists were documented in the charts of 60%, 51%, 22%, and 3% of subjects, respectively. Thirty-three percent of charts had SBHC clinician-documented severity classifications, of which 70% had appropriate medications prescribed. Asthma education and an asthma plan were documented in 18% and 10% of charts, respectively. Environmental triggers and tobacco exposures were documented in 71% and 49% of charts, respectively. Older children (> 8 years) were more likely to have documentation of peak flow use for asthma management, asthma education, follow-up visits, and written asthma plans, whereas younger children (< 8 years) were more likely to miss more days of school (all $p < .05$). Overall, provider adherence to NHLBI guidelines was inadequate, with adherence somewhat better for older children.

Osborn T.M. et al. *The PEAK study: does pharmaceutical care make a difference?* J Am Pharm Assoc (Wash DC). 2003; 43(5) : 548, 550.p

Osborne M. et al. *The epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) study.* Ann Allergy Asthma Immunol. 2004; 92(1) : 3-4.p

Oymar K. *High levels of urinary eosinophil protein X in young asthmatic children predict persistent atopic asthma.* Pediatr Allergy Immunol. 2001; 12(6) : 312-7.p **Abstract:** Levels of urinary eosinophil protein X (U-EPX) and eosinophil counts were measured in 32 children (12-36 months of age) who were hospitalized for acute asthma, and the U-EPX levels were measured in 20 healthy children of the same age. The ability of these parameters to predict persistent asthma (at least one wheezing episode during the last 6 months) and atopic asthma (a positive skin-prick test [SPT]), was evaluated at a follow-up 2 years later. On admission, levels of U-EPX were higher in children with asthma (median: 120 microg/mmol of creatinine; quartiles: 67-123 microg/mmol of creatinine) than in controls (60 microg/mmol of creatinine, 38-74 microg/mmol of creatinine; $p<0.001$). The U-EPX level was higher in those with persistent atopic

asthma at follow-up (173 microg/mmol of creatinine, 123-196 microg/mmol of creatinine, n = 16), than in those with persistent non-atopic asthma (73 microg/mmol creatinine, 46-105 microg/mmol of creatinine, n = 8; p < 0.05), and higher than in those with transient asthma (no symptoms at follow-up) (106 microg/mmol creatinine; 42-167 microg/mmol of creatinine, n = 8; p < 0.05). By multiple logistic regression analysis, U-EPX was the only parameter able to predict persistent atopic asthma; eosinophil counts, parental atopy, age or gender could not. Parental atopy was the only parameter predictive for persistent asthma, regardless of atopic status. In conclusion, levels of U-EPX, but not eosinophil counts, measured in young children hospitalized with acute asthma can predict the persistence of atopic asthma 2 years later.

Ozbek Z. et al. *Rapid healing of vernal shield ulcer after surgical debridement: A case report.* *Cornea.* 2006; 25(4) : 472-3.p **Abstract:** **PURPOSE:** This study was designed to report a patient with a vernal shield ulcer that did not respond to medical therapy but healed in 1 week after surgical debridement of the ulcer base. **METHODS:** Case report and literature review. **RESULTS:** A 12-year-old girl with a history of asthma and eczema was seen with a 5.7- x 5.7-mm corneal epithelial defect in the right eye. Her uncorrected visual acuity was 20/200 OD and 20/70 OS. Slit-lamp examination revealed giant papillae on the tarsal conjunctivae, diffuse punctate epitheliopathy, and a thick mucoid discharge in both eyes. A diagnosis of vernal keratoconjunctivitis both eyes (OU) with a shield ulcer OD was made and prednisolone 1% was started 4 times per day OD. Topical ofloxacin 0.3% 3 times per day and topical cyclosporine 0.05% every 2 hours were added OD 2 days later. On minimal improvement in the epithelial defect in 1 week, surgical debridement of the ulcer base was performed. The epithelial defect healed smoothly in 1 week with an underlying stromal scar and the uncorrected visual acuity improved to 20/70 OD at 1 month and 20/40 at 10 months. **CONCLUSION:** Corneal shield ulcers and plaques are rare but serious complications of vernal keratoconjunctivitis, which may be unresponsive to standard medical therapy. Surgical debridement is a fast and effective procedure yielding rapid healing of the ulcer and minimizing complications, such as infections.

Ozer A. et al. *Effect of BCG vaccination on cytokine mRNA expression in atopic children with asthma.* *Immunol Lett.* 2003; 86(1) : 29-35.p **Abstract:** **BACKGROUND:** To investigate whether a preexisting T(H2)-type immune response could be suppressed by BCG immunization in atopic children with asthma. **METHODS AND RESULTS:** We have used PCR to amplify reverse transcribed (RT) IFN-gamma and IL-5 mRNA expressed by peripheral blood mononuclear cells (PBMCs) in response to in vitro phytohemagglutinin A, purified protein derivative and Dermatophagoides pteronyssinus II stimulation from nine atopic children, both before and 8 weeks after BCG vaccination. We have demonstrated that IFN-gamma expression was induced in response to all stimulants (IFN-gamma/beta-actin) after the vaccination, whereas there was no expression before (P<0.001). Although there was a tendency to diminish in the expression of IL-5 mRNA in response to the stimulants, only PHA rendered a statistically significant decrease after the vaccination. **CONCLUSIONS:** These results provide some evidence of TH1 dominance after BCG administration in atopic children.

P

Pace E. et al. *Synergistic effects of fluticasone propionate and salmeterol on in vitro T-cell activation and apoptosis in asthma.* *J Allergy Clin Immunol.* 2004; 114(5) : 1216-23.p **Abstract:** **BACKGROUND:**

In asthma T cells are characterized by an increased activation state and by reduced apoptosis. **OBJECTIVE:** Because the clinical efficacy of inhaled corticosteroids combined with long-acting beta 2-agonists has been widely demonstrated in asthma, we studied, in vitro, the effect of fluticasone propionate (FP) and salmeterol alone and in combination on the activation and apoptosis of peripheral blood T cells (PBTs), on the expression of phosphorylated nuclear factor kappaB inhibitor (IkappaBalpha), and on the nuclear translocation of glucocorticoid receptor (GR) in PBTs from asthmatic subjects. **METHODS:** Apoptosis was evaluated on the basis of annexin V binding, whereas the expression of caspases 8 and 3 and phosphorylated IkappaBalpha, as well as the nuclear translocation of the GR, were evaluated by means of Western blot analysis. **RESULTS:** FP alone increases and salmeterol alone does not affect T-cell apoptosis. The combination of FP and salmeterol significantly increases PBT apoptosis in comparison with FP alone. FP at the lower concentration, when combined with salmeterol, is equivalent to FP at the higher concentration in inducing PBT apoptosis. The synergy in the induction of cell apoptosis is associated with more efficient activation of caspases 8 and 3. FP plus salmeterol is also able to synergistically reduce the expression of phosphorylated IkappaBalpha, thus limiting nuclear factor kappaB activation. The synergy was related to an increased nuclear translocation of the GR. **CONCLUSION:** This study shows that the combination of FP and salmeterol is able to control PBT activation in asthmatic patients more efficiently than FP alone and with a lower concentration of steroids.

Palacios-Nava M.E. et al. *[Health differences between male and female migrant agricultural workers in Sinaloa, Mexico].* *Salud Publica Mex.* 2004; 46(4) : 286-93.p **Abstract:** **OBJECTIVE:** To assess the differences in the prevalence of muscarinic and nicotinic type symptoms and the level of erythrocytic cholinesterase, prior to pesticide exposure, in male and female migrant agricultural workers. **MATERIAL AND METHODS:** A cross-sectional study was carried out in 2001 in Sinaloa State, Mexico, among 488 migrant workers. A questionnaire was applied and erythrocytic cholinesterase levels were measured before the beginning of the agricultural season. The differences by sex were compared using the "t" test for continuous variables and chi2 test for categorical variables. Prevalence odds ratios were also estimated. Statistical significance was assessed using p-values <0.05 and 95% confidence intervals. **RESULTS:** Significant differences were found by age, migration type, place of origin, education, and migration time (p=0.000). Women were six times more likely to have anemia and asthma, twice more likely to have parasites and respiratory and gastrointestinal diseases and 38% more likely to suffer from heart disease. They were also at greater prevalence in thirteen of nineteen investigated symptoms. The average cholinesterase level was within normal limits (4.22 U/ml +/- 0.77) and it was similar to the levels reported using the Magnotti method. **CONCLUSIONS:** The prevalence of symptoms, illnesses and cholinesterase levels found in this study may serve as baseline values for future comparisons of the health effects of pesticide exposure. The English version of this paper is available at: <http://www.insp.mx/salud/index.html>.

Palmer C.N. et al. *Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis.* *Nat Genet.* 2006; 38(4) : 441-6.p **Abstract:** Atopic disease, including atopic dermatitis (eczema), allergy and asthma, has increased in frequency in recent decades and now affects approximately 20% of the population in the developed world. Twin and family studies have shown that predisposition to atopic disease is highly heritable. Although most genetic studies have focused on immunological mechanisms, a primary epithelial barrier defect has been anticipated. Filaggrin is a key protein that facilitates terminal differentiation of the epidermis and formation of the skin barrier. Here we show that two independent loss-of-function genetic variants (R510X and 2282del4) in the gene encoding filaggrin (FLG) are very

strong predisposing factors for atopic dermatitis. These variants are carried by approximately 9% of people of European origin. These variants also show highly significant association with asthma occurring in the context of atopic dermatitis. This work establishes a key role for impaired skin barrier function in the development of atopic disease.

Palmer L.J. et al. *Ascaris lumbricoides infection is associated with increased risk of childhood asthma and atopy in rural China.* Am J Respir Crit Care Med. 2002; 165(11): 1489-93.p **Abstract:** There is growing international interest in the possible relationships between helminthic infection and allergic disease, although the nature of the relationships remains uncertain and controversial. The interrelationships of current and past infection with *Ascaris lumbricoides* and asthma and atopy were investigated in a cross-sectional sample of 2,164 children between the ages of 8 and 18 years from Anqing Province, China. The children were sampled from a larger family-based study of the genetics of asthma. The prevalence of either a history of or a positive stool examination for *Ascaris* was 24.5%. Asthma was defined for analytic purposes using previously validated, stringent criteria including airways responsiveness to methacholine. Independently of the other factors assessed, infection with *A. lumbricoides* was associated with increased risk of asthma ($p < 0.001$), an increased number of skin tests positive to aeroallergens ($p < 0.001$), and an increased dose-response slope to methacholine ($p = 0.003$). The association of sensitization to common aeroallergens with increased asthma risk was enhanced in those children infected with *Ascaris*, and such infection was associated with an increased risk of asthma independent of sensitization to aeroallergens in this selected population. These data suggest a complex relationship between ascariasis and susceptibility to childhood asthma among predisposed children that may involve an interaction with the immune response to inhaled aeroallergens.

Pampura A.N. *Prevalence of atopic diseases and the use of topical corticosteroids. Is there any connection?* Med Hypotheses. 2005; 64(3): 575-8.p **Abstract:** The prevalence of atopic diseases (atopic dermatitis, bronchial asthma, allergic rhinitis) has considerably increased for the last 40 years. This tendency has coincided with the beginning of the epoch of the use of the topical corticosteroids, which have a potent immunomodulation action. This fact itself as well as a number of research results has allowed to formulate the following hypothesis: the use of topical corticosteroids in children of early age contributes to the increase of prevalence of atopic diseases in the developed countries. The offered hypothesis can explain lower prevalence of atopic diseases in rural areas and in children from families with the anthroposophic life style. In other side this hypothesis also capable to give explanation of increased level of atopic diseases among people with high socioeconomic level and in children from 1 child families. It is of a note that corticosteroids use in developing countries is limited due to economic reasons and active use of complementary medicine. If the proposed hypothesis is correct, a revision of the therapeutic approaches is necessary concerning the attitude towards application of topical corticosteroids in children suffering from various forms of eczema. The direct proof of this hypothesis can be found during prospective studies.

Panditi S. et al. *Perception of exercise induced asthma by children and their parents.* Arch Dis Child. 2003; 88(9): 807-11.p **Abstract:** BACKGROUND: Exercise induced asthma (EIA) plays an important role in clinical evaluation. There has been little previous work validating EIA as reported directly by children and indirectly by their parents. AIMS: (1) To determine the strength of the association between children's symptoms of EIA and their physiological response to exercise in a laboratory setting. (2) To compare parents' perception of EIA with that of their children. (3) To seek factors influencing the perception of EIA. METHODS: Forty three asthmatic children and their parents answered a questionnaire, which included

measures of symptom perception in EIA using visual analogue (VAS) and Likert scales. The children underwent a standardised treadmill exercise challenge, using spirometry to measure the physiological outcome, after which they and their parents independently completed the symptom scores. Twenty four subjects agreed to return for a second visit, in order to assess repeatability. RESULTS: The VAS and Likert scales were highly correlated. Children's symptom perception as measured by change in VAS scores related weakly to change in FEV(1) after exercise, and was unaffected by confounding factors such as age, gender, medication, and habitual exercise. Parents' perception of symptoms was unrelated to any physiological measure. There was no significant relation between parent and child VAS scores after exercise, and there was poor agreement between the Likert scale scores after exercise. The repeatability of the perception of change in FEV(1) after exercise was poor for both parents and children. CONCLUSION: Physicians should obtain reports of EIA from children rather than parents, but be aware of their limited accuracy and repeatability.

Panickar J.R. et al. *Trends in deaths from respiratory illness in children in England and Wales from 1968 to 2000.* Thorax. 2005; 60(12): 1035-8.p **Abstract:** BACKGROUND: Childhood mortality has decreased markedly over the last three decades. A study was undertaken to determine trends in deaths from respiratory illness in children in England and Wales. METHODS: Mortality data collected by the Office for National Statistics were analysed. The data included all deaths registered from all causes in children aged between 28 days and 16 years in England and Wales from 1 January 1968 to 31 December 2000. The main outcome measures were overall and age-specific mortality rates due to all respiratory disorders and specific rates for pneumonia, asthma, cystic fibrosis (CF), and bronchiolitis. RESULTS: In children aged 1-16 years the overall mortality rate (per 100,000 children) declined from 49.9 in 1968 to 16.3 in 2000, and rates due to respiratory illness fell from 8.6 to 1.3. The proportion of all deaths caused by respiratory illness in children aged 28 days to 16 years fell from 30.8% in 1968 to 9.9% in 2000. In post-neonatal infants (aged 28-364 days), the "all cause" mortality rate fell from 592.8 in 1968 to 176 in 2000 and the rates due to respiratory illness fell from 280 to 22.8. In 2000, pneumonia, asthma and CF together accounted for 73% of all respiratory deaths in 1-16 year olds. In this age group, mortality rates per 100,000 for pneumonia fell from 4.22 to 0.57, for asthma from 0.83 to 0.25, and for CF from 0.66 to 0.12 between 1968 and 2000. Over the same period mortality rates for pneumonia in post-neonatal infants fell from 165 to 6.78 per 100,000 and for CF from 4.88 to 0.33. Bronchiolitis mortality rates per 100,000 in post-neonatal infants fell from 21.47 in 1979 to 1.82 in 2000. CONCLUSIONS: Mortality rates due to all respiratory illnesses in children have fallen markedly in the last three decades. This decline has been more rapid than the overall decline in childhood mortality and respiratory diseases are now responsible for a smaller proportion of deaths in children. These data could provide a foundation for assessing the impact on mortality of future health initiatives such as the introduction of a universal pneumococcal vaccination programme in England and Wales.

Panickar J.R. et al. *Intramuscular triamcinolone for difficult asthma.* Pediatr Pulmonol. 2005; 39(5): 421-5.p **Abstract:** We treated a selected group of children attending a difficult asthma clinic with intramuscular triamcinolone acetonide. This study retrospectively reviews markers of asthma severity in those who received one or more monthly doses for three periods: 1) 3 months preceding the first injection (pretreatment), 2) from the first injection to 1 month after the last injection (treatment period), and 3) 3 months after the treatment period (follow-up period). Severity markers during the treatment and follow-up periods were compared with the pretreatment period by paired t-test. Five children (5-13 years old) received a single dose, and 8 children (12-15 years old) received multiple doses. Multiple doses of triamcinolone ($n = 3-5$) were associated with a fall in the number of asthma exacerbations ($P <$

0.01) and hospital admissions ($P < 0.01$) in both the treatment and follow-up periods. A single dose reduced exacerbations ($P < 0.05$, treatment vs. pretreatment) but not hospital admissions. We conclude that intramuscular triamcinolone is a useful short-term therapy in difficult asthma. Whether its efficacy is due to improved compliance, or an improved anti-inflammatory profile compared with oral steroids, remains unclear.

Parapanissiou E. et al. *HLA antigens in Greek children with allergic bronchial asthma.* Tissue Antigens. 2005; 65(5) : 481-4.p
Abstract: The aim of our study was to investigate the genetic linkage between mite allergic bronchial asthma and HLA class I and II antigens and haplotypes. Sixty Greek children with allergic bronchial asthma due to mite sensitivity (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and their family members were typed for HLA class I and II antigens (total 263 subjects). One hundred and twenty-five healthy, unrelated Greek children without medical history of atopy were also typed as control group. Major histocompatibility complex class I and II gene analysis revealed that only HLA-DRB1*04 and HLA-DQA1*0301 alleles are possibly important factors in the development of atopic asthma in Greek children with sensitivity to mites. No significant differences among the HLA-DRB1*04 subtypes have been established. Transmission disequilibrium test revealed that no specific HLA-A, -B, -DRB1, -DQA1 and -DQB1 alleles were transmitted preferentially to the affected children. HLA-DQB1*0301-4 alleles were associated with high levels of total serum immunoglobulin E in affected children. The study of the HLA haplotypes failed to demonstrate any significant association between any extended or natural selection haplotype and mite allergic bronchial asthma in Greek children.

Park B.L. et al. *Interleukin 3 (IL3) polymorphisms associated with decreased risk of asthma and atopy.* J Hum Genet. 2004; 49(10) : 517-27.p
Abstract: Cytokines, having central functions in immunological and inflammatory process, are always expected to play important roles in the pathogenesis of various diseases, such as asthma. Genetic polymorphisms of those cytokine and cytokine receptor genes are the focus of genetic association studies. In an effort to identify gene(s) whose variant(s) are involved in the development of asthma, we examined the genetic effects of 19 single nucleotide polymorphisms in eight cytokine and cytokine receptor genes, including IL1A, IL1B, IL2, IL3, IL4, IL8, IL10, and IL5RA, on asthma and atopy. Nineteen single nucleotide polymorphisms in eight cytokine and cytokine receptor genes were genotyped using the single-base extension method in a Korean asthma cohort ($n = 723$). Logistic regression and multiple regressions were used for statistical analyses controlling for smoking, age, and gender as covariables. Genetic association analysis of polymorphisms revealed that one exonic (exon 1), IL3 + 79T > C (Ser27Pro), showed significant association with the risk of asthma and atopy. The Pro allele had shown dominant and protective effects on development of asthma in nonatopic subjects ($P = 0.002$) and also showed significant association with the risk of atopy in normal control subjects ($P = 0.007$). This information about the genetic association of important genes with asthma might provide valuable insights into strategies for the pathogenesis of asthma and atopy.

Patel B.D. et al. *Childhood smoking is an independent risk factor for obstructive airways disease in women.* Thorax. 2004; 59(8) : 682-6.p
Abstract: OBJECTIVE: To assess whether starting to smoke in childhood increases the risk of obstructive airways disease (OAD) in adult life. METHODS: A retrospective cohort analysis was undertaken of 12 504 current and ex-smokers in the EPIC-Norfolk cohort. The main exposure was starting to smoke during childhood (age <16 years). Three definitions of OAD were used: doctor diagnosed asthma, doctor diagnosed bronchitis/emphysema, and "any OAD" (doctor diagnosed asthma or bronchitis/emphysema, or taking medication used in the treatment of OAD). RESULTS: Childhood

smokers had significantly more pack years of exposure and poorer lung function than subjects who started to smoke in adulthood (≥ 16 years). Compared with starting in adulthood, starting to smoke in childhood was associated with a greater risk of bronchitis/emphysema in female smokers (OR 1.79, 95% CI 1.25 to 2.56) and ex-smokers of both sexes (OR 1.29, 95% CI 1.07 to 1.55 in men and OR 1.40, 95% CI 1.05 to 1.85 in women), and of "any OAD" in female smokers (OR 1.72, 95% CI 1.24 to 2.38) and male and female ex-smokers (OR 1.20, 95% CI 1.03 to 1.40 in men and 1.34, 95% CI 1.07 to 1.57 in women). After adjustment for pack years, childhood smoking was associated with poorer lung function (FEV₁) 92.3% predicted in adult smokers and 89.5% in childhood smokers, $p = 0.03$) and a greater risk of bronchitis/emphysema (adjusted OR 1.55, 95% CI 1.08 to 2.24) and for "any OAD" (OR 1.54, 95% CI 1.10 to 2.13) in female smokers but not in male and female ex-smokers. CONCLUSION: Starting to smoke in childhood is associated with an increased risk of airways disease because of the extra pack years smoked. In women, childhood smoking is itself an independent risk factor for the development of airways disease.

Patel N. et al. *Does adding ipratropium to salbutamol (albuterol) help children with asthma?* Arch Dis Child. 2001; 85(5) : 432-3.p

Patel N.J. et al. *Concurrent laryngeal abnormalities in patients with paradoxical vocal fold dysfunction.* Otolaryngol Head Neck Surg. 2004; 130(6) : 686-9.p
Abstract: OBJECTIVE: Our goal was to investigate the presence of laryngeal abnormalities in patients with paradoxical vocal fold dysfunction (PVFD). STUDY DESIGN AND SETTING: A retrospective chart review was performed of patients referred for evaluation of paradoxical vocal fold dysfunction between July 2002 and December 2002. The patients completed questionnaires at the time of the office visit. Data collected from the medical record included age, gender, duration of symptoms before evaluation, asthma, gastroesophageal reflux symptoms, and laryngoscopic findings. Exercise stress test was performed when suitable. The diagnosis of PVFD was made based on patient history and laryngoscopy. RESULTS: Thirty patients were identified. There was a 27:3 (90%) female predominance, and mean age of presentation at was 28 years (range, 12 to 67 years). The median time from the onset of respiratory symptoms to diagnosis was 4.5 years (range, 0.5 to 30 years). Of the 30 patients, 17 (56%) had asthma, 16 had laryngeal findings suggestive of gastroesophageal reflux disease, 4 (12%) had laryngoscopic findings of chronic laryngitis, and 10 (33%) had additional findings, including laryngomalacia, vocal fold motion impairment, sulcus vocalis, nodules, and subglottic stenosis, mostly in the exercise-induced group. CONCLUSIONS: Concomitant laryngeal abnormalities are present in a many patients with PVFD, particularly in those with exercise-induced symptoms. Laryngoscopy is important in the management of these patients.

Patel R. et al. *Ten puffs too many.* Arch Dis Child. 2004; 89(12) : 1129.p

Patriarca G. et al. *Sublingual desensitization: a new approach to latex allergy problem.* Anesth Analg. 2002; 95(4) : 956-60, table of contents.p
Abstract: The prevalence of latex allergy has rapidly increased. Clinical manifestations range from contact urticaria-angioedema and rhinoconjunctivitis to more severe bronchial asthma and anaphylactic shock. The only effective therapy is desensitization. We studied 24 patients allergic to latex: 12 of them underwent a rush (4-day) sublingual desensitization to latex, performed by putting increasing doses of latex extract under the patients' tongues for 3 min every 20 min, followed by a maintenance therapy. The other 12 patients were considered controls. The sublingual rush desensitization protocol was successfully completed in all patients with no side effects. After 3 mo, all patients underwent an allergological evaluation, which showed a significant improvement of symptoms scores after challenges in the treated group as compared with the controls. All the desensitized patients can now wear latex

gloves and undergo medical procedures without any symptoms. IMPLICATIONS: We present 12 cases of latex allergy in patients who underwent desensitization by a sublingual exposure protocol. This study provides evidence that a safe therapeutic approach to latex allergy is possible.

Paulley J.W. *Asthma attacks and thunderstorms.* QJM. 2002; 95(4) : 253.p

Paulley J.W. *Asthma attacks and thunderstorms.* QJM. 2002; 95(7) : 485-6.p

Pauwels R.A. et al. *The inhaled Steroid Treatment as Regular Therapy in early asthma (START) study: rationale and design.* Control Clin Trials. 2001; 22(4) : 405-19.p **Abstract:** Although the beneficial effects of treatment with inhaled steroids in asthma are widely accepted, the role of early intervention in patients with mild asthma remains unsettled. Conventional efficacy trials are often of short duration and involve highly selected patient populations that exclude many patients typical of those encountered in routine clinical practice. Hence, a large "real-world" effectiveness study is needed to evaluate the benefits of early intervention with inhaled steroids in patients with mild, persistent asthma. In the START (inhaled Steroid Treatment As Regular Therapy in early asthma) study, patients ages 6-60 years, from 31 countries and districts worldwide with mild persistent asthma, have been randomized to once-daily treatment with budesonide, 200 microg (for patients < 11 years) or 400 microg (for patients > or = 11 years), or placebo via Turbuhaler for 3 years. The double-blind treatment period will be followed by a 2-year period of open budesonide treatment. Throughout the study, other asthma medication including glucocorticosteroids can be given as judged appropriate by the investigator. Lung function will be measured by spirometry using standardized techniques at 3-month intervals throughout the study, and bronchodilator reversibility will be measured annually. The primary outcome measures are the time to the first severe asthma-related event during the first 3 years of the study and the change in postbronchodilator forced expiratory volume in 1 second (FEV₁) from baseline during the entire 5-year study period. These measures have been chosen to reflect the progression of mild asthma toward more severe asthma and the extent of irreversible airflow limitation, which should reflect the degree of airway remodeling.

Pauwels R.A. et al. *Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial.* Lancet. 2003; 361(9363) : 1071-6.p **Abstract:** **BACKGROUND:** Although inhaled glucocorticosteroids are recommended for persistent asthma, their long-term effect on recent onset, mild, persistent asthma has yet to be established. **METHODS:** We did a randomised, double-blind clinical trial in 7241 patients in 32 countries to assess the effects of budesonide in patients who had had mild persistent asthma for less than 2 years and who had not had previous regular treatment with glucocorticosteroids. Patients aged 5-66 years received either budesonide or placebo once daily for 3 years in addition to their usual asthma medications. The daily budesonide dose was 400 microg, or 200 microg for children younger than 11 years. The primary outcome was time to first severe asthma-related event, and analysis was by intention to treat. **FINDINGS:** 198 of 3568 patients on placebo and 117 of 3597 on budesonide had at least one severe asthma exacerbation; hazard ratio 0.56 (95% CI 0.45-0.71, p<0.0001). Patients on budesonide had fewer courses of systemic corticosteroids and more symptom-free days than did those on placebo. Compared with placebo, budesonide increased postbronchodilator forced expiratory volume in 1 s (FEV₁) from baseline by 1.48% (p<0.0001) after 1 year and by 0.88% (p=0.0005) after 3 years (expressed as percent of the predicted value). The corresponding increase in prebronchodilator FEV₁ was 2.24% after 1 year and 1.71% after 3 years (p<0.0001 at both timepoints). The

effect of treatment on all outcome variables was independent of the baseline lung function (prebronchodilator or postbronchodilator) or baseline medication. In children younger than 11 years, 3-year growth was reduced in the budesonide group by 1.34 cm. The reduction was greatest in the first year of treatment (0.58 cm) than years 2 and 3 (0.43 cm and 0.33 cm, respectively). **INTERPRETATION:** Long-term, once-daily treatment with low-dose budesonide decreases the risk of severe exacerbations and improves asthma control in patients with mild persistent asthma of recent onset.

Pauwels R.A. et al. *Formoterol as relief medication in asthma: a worldwide safety and effectiveness trial.* Eur Respir J. 2003; 22(5) : 787-94.p **Abstract:** The aim of the study was to compare the safety and effectiveness of as-needed formoterol with salbutamol in a large international real-life asthma study. Children and adults (n=18,124) were randomised to 6 months as-needed treatment with open-label formoterol 4.5 microg Turbuhaler or salbutamol 200 microg pressurised metered dose inhaler or equivalent. Primary safety variables were asthma-related and nonasthma-related serious adverse events (SAE)s and adverse events (AE)s resulting in discontinuation (DAE)s. The primary efficacy variable was time to first asthma exacerbation. The incidences of AEs, SAEs and DAEs arising from SAEs were not significantly different between treatments. DAEs for nonserious AEs were higher with formoterol. Asthma-related AEs decreased with formoterol (1,098 (12.3%) versus 1,206 (13.5%)), asthma-related SAEs were similar (108 (1.2%) versus 121 (1.4%)) but more asthma-related DAEs occurred in the formoterol group (89 (1.0%) versus 48 (0.5%)). Time to first exacerbation was prolonged (hazard ratio 0.86) and less as-needed and maintenance medication was used with formoterol. Reductions of exacerbations with as-needed formoterol versus salbutamol increased with increasing age and asthma medication level. This real-life study demonstrates that formoterol as-needed has a similar safety profile to salbutamol, and its use as a reliever therapy is associated with fewer asthma symptoms and exacerbations.

Pearce M. et al. *The effects of aerial spraying with Bacillus thuringiensis Kurstaki on children with asthma.* Can J Public Health. 2002; 93(1) : 21-5.p **Abstract:** **OBJECTIVE:** To determine if aerially spraying a biological pesticide was associated with an increase in the symptoms or change in the Peak Expiratory Flow Rate of children with asthma. **METHODS:** A pre/post matched pairs cohort design was used. Children living in the spray zone were matched with children outside of the spray zone. Peak Expiratory Flow Rates, asthma symptoms and non-asthma symptoms were recorded in diaries. **RESULTS:** There were no differences in asthma symptom scores between subjects and controls, neither before nor after the spray; nor were there significant changes in Peak Expiratory Flow Rates for subjects after the spray period. **CONCLUSIONS:** No evidence of adverse effects from the use of the biological pesticide was found. We believe that this is the first paper to address the issue of whether or not aerial spraying with Btk has a harmful effect on children with asthma.

Pearlman D.S. et al. *Formoterol delivered via a dry powder inhaler (Aerolizer): results from long-term clinical trials in children.* Curr Med Res Opin. 2002; 18(8) : 445-55.p **Abstract:** Over 500 children with asthma, aged 5-12 years, have been treated with formoterol fumarate (Foradil) delivered via the Aerolizer dry powder inhaler in clinical trials, with treatment periods of up to 15 months. In pivotal double-blind trials, two dose levels, 12 and 24 microg taken twice daily, provided significant benefit in terms of lung function measurements and symptom control (a lower dose of 6 microg twice daily appeared insufficient with this formulation). The higher, 24 microg dose appeared to provide an additional margin of benefit in a subgroup of children with more unstable/severe disease when the results from long-term follow-up (12-15 months) were analysed.

Formoterol was shown to have a good safety profile when taken as regular maintenance treatment and when used as rescue medication by patients already receiving formoterol as regular maintenance treatment. In this flexible regimen, with formoterol used for rescue and maintenance, the overall daily intake of formoterol was low, with 96.1% of all treatment days (n = 2452) covered by a total daily dose (regular + rescue) of 48 microg (four doses) or less. There was no increase in the average daily intake of rescue formoterol over time. The clinical efficacy associated with this regimen was maintained over time and, in the case of morning peak expiratory flow rate, steadily improved over time. The Foradil Aerolizer inhalation system is simple to use and has a low resistance to inspiratory airflow that maximises the patient's control over dosing, while minimising the risk of under- and overdosing. These features may be especially valuable in a young patient population.

Pedersen S. *Progression of asthma: small steps and a long way to go.* Am J Respir Crit Care Med. 2004; 170(3): 206-7.p

Pedersen S. et al. *Growth, systemic safety, and efficacy during 1 year of asthma treatment with different beclomethasone dipropionate formulations: an open-label, randomized comparison of extrafine and conventional aerosols in children.* Pediatrics. 2002; 109(6): e92.p **Abstract:** **OBJECTIVE:** To assess the long-term safety of hydrofluoroalkane 134a (HFA)-beclomethasone dipropionate (BDP) extrafine aerosol administered by the Autohaler compared with chlorofluorocarbon (CFC)-BDP administered by a press-and-breathe metered-dose inhaler (pMDI) and spacer (+S) in the treatment of children with asthma. **METHODS:** This 12-month, open-label, randomized, multicenter study enrolled 300 children who were aged 5 to 11 years and had well-controlled asthma on inhaled CFC-BDP or budesonide; 256 patients were using doses within the recommended range (200-400 microg) and were analyzed separately. Patients were randomized in a 1:3 ratio to continue on CFC-BDP+S at approximately the same dose as they were using before study entry or switch to HFA-BDP at half the daily dose. **RESULTS:** Asthma control was well maintained in the HFA-BDP group as evidenced by lung function tests and asthma symptoms compared with CFC-BDP+S at approximately twice the dose. There were no significant differences between the HFA-BDP 100 to 200 microg and CFC-BDP+S 200 to 400 microg treatment groups in mean change from baseline in height (5.23 cm vs 5.66 cm at month 12, respectively) or mean growth velocity from day 1 to month 12 (5.27 cm/y vs 5.71 cm/y, respectively). There were no significant differences between groups in adrenal function tests or markers of bone metabolism. **CONCLUSIONS:** In this long-term study in children with asthma, extrafine HFA-BDP provided long-term maintenance of asthma control at approximately half the dose compared with CFC-BDP+S. There were no clinically meaningful differences between HFA-BDP extrafine aerosol and conventional CFC-BDP+S with regard to growth or other systemic effects.

Peel J.L. et al. *Ambient air pollution and respiratory emergency department visits.* Epidemiology. 2005; 16(2): 164-74.p **Abstract:** **BACKGROUND:** A number of emergency department studies have corroborated findings from mortality and hospital admission studies regarding an association of ambient air pollution and respiratory outcomes. More refined assessment has been limited by study size and available air quality data. **METHODS:** Measurements of 5 pollutants (particulate matter [PM10], ozone, nitrogen dioxide [NO2], carbon monoxide [CO], and sulfur dioxide [SO2]) were available for the entire study period (1 January 1993 to 31 August 2000); detailed measurements of particulate matter were available for 25 months. We obtained data on 4 million emergency department visits from 31 hospitals in Atlanta. Visits for asthma, chronic obstructive pulmonary disease, upper respiratory infection, and pneumonia were assessed in relation to air pollutants using Poisson generalized estimating equations. **RESULTS:** In single-pollutant models examining 3-day moving averages of pollutants (lags 0, 1,

and 2): standard deviation increases of ozone, NO2, CO, and PM10 were associated with 1-3% increases in URI visits; a 2 microg/m increase of PM2.5 organic carbon was associated with a 3% increase in pneumonia visits; and standard deviation increases of NO2 and CO were associated with 2-3% increases in chronic obstructive pulmonary disease visits. Positive associations persisted beyond 3 days for several of the outcomes, and over a week for asthma. **CONCLUSIONS:** The results of this study contribute to the evidence of an association of several correlated gaseous and particulate pollutants, including ozone, NO2, CO, PM, and organic carbon, with specific respiratory conditions.

Peisong G. et al. *An asthma-associated genetic variant of STAT6 predicts low burden of ascaris worm infestation.* Genes Immun. 2004; 5(1): 58-62.p **Abstract:** Th-2 immune mechanisms are involved in the pathology of asthma and in the protective immune response to parasitic worms. Common upregulating genetic variants of Th-2 immune signalling are risk factors for asthma, and we tested whether they may confer a counteradvantage in protecting against parasitic worms. We examined the intensity of infection by the parasitic worm, *Ascaris lumbricoides*, by microscopic counting of ascaris eggs in the stool of 614 schoolchildren from an area of endemic ascaris infection in China. We investigated the relationship between the intensity of ascaris infection and common, asthma-associated genetic variants of Th-2 and Th-1 immune signalling. Ascaris egg counts per gram of stool (egg), mean 1068 egg, ranged from barely detectable (<240 egg) to heavy (approximately 9600 egg) in a skewed distribution. Logistic regression, after exploratory discriminant analysis, showed a major association between a common genetic variant of the 3'-UTR regulatory elements of the signal transducer and transactivating factor (STAT6) (P=0.0002) and egg counts, at the 77 th centile. Linear regression after log transformation of egg counts confirmed a highly significant association with this STAT6 variant (P=0.001). Thus, a common, asthma-associated, genetic variant of the pivotal transduction and transactivating factor for Th-2 immune signalling, STAT6, predicts increased resistance to ascaris worm infection. The evolution of enhanced resistance to parasitic worm infection, through human genetic variation in Th-2 immune signalling, may represent one origin for asthma.

Pelletier A.R. et al. *Roller coaster related fatalities, United States, 1994--2004.* Inj Prev. 2005; 11(5): 309-12.p **Abstract:** **OBJECTIVE:** To determine the number of fatalities related to roller coasters and examine factors common to multiple incidents. **METHODS:** A case was defined as the death of a person, which was associated with a roller coaster in the United States between 15 May 1994 and 14 May 2004. Cases were identified from four **DATA SOURCES:** (1) Consumer Product Safety Commission, (2) Lexis-Nexis, (3) Medline, and (4) Safer parks. **RESULTS:** Forty people, ranging in age from 7 to 77 years, were killed in 39 separate incidents. Twenty nine (73%) deaths occurred among roller coaster patrons. Eleven fatalities resulted from external causes related to injuries from falls or collisions. Eighteen people died from medical conditions that might have been caused or exacerbated by riding a roller coaster; 15 were the result of intracranial hemorrhages or cardiac problems. Eleven (28%) deaths involved employees; all were caused by injuries. **CONCLUSIONS:** Approximately four deaths annually in the United States are associated with roller coasters. Prevention of roller coaster fatalities is dependent on establishing an effective surveillance system for amusement ride injuries, engineering rides to better protect both patrons and employees, improving training and supervision of employees regarding safety precautions, and posting cautionary notices near roller coasters for people with specified medical conditions. Further research is needed on roller coaster related deaths resulting from intracranial hemorrhages and cardiac problems.

Pena M.T. et al. *Immunohistochemical analyses of MUC5AC mucin expression in sinus mucosa of children with sinusitis and controls.* Ann Otol Rhinol Laryngol. 2005; 114(12) : 958-65.p **Abstract:** **OBJECTIVES:** The purpose of this study was to analyze MUC5AC protein expression in sinus mucosal specimens of children with and without chronic sinusitis. **METHODS:** Morphometric, histologic, and immunohistochemical analyses were carried out on sinus mucosa of 7 children with chronic sinusitis and 6 children without sinusitis. **RESULTS:** MUC5AC protein was expressed in a subset of goblet cells in the surface epithelium, but not in the submucosal glands in either pediatric population. The number of goblet cells that expressed MUC5AC mucin was not significantly different in patients with and without chronic sinusitis. All specimens had similar numbers of goblet cells in the surface epithelium. **CONCLUSIONS:** The data demonstrate that neither goblet cell hyperplasia nor increased MUC5AC expression occurs in the sinus mucosa of children with chronic sinusitis. This suggests that in contrast to asthma, in which goblet cell hyperplasia is present in the lower respiratory tract, mucus hypersecretion in pediatric chronic sinusitis may involve other secretory cells, eg, submucosal glandular cells, and mucins secreted by these glandular cells.

Penny M.E. et al. *Respiratory symptoms, asthma, exercise test spirometry, and atopy in schoolchildren from a Lima shanty town.* Thorax. 2001; 56(8) : 607-12.p **Abstract:** **BACKGROUND:** Little is known about the associations between symptoms of asthma, pulmonary function tests, and atopy in developing countries. While asthma in children is often associated with atopy, some studies of wheezing illness have found little or no association, leading to suggestions that there are subgroups of wheezing illness. The ISAAC study recently reported that the prevalence of reported asthma symptoms in Lima, Peru was among the highest in the world, but did not report on the atopic status of the subjects. **METHODS:** A cross sectional survey was conducted of children aged 8-10 years who had previously participated in a cohort study of respiratory and diarrhoeal illnesses in infancy. Questionnaires were administered asking about respiratory symptoms and asthma diagnoses, pulmonary function tests were performed before and after exercise on a treadmill, and atopy was determined from skin prick tests and specific serum IgE levels. **RESULTS:** A total of 793 children participated in the survey. The prevalence of asthma related symptoms in the last 12 months was 23.2%, but only 3.8% of children reported a recent asthma attack. The mean differences in pretest percentage predicted forced expiratory volume in one second (FEV₁) were 8.1% (95% CI 2.4 to 13.8) between children who did and did not report an asthma attack in the last 12 months, and 5.3% (95% CI 2.8 to 7.9) in children who did and did not report respiratory symptoms. The corresponding differences in mean percentage fall in FEV₁ after exercise were 3.1% (95% CI -1 to 7.1) and 5.1% (95% CI 3.4 to 6.8). Recent asthma or respiratory symptoms were not associated with atopy in this population (odds ratios 1.29 (95% CI 0.56 to 2.97) and 0.91 (95% CI 0.61 to 1.37), respectively). **CONCLUSIONS:** Most asthma in these children was unrecognized and mild. Asthma and asthma symptoms in this population do not seem to be related to atopy.

Pereira E.A. et al. *IgE, IgG1, and IgG4 antibody responses to Blomia tropicalis in atopic patients.* Allergy. 2005; 60(3) : 401-6.p **Abstract:** **BACKGROUND:** Allergens from house dust mites (HDMs), Dermatophagoides pteronyssinus and Blomia tropicalis are clinically relevant in atopic respiratory diseases in tropical countries. **AIMS OF THE STUDY:** To evaluate immunoglobulin (Ig)E, IgG1, and IgG4 antibody responses to B. tropicalis in Brazilian atopic patients. **METHODS:** About 110 patients with allergic rhinitis with/without asthma and 33 control subjects underwent skin prick testing (SPT) with HDM extracts, and their sera were tested for IgE and IgG subclass antibodies to D. pteronyssinus and B. tropicalis by enzyme-linked immunosorbent assay (ELISA) and immunoblotting. **RESULTS:** Most patients (56%) had positive SPT to B. tropicalis extract (B. tropicalis+ group), although 51% were reactive to both B.

tropicalis and D. pteronyssinus and 6% were sensitized to B. tropicalis only. IgE-ELISA detected 43% B. tropicalis positivity with high-specific IgE levels in B. tropicalis+ patients. Specific IgG4 levels were higher in B. tropicalis+ than B. tropicalis- groups and correlated with specific IgE levels. The IgG1 levels to B. tropicalis were higher in patients than controls. The major allergenic B. tropicalis components recognized by B. tropicalis+ patient sera were the 54, 66, and 68 kDa proteins. The IgG4-binding protein profiles closely resembled that of IgE. The IgG1 antibodies recognizing multiple B. tropicalis protein species were detected in sera of all three patient groups. **CONCLUSIONS:** A large percentage of our allergic patients are B. tropicalis+. They are more frequently sensitized to high-molecular weight (HMW) B. tropicalis components than the major low-molecular weight (11-15 kDa) allergens detected in other studies. The results suggest that HMW B. tropicalis antigenic components are potential candidates for evaluating allergen exposure and sensitization, and for immunotherapy treatment.

Pereira L.S. et al. *[Maternal morbidity in adolescent pregnancy].* Ginecol Obstet Mex. 2002; 70 : 270-4.p **Abstract:** **OBJECTIVE:** To evaluate the maternal morbidity in < or = 16 year old pregnant teenagers. **MATERIAL AND METHODS:** A prospective study of the reviewed cases was carried out from June 1998 to May 1999. All pregnant teenagers which attended the Coordination for the Attention of the Teenage Patient and whose pregnancy came to term during the study period were included. The following variables were analyzed: maternal age, preexisting related diseases, number of pregnancies, number of prenatal control medical visits and the time at which these were started, and maternal morbidity secondary to pregnancy. **RESULTS:** Two hundred and ninety six of 330 case were included. The average maternal age was 15.1 years old (10-16 range); 68.9% had finished middle school; 82.2% were housekeepers, and 61.4% were single. Prenatal control was initiated in the 2nd trimester by 50.7% of them, while 39.5% started it in the 3rd trimester and the remaining 9.8% in the 1st trimester. The most frequent previous pathologies were: bronchial asthma (2.5%), drug addiction (2%), hypothyroidism (2%), cardiopathy (1.5%). The most common complications during pregnancy: urinary system infections (20.4%), anemia (9.8%), threats of premature labour (9.8%), premature membrane rupture (9%), hypertensive disease induced by pregnancy (3.2%), delayed intrauterine growth (2.4%) and fetal malformation (2.4%). About 44.1% of the pregnancies were interrupted by cesarean section, 35.6% by eutocchia and 20.3% by instrumented labour. The most frequent complications during the puerperium were: tearing of the canal of the cervix (7%), decidual endometritis (3.3%), dehiscence of surgical wounds (2.7%), and pyelonephritis (1.6%). **CONCLUSIONS:** The pregnant teenager is a "special" patient from the biopsychosocial point of view, thus, she must be managed by a multidisciplinary team, with special emphasis in the problems analyzed in this study.

Perez Martin J. *[Early childhood infections and the development of allergy and asthma].* Rev Alerg Mex. 2002; 49(2) : 25-6.p

Perez-Padilla R. et al. *Obesity among children residing in Mexico City and its impact on lung function: a comparison with Mexican-Americans.* Arch Med Res. 2006; 37(1) : 165-71.p **Abstract:** **BACKGROUND:** The objective of the study was to describe the prevalence of obesity among Mexican children and its impact on ventilatory lung function. **METHODS:** We studied cross-sectionally 6784 students between 8 and 20 years of age attending schools located <2 km away from ten air pollution monitors located throughout metropolitan Mexico City. The comparison group was made up of 1924 Mexican-Americans of the same age, studied during the NHANES-III examination, which included information on spirometry and body mass index (BMI). **RESULTS:** Of all our subjects, 9.7% had a BMI >95(th) percentile of CDC growth charts (compared to 15.1% in Mexican-Americans) and 6.6% fulfilled the

obesity criteria of the International Obesity Task Force (vs. 12.2%). Obesity was related to male gender, asthma and passive smoking. At the same height and gender, lung function was higher in Mexicans than in Mexican-Americans, perhaps due to altitude. In children 8-11 years of age, lung function increased in heavier subjects but, in older children and youths, function reached a plateau and decreased among children with highest BMI (inverted U pattern, seen in adults). CONCLUSIONS: Obesity is higher in Mexican-American children and youths than in Mexicans. Spirometric function is affected adversely by obesity, especially in young people.

Peroni D.G. et al. *Rhinitis in pre-school children: prevalence, association with allergic diseases and risk factors.* Clin Exp Allergy. 2003; 33(10) : 1349-54.p **Abstract:** BACKGROUND: The aim of our study was to assess the prevalence of rhinitis, sneezing, runny or blocked nose apart from colds in a pre-school children population and to evaluate the risk factors and relationship with allergic diseases and sensitization. METHODS: Eighteen nursery schools were randomly selected. The International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire (WQ) was distributed and filled by parents of pre-school children (3-5 years). The allergic sensitization to common aeroallergens and foods was evaluated by skin prick test (SPT). chi2 tests were used to compare proportions between rhinitic and non-rhinitic children. RESULTS: One thousand four hundred and two (92%) valuable questionnaires were returned. Prevalence of rhinitis in the last 12 months was 16.8%. Rhinitic children compared to non-rhinitic children presented a significant increase of diagnosed asthma (20.8% vs. 6.2%, P<0.001), lifetime wheezing (43.2% vs. 21.6%, P<0.001), wheezing in the last 12 months (25.0% vs. 9.4%, P<0.001), atopic dermatitis (22.9% vs. 13.9%, P<0.001) and allergic sensitization (29.9% vs. 13.7%, P<0.001). Sensitization to grass pollen and house dust mites were significant risk factors for rhinitis (P<0.01). A family history of atopy, having pets at home, male gender and greater age were significant risk factors for rhinitis, but not smoking exposure, sharing a bedroom or breastfeeding. CONCLUSIONS: In pre-school children rhinitis has a strong association with wheezing symptoms, asthma and atopic dermatitis. Allergic sensitization is a risk factor for rhinitis and should be evaluated even in pre-school children.

Perzanowski M.S. et al. *Atopy, asthma, and antibodies to Ascaris among rural and urban children in Kenya.* J Pediatr. 2002; 140(5) : 582-8.p **Abstract:** OBJECTIVE: The purpose of this study was to evaluate differences in the relationship between asthma and immune responses to allergens in children living in rural and urban areas of Kenya. STUDY DESIGN: Children (mean age, 11 years) from Kabati (n = 136), a rural village, and Thika (n = 129), a small town, were studied by skin testing and serum immunoglobulin E (IgE) and immunoglobulin G (IgG) antibody measurement. Asthma was evaluated by symptoms, as well as spirometry before and after vigorous exercise to test for exercised-induced bronchospasm (EIB). School children from a study performed in Atlanta, Georgia, were used for comparison of anthropometric and immunologic results. RESULTS: Compared with the urban area of Kenya, children living in the rural area had a lower percentage of body fat, smaller and fewer skin test responses to allergens, a higher prevalence of IgE antibodies to Ascaris (67% vs 26%) and 10-fold higher total IgE. In the urban area of Kenya, there was a strong correlation between EIB and atopy determined both by IgE antibodies (P =.02) and skin tests (P =.002). By contrast, in the rural area, none of the 13 children with EIB were skin-test positive (vs 13/109 of children without EIB). CONCLUSIONS: Among the rural children, there was no association between immune responses to allergens and airway-related symptoms or reactivity. The association between asthma and atopy seen in the town of Thika may represent an important step in the increase in asthma seen both in urban Africa and in the West.

Perzanowski M.S. et al. *Endotoxin and asthma.* N Engl J Med. 2003; 348(2) : 171-4; author reply 171-4.p

Perzanowski M.S. et al. *Effect of cat and dog ownership on sensitization and development of asthma among preteenage children.* Am J Respir Crit Care Med. 2002; 166(5) : 696-702.p **Abstract:** An inverse relationship has been proposed between exposure to high quantities of cat allergen at home and both asthma and cat allergy. First- and second-grade children from Lulea, Kiruna, and Pitea, Sweden participated in an asthma questionnaire study (n = 3,431) and incidence was evaluated over the next 3 years. Skin testing was performed on the children in Lulea and Kiruna (n = 2,149). The strongest risk factor for incident cases of asthma was Type 1 allergy (relative risk [RR], 4.9 [2.9-8.4]), followed by a family history of asthma (RR, 2.83 [1.8-4.5]). Living with a cat was inversely related both to having a positive skin test to cat (RR, 0.62 [0.47-0.83]) and incidence of physician-diagnosed asthma (RR, 0.49 [0.28-0.83]). This effect on incident asthma was most pronounced among the children with a family history of asthma (RR, 0.25 [0.08-0.80]). The evidence also suggests that many of the children exposed to cats at home can develop an immune response that does not include immunoglobulin E. Weaker protective trends were seen with dog ownership. The traditional thinking that not owning cats can provide protection against developing allergy and asthma among those with a family history of allergy needs to be re-evaluated. In a community where cat sensitization was strongly associated with asthma, owning a cat was protective against both prevalent and incident asthma.

Pescollerung L. et al. *Inhaled corticosteroids and urinary free cortisol.* Pediatrics. 2003; 112(6 Pt 1) : 1464-5.p

Pescollerung L. et al. *Inhaled fluticasone in asthmatic children.* Ann Allergy Asthma Immunol. 2002; 89(3) : 328-9; author reply 329.p

Pescollerung L. et al. *Systemic activity of inhaled corticosteroid treatment in asthmatic children: corticotrophin releasing hormone test.* Thorax. 2003; 58(3) : 227-30.p **Abstract:** BACKGROUND: A study was undertaken to assess the function of the hypothalamic-pituitary-adrenal axis (HPA) in a group of asthmatic children before and after treatment with inhaled corticosteroids. METHODS: Thirty prepubertal patients of mean (SD) age 6.7 (1.8) years were treated with inhaled corticosteroids. All children underwent a corticotrophin releasing hormone (CRH) test with evaluation of serum cortisol and adrenocorticotrophin hormone (ACTH) levels before and after 3 months of treatment. Twenty four hour urine samples were also collected to measure free cortisol (UFC) excretion. RESULTS: Subjects showed no difference between basal serum cortisol levels (mean change -18; 95% CI -41 to 5; p=0.118) and delta (peak minus basal) levels (mean change -13; 95% CI -38 to 12; p=0.308) before and after treatment, whereas the peak cortisol level (mean change -31; 95% CI -55 to -7; p=0.013) and area under the curve (AUC) (mean change -175; 95% CI -288 to -63; p=0.003) after CRH were significantly lower following treatment. Basal, peak and AUC ACTH were significantly lower after treatment (p<0.05, p=0.004 and p=0.003, respectively), while delta ACTH was similar before and after treatment ((mean change -12; 95% CI -31 to -7; p=0.199). No significant reduction in 24 hour UFC was observed after the treatment period (before 14.9 (7.1), after 15.0 (11.6); mean change 0.1, 95% CI -5.2 to 5.4; p=0.967). No correlation was found between UFC and any of the parameters of cortisol excretion following the CRH test, either before or after treatment. CONCLUSIONS: These data suggest that, at the dosage and for the treatment period used, inhaled steroids do not seem to suppress the HPA axis in the majority of patients. The CRH test may be more sensitive than 24 hour UFC and morning plasma cortisol levels in evaluating systemic activity of inhaled corticosteroid treatment.

Peters U. et al. *Causes of death in patients with celiac disease in a population-based Swedish cohort.* Arch Intern Med. 2003; 163(13) : 1566-72.p **Abstract:** BACKGROUND: Patients with celiac disease have an increased risk of death from gastrointestinal malignancies and lymphomas, but little is known about mortality from other causes and few studies have assessed long-term outcomes. METHODS: Nationwide data on 10 032 Swedish patients hospitalized from January 1, 1964, through December 31, 1993, with celiac disease and surviving at least 12 months were linked with the national mortality register. Mortality risks were computed as standardized mortality ratios (SMRs), comparing mortality rates of patients with celiac disease with rates in the general Swedish population. RESULTS: A total of 828 patients with celiac disease died during the follow-up period (1965-1994). For all causes of death combined, mortality risks were significantly elevated: 2.0-fold (95% confidence interval [CI], 1.8-2.1) among all patients with celiac disease and 1.4-fold (95% CI, 1.2-1.6) among patients with celiac disease with no other discharge diagnoses at initial hospitalization. The overall SMR did not differ by sex or calendar year of initial hospitalization, whereas mortality risk in patients hospitalized with celiac disease before the age of 2 years was significantly lower by 60% (95% CI, 0.2-0.8) compared with the same age group of the general population. Mortality risks were elevated for a wide array of diseases, including non-Hodgkin lymphoma (SMR, 11.4), cancer of the small intestine (SMR, 17.3), autoimmune diseases (including rheumatoid arthritis [SMR, 7.3] and diffuse diseases of connective tissue [SMR, 17.0]), allergic disorders (such as asthma [SMR, 2.8]), inflammatory bowel diseases (including ulcerative colitis and Crohn disease [SMR, 70.9]), diabetes mellitus (SMR, 3.0), disorders of immune deficiency (SMR, 20.9), tuberculosis (SMR, 5.9), pneumonia (SMR, 2.9), and nephritis (SMR, 5.4). CONCLUSION: The elevated mortality risk for all causes of death combined reflected, for the most part, disorders characterized by immune dysfunction.

Peterson J.W. et al. *Community's voice in managing childhood asthma: the assessment phase of research.* J Health Care Poor Underserved. 2005; 16(4) : 747-59.p **Abstract:** This study was designed to investigate community beliefs about caring for childhood asthma and to elicit suggestions for interventions to improve asthmatic children's health. Focus groups were conducted with parents of children with asthma, children with asthma, school staff, and health care and childcare professionals. Data were analyzed for themes, such as disruption of normal living and having to work in a chaotic system, enabling researchers to posit a core belief for each group. These core beliefs, together with encompassed other, related beliefs held by group members, guide attitudes and actions about asthma. Interventions recommended by focus group participants included creating an asthma play, asthma education, and developing a clinic-based registry to standardize asthma documentation. The community's voice is important in assessment and design of health improvement projects. Incorporating the community's suggestions gives the community a sense of contributing to the health care of their children with asthma.

Peterson-Sweeney K. et al. *Parental perceptions of their child's asthma: management and medication use.* J Pediatr Health Care. 2003; 17(3) : 118-25.p **Abstract:** INTRODUCTION: Adequate treatment for asthma depends on accurate assessment and intervention by the parent and child and timely communication with the provider. These actions by the parent may be affected by their understanding of asthma management and their concerns about medications being prescribed. This research reports parental experiences with their children with asthma, specifically their beliefs, knowledge, and attitudes about asthma management, including medication use. METHODS: Data reported are from a study investigating parental attitudes and beliefs affecting antiinflammatory medication use in childhood asthma. These qualitative findings emerged from one-on-one semistructured qualitative interviews with 18 parents of children 2 to 18 years of age who were from diverse racial and socioeconomic

backgrounds and who represented the spectrum of illness severity. RESULTS: Eight main themes within the domain of asthma management and medication use were identified: "I know my child," "trial and error," "partnership," "need for education," "negotiating responsibility," "hassles with medication administration," "preferences," and "the benefits outweigh the risks of side effects." DISCUSSION: These themes emphasize parents' need to partner with providers in their child's asthma management, as well as their need for ongoing asthma education. Parents also expressed concern about adverse effects of antiinflammatory medication but acknowledged the importance of controlling asthma symptoms. Based on these findings, systematic practice changes are recommended that provide regular opportunities for parent and child asthma education in a structured asthma wellness or "tune-up" visit.

Petrillo T.M. et al. *Emergency department use of ketamine in pediatric status asthmaticus.* J Asthma. 2001; 38(8) : 657-64.p **Abstract:** The objective of this study was to evaluate the effects of adding ketamine to standard emergency department (ED) therapy for patients with status asthmaticus. This was a prospective observational study. Ten patients with an acute exacerbation of asthma who were unresponsive to standard therapy were enrolled in the ED. Upon enrollment, children received ketamine at a loading dose of 1 mg/kg intravenously (i.v.), followed by a continuous infusion of 0.75 mg/kg/hr (12.5 microg/kg/min) for 1 hr. Clinical asthma score (CAS), vital signs, and peak expiratory flow (PEF) measurements were obtained prior to ketamine administration, within 10 min after ketamine administration was completed, and 1 hr after infusion. Median CAS on ED arrival was 15 (range 7-23) and did not significantly change immediately prior to infusion of ketamine (median 14, range 8-21). Median CAS decreased to 10.5 immediately after infusion and to 9.51 hr post ketamine infusion (37% reduction, $p < 0.05$ by ANOVA vs. preketamine CAS). Median respiratory rate (RR) also decreased from 39 prior to ketamine to 30 immediately following ketamine administration (25% decrease vs. preketamine; $p < 0.05$). Oxygen saturation significantly improved after ketamine infusion, although 5 patients remained on oxygen. Median PEF improved after infusion, but was not statistically significant. Four patients experienced mild side effects including mild hallucinations, diffuse flushing, and moderate hypertension. Side effects resolved with benzodiazepines or with discontinuation of the infusion. Addition of ketamine to standard therapy was associated with improved indices of acute asthma severity. Side effects were transitory and comparable to previous studies. However, a double-blinded randomized controlled trial needs to be conducted to determine if improvement is attributable to the addition of ketamine to standard asthma therapy.

Pettigrew M.M. et al. *Association of early-onset otitis media in infants and exposure to household mould.* Paediatr Perinat Epidemiol. 2004; 18(6) : 441-7.p **Abstract:** Otitis media is one of the most common infections of early childhood. Children who first experience acute otitis media at an early age (before 6 months) are at increased risk for recurrent otitis media. This prospective study investigated exposure to measured levels of airborne household mould and the risk of early otitis media in the first 6 months of life among a cohort of infants at high risk for asthma. Between September 1996 and December 1998, women were invited to participate if they had at least one other child with physician-diagnosed asthma. Mothers were given a standardised questionnaire within 4 months of their infant's birth. Airborne mould samples were also taken at this time, and culturable fungi were categorised into four levels according to the report of the Commission of European Communities: 0 (undetectable), 1-499 colony forming units (CFU)/m³ (low), 500-999 CFU/m³ (medium), > or =1000 CFU/m³ (high). Infant respiratory symptoms were collected during quarterly telephone interviews at 6, 9 and 12 months of age. Of the 806 children in the study, 27.8% experienced otitis media before six months of age. Household levels of Penicillium and Cladosporium were modestly associated with the

number of otitis media episodes ($P = 0.056$ and 0.081 respectively). After controlling for potential confounders, *Penicillium* and *Cladosporium* were not associated with early otitis media. High levels of 'other' mould (defined as total spore count minus counts for *Penicillium*, *Cladosporium*, and yeast) were associated with early otitis media (OR 3.49; 95% CI [1.38, 8.79]). We also found associations between day-care outside of the home and birth during the summer or fall season with early otitis media. This study is suggestive of a relationship between otitis media and mould that warrants further study.

Pettigrew M.M. et al. *Infant otitis media and the use of secondary heating sources.* *Epidemiology.* 2004; 15(1) : 13-20.p **Abstract:** **BACKGROUND:** This prospective study investigated the association of exposure to indoor secondary heating sources with otitis media and recurrent otitis media risk in infants. **STUDY DESIGN:** We enrolled mothers living in nonsmoking households and delivering babies between 1993 and 1996 in 12 Connecticut and Virginia hospitals. Biweekly telephone interviews during the first year of life assessed diagnoses from doctors' office visits and use of secondary home heating sources, air conditioner use, and day care. Otitis media episodes separated by more than 21 days were considered to be unique episodes. Recurrent otitis media was defined as 4 or more episodes of otitis media. Repeated-measures logistic regression modeling evaluated the association of kerosene heater, fireplace, or wood stove use with otitis media episodes while controlling for potential confounders. Logistic regression evaluated the relation of these secondary heating sources with recurrent otitis media. **RESULTS:** None of the secondary heating sources were associated with otitis media or with recurrent otitis media. Otitis media was associated with day care, the winter heating season, birth in the fall, white race, additional children in the home, and a maternal history of allergies in multivariate models. Recurrent otitis media was associated with day care, birth in the fall, white race, and a maternal history of allergies or asthma. **CONCLUSION:** We found no evidence that the intermittent use of secondary home heating sources increases the risk of otitis media or recurrent otitis media. This study confirms earlier findings regarding the importance of day care with respect to otitis media risk.

Phipatanakul W. et al. *Endotoxin exposure and eczema in the first year of life.* *Pediatrics.* 2004; 114(1) : 13-8.p **Abstract:** **OBJECTIVE:** Exposure to endotoxin in early life has been proposed as a factor that may protect against the development of allergic diseases such as eczema. The objective of this study was to examine the relation between endotoxin exposure in early life and eczema in the first year of life in children with parental history of asthma or allergies. **METHODS:** This study used a prospective birth cohort study of 498 children who had a history of allergy or asthma in at least 1 parent and lived in metropolitan Boston. A subset of 401 living rooms had house dust samples adequate for analysis of endotoxin. **RESULTS:** In multivariate analyses adjusting for gender, income, and season of birth, endotoxin levels in the living room at 2 to 3 months of age was inversely associated with physician- or nurse-diagnosed eczema in the first year of life (odds ratio [OR] for each quartile increment: 0.76; 95% confidence interval [CI]: 0.61-0.96). Exposure to a dog in the home at age 2 to 3 months was also inversely associated with eczema in the first year of life, but the CI widened when endotoxin was included in the multivariate model (OR: 0.54; 95% CI: 0.27-1.09). Other variables associated with eczema in the first year of life included paternal history of eczema (OR: 1.91; 95% CI: 1.03-3.55) and maternal specific immunoglobulin E positivity to $> \text{or} = 1$ allergen (OR: 1.61; 95% CI: 1.01-2.56). **CONCLUSIONS:** Among children with parental history of asthma or allergies, exposure to high levels of endotoxin in early life may be protective against eczema in the first year of life. In these children, paternal history of eczema and maternal sensitization to at least 1 allergen are associated with an increased risk of eczema in the first year of life.

Phipatanakul W. et al. *Montelukast improves asthma control in asthmatic children maintained on inhaled corticosteroids.* *Ann Allergy Asthma Immunol.* 2003; 91(1) : 49-54.p **Abstract:** **BACKGROUND:** Because of potential toxicities of inhaled corticosteroid (ICS) use in pediatric asthma, alternative or steroid-sparing therapy is desirable. There are no previous studies evaluating montelukast's steroid-sparing effects in children with asthma. **OBJECTIVE:** To evaluate whether (1) montelukast as add-on therapy improves asthma symptom control and (2) montelukast provides steroid-sparing effects in children with asthma treated with low to moderate doses of ICS therapy. **METHODS:** In a double-blind, placebo-controlled trial, 36 children ages 6 to 14 years with symptomatic asthma maintained on a stable low to moderate dose of ICSs were randomly assigned to receive montelukast or matching placebo for 24 weeks after a run-in period of 2 weeks (period I). During the trial, subjects kept daily asthma diary cards and monthly spirometry was performed. After a 4 week add-on period (period II), the subjects completed a 20-week (period III) ICS tapering period based on a predetermined protocol. **RESULTS:** In period II, the difference in the number of rescue-free days was significantly higher in the montelukast group ($P = 0.0001$), and the number of rescue-free days per week was also significantly higher in montelukast-treated subjects compared with placebo subjects ($P = 0.002$). In period III, the percentage reduction in ICS dose was not significant between montelukast and placebo ($P = 0.10$), but the montelukast group experienced an average 17% decrease in ICS dose and the control group experienced an average 64% increase in ICS dose. **CONCLUSIONS:** Montelukast treatment significantly increased the number of rescue-free days in symptomatic children with asthma.

Phipatanakul W. et al. *The efficacy of montelukast in the treatment of cat allergen-induced asthma in children.* *J Allergy Clin Immunol.* 2002; 109(5) : 794-9.p **Abstract:** **BACKGROUND:** Montelukast is a leukotriene antagonist approved for the treatment of childhood asthma in children age 2 years and older. There are limited studies on its effects on allergic asthma in children. **OBJECTIVE:** We sought to evaluate montelukast's effects on upper and lower airway responses to intense cat allergen exposure. **METHODS:** In a double-blind, placebo-controlled, cross-over trial 18 subjects aged 6 to 14 years with cat-induced asthma were randomly assigned to receive 1 week each of either montelukast or placebo, followed by a 1-hour cat challenge in an environmental exposure unit. Upper and lower respiratory tract symptoms were rated, and spirometry and acoustic rhinometry were performed. Challenges were stopped early if the subject became too uncomfortable or had a greater than 50% decrease in FEV1. **RESULTS:** Overall changes in FEV1 were significantly different with montelukast treatment and remained significant after adjusting for allergen level ($P = .02$; adjusted $P = .01$). Lower respiratory tract symptom scores were significantly reduced with montelukast versus placebo ($P = .007$) but lost significance after adjusting for allergen level ($P = .16$). Challenge length was significantly longer with montelukast versus placebo ($P < .001$) and remained significant after adjusting for allergen level ($P = .019$). Montelukast did not significantly affect upper respiratory responses, as measured by means of symptom scores ($P = .43$) and changes in acoustic rhinometry ($P = .078$). **CONCLUSIONS:** Montelukast was significantly more effective than placebo in attenuating lower respiratory responses and extending challenge length when cat-sensitive children with mild persistent asthma were exposed to high levels of cat allergen.

Piacentini G.L. et al. *Reduction in exhaled nitric oxide immediately after methacholine challenge in asthmatic children.* *Thorax.* 2002; 57(9) : 771-3.p **Abstract:** **BACKGROUND:** The measurement of exhaled nitric oxide (NO) has recently been proposed as a useful technique for the evaluation of airway inflammation in asthma. The purpose of this study was to determine the effect of methacholine bronchial provocation on the levels of exhaled NO in asthmatic children. **METHOD:** Exhaled NO was measured immediately before and

after methacholine provocation in 51 children with mild to moderate asthma. RESULTS: A significant decrease occurred in the level of exhaled NO ($p < 0.0001$) after methacholine bronchial provocation which was not correlated with the percentage fall in forced expiratory volume in 1 second (FEV₁). CONCLUSIONS: The methacholine test should not be used immediately before measurement of exhaled NO in children with asthma.

Piazza-Waggoner C. et al. *Child and caregiver psychosocial functioning in pediatric immunodeficiency disorders.* Ann Allergy Asthma Immunol. 2006; 96(2) : 298-303.p **Abstract:** BACKGROUND: Children with chronic illness have been found to be at an increased risk of behavioral and emotional difficulties. To date, children with pediatric immunodeficiency disorders (PIDDs) and their families have not been the focus of extensive published psychosocial research. OBJECTIVE: To determine if children with PIDDs and their caregivers have altered psychosocial function and whether the severity of the PIDD was associated with such difficulties. METHODS: Twenty children with PIDDs and 20 children with asthma were recruited for this study. Children and their caregivers completed various psychosocial questionnaire forms. Responses were compared with normative data for the appropriate measure and with other variables. RESULTS: Higher frequencies of children with PIDDs were found to have a number of elevated psychosocial concerns when contrasted with normative data, particularly from parent report. These concerns included depression, anxiety, somatization, social withdrawal, and social skills. The severity of the PIDDs was significantly associated with a number of behavioral adjustment issues, including receiving psychiatric diagnoses and special education services. Although children with PIDDs had significantly more psychiatric diagnoses than did asthmatic children, these groups did not differ significantly on questionnaire scores regarding child or caregiver psychosocial adjustment. CONCLUSIONS: Children with PIDDs have significant behavioral problems. Children receiving intravenous immunoglobulin or immunomodulatory treatments were reported to have more problems than children not receiving them. This study highlights the need for further research in psychosocial functioning of children with PIDDs in an effort to develop interventions to promote their overall adjustment.

Picard E. et al. *Rate and place of death from asthma among different ethnic groups in Israel: national trends 1980 to 1997.* Chest. 2002; 122(4) : 1222-7.p **Abstract:** STUDY OBJECTIVES: To compare the trends of asthma mortality and place of death in young patients (ages 5 to 34 years) from different major population groups in Israel. DESIGN: Retrospective study. Patients and participants: Patients who died from asthma between the years 1980 and 1997 according to the death record of the National Israeli Health Registry. RESULTS: During the period studied, 100 asthma mortality cases were reported, which yields a mean mortality rate of 0.226 per 100,000 population. There were no significant changes in the mortality rates over the years. The mean (+/- SD) age of death was 23 +/- 7 years. Of this population, 84.5% were Jews and 15.5% were Arabs, which is proportionate to the general Israeli population. In 52% of the cases, the patients died outside a hospital. There was no significant difference in the place of death between Jews and Arabs. Significantly more men (62.5%) than women (40%) died outside the hospital ($p = 0.025$). CONCLUSIONS: The asthma mortality rate in Israel during the years 1980 to 1997 was low and stable. Most of the patients still died outside the hospital. There was no difference in the asthma death rate and place of death between Jews and Arabs, suggesting that in our population genetic predisposition is not likely to be a risk factor for mortality.

Pifferi M. et al. *Montelukast and airway remodeling in children with chronic persistent asthma: an open study.* Pediatr Allergy Immunol. 2004; 15(5) : 472-3.p **Abstract:** We report a 4 yr follow up study of

seven asthmatic children with chronic persistent asthma, high-residual volume and low-density areas at high-resolution computerized tomography after treatment with salmeterol and fluticasone. Improvement of lung function with disappearance of low-density areas in six patients after treatment with fluticasone and montelukast was obtained.

Pijnenburg M.W. et al. *High fractional concentration of nitric oxide in exhaled air despite steroid treatment in asthmatic children.* Clin Exp Allergy. 2005; 35(7) : 920-5.p **Abstract:** BACKGROUND: The fractional concentration of nitric oxide in exhaled air (FENO) is elevated in atopic asthma and typically responds to treatment with inhaled corticosteroids (ICS). However, some patients have persistently high FENO levels despite treatment. OBJECTIVE: We studied how optimizing the inhalation technique and increasing ICS doses would affect FENO in stable atopic asthmatic children who had elevated FENO while using ICS. METHODS: In 41 stable asthmatic children who were treated with ICS (median daily dose 800 microg budesonide equivalent, range 100-1600 microg) and maintained FENO $> \text{or} = 20$ p.p.b., we optimized the inhalation technique by thorough instruction and measured FENO 2 weeks later. Then, if FENO remained $> \text{or} = 20$ p.p.b., we increased the ICS dose and reassessed FENO 2 weeks later. RESULTS: Improving the inhalation technique did not reduce FENO. Increasing ICS from a daily median dose of 800 to 1200 microg budesonide had no significant effect on FENO. FENO correlated positively with symptom scores in the following 2 and 4 weeks ($P = 0.001, 0.002$) and beta2-agonist use the 2 and 4 weeks following FENO measurement ($P = 0.02, 0.004$). CONCLUSION: We conclude that common steps in asthma treatment, i.e. inhalation instruction and increasing ICS dose, were both ineffective in reducing FENO in atopic asthmatic children with elevated FENO values despite treatment with ICS. This implies that FENO cannot simply be incorporated in current treatment guidelines.

Pijnenburg M.W. et al. *Exhaled nitric oxide measurements with dynamic flow restriction in children aged 4-8 yrs.* Eur Respir J. 2002; 20(4) : 919-24.p **Abstract:** Fractional exhaled nitric oxide concentration (FENO) depends on exhalation flow; however, children often are unable to perform controlled flow procedures. Therefore, a device was developed for off-line FENO sampling, with dynamic flow restriction (DFR). The authors compared off-line with on-line FENO, assessed feasibility, and obtained normal values for FENO in children aged 4-8 yrs. Subjects inhaled nitric oxide (NO)-free air and exhaled into the device, where DFR kept exhalation flow constant at 50 mL x s⁻¹. Dead space air was discarded. Exhaled air was collected in a 150 mL mylar balloon. On-line measurements were performed and values compared with off-line FENO in 19 adult volunteers. Seventy-nine children performed off-line sampling. All samples were analysed with a chemiluminescence NO-analyser. Normal values were obtained in 34 healthy children. There was an excellent correlation between on- and off-line values. Bland and Altman plots showed good agreement between on- and off-line FENO. Seventy-four out of 79 children were able to perform a correct off-line procedure. Geometric mean +/- SEM FENO in healthy children was 4.9 +/- 1.2 parts per billion (ppb) for male children and 7.6 +/- 1.1 ppb for female children. It can be concluded that off-line fraction of exhaled nitric oxide measurements with dynamic flow restriction are feasible in young children and correspond to on-line values.

Pillai S.G. et al. *A genome-wide search for linkage to asthma phenotypes in the genetics of asthma international network families: evidence for a major susceptibility locus on chromosome 2p.* Eur J Hum Genet. 2006; 14(3) : 307-16.p **Abstract:** Asthma is a complex disease and the intricate interplay between genetic and environmental factors underlies the overall phenotype of the disease. Families with at least two siblings with asthma were collected from Europe, Australia and

the US. A genome scan using a set of 364 families with a panel of 396 microsatellite markers was conducted. Nonparametric linkage analyses were conducted for asthma and three asthma-related phenotypes: bronchial hyper-reactivity (BHR), strict definition of asthma and atopic asthma. Nine chromosomal regions with LOD scores greater than 1.5 were identified (chromosomes 1q, 2p, 3q, 4p, 4q, 6q, 12q, 20p and 21). Linkage refinement analysis was performed for three BHR loci by genotyping single nucleotide polymorphisms at an average marker density of 1 cM. The LOD scores increased to 3.07 at chromosome 4p and 4.58 at chromosome 2p, while the chromosome 6p locus did not refine. The LOD score at the chromosome 2p locus is highly significant on a genome-wide basis. The refined locus covers a region with a physical size of 12.2 Mb. Taken together, these results provide evidence for a major asthma susceptibility locus on chromosome 2p.

Pilotto L.S. et al. *Randomized controlled trial of unflued gas heater replacement on respiratory health of asthmatic schoolchildren.* *Int J Epidemiol.* 2004; 33(1) : 208-14.p **Abstract:** BACKGROUND: Previous studies do not provide a clear picture of the relationship between nitrogen dioxide (NO₂) exposure and asthma. METHODS: Eighteen schools using unflued gas heating in winter were randomly allocated to either retain their heaters (10 control schools) or to have replacement flued gas or electric heaters installed at the beginning of winter (8 intervention schools). Fortnightly telephone interviews were used to record daily individual asthma symptoms that occurred over 12 weeks (including winter). Lung function and histamine challenge tests were performed at baseline and the end of the study. NO₂ was measured in each school classroom on 9 days and in each household on 3 days spread over the study period. RESULTS: From 199 primary school children that met the eligibility criteria, 45 intervention and 73 control children agreed to participate. Baseline characteristics were similar between groups. Difficulty breathing during the day (Relative Risk [RR] = 0.41; 95% CI: 0.07, 0.98) and night (RR = 0.32; 95% CI: 0.14, 0.69), chest tightness during the day (RR = 0.45; 95% CI: 0.25, 0.81), and daytime asthma attacks (RR = 0.39; 95% CI: 0.17, 0.93) were significantly reduced in the intervention group. Percentage predicted forced expiratory volume in one second (FEV₁), the concentration of histamine inducing a 20% fall in FEV₁ (PD₂₀), and the dose-response slope (DRS) were similar between groups at follow-up. Mean (standard deviation) NO₂ levels were 15.5 (6.6) parts per billion (ppb) and 47.0 (26.8) ppb in the intervention and control schools respectively (P < 0.001). CONCLUSIONS: Asthma symptoms were reduced following a replacement intervention that removed high exposure to NO₂. Such replacement should be considered a public health priority for schools using unflued gas heating during winter.

Pines J.M. et al. *Predictors of frequent emergency department utilization in Southeastern Pennsylvania.* *J Asthma.* 2006; 43(3) : 219-23.p **Abstract:** STUDY OBJECTIVE: We sought to determine socioeconomic and demographic factors that predict frequent emergency department (ED) use among asthmatics in Southeastern Pennsylvania. DESIGN: Retrospective cohort study using the 2004 Philadelphia Health Management Corporation's Southeastern Pennsylvania Household Health Survey. SETTING AND PARTICIPANTS: Health behaviors were surveyed using telephone interviews (random-digit dialing) in Bucks, Montgomery, Delaware, Philadelphia, and Chester counties. Response rate was 30%. RESULTS: Of 13,342 respondents, 1,799 (13%) stated that they had asthma. The mean reported visits in 12 months were as follows: clinic--1.2 (SD 2.7); doctor's office--4.7 (SD 5.6); ED--0.8; (SD 1.8); overnight hospitalizations--0.4 (SD 0.9). Most (91%) reported that a primary care doctor was their principal source of care, whereas 2% reported the ED as their principal source of care. Frequent ED use (>or=3 visits/12 months) was reported in 180 (10%). Frequent ED use was associated with race, education, diabetes, mental illness, smoking at home, and language barriers (p < 0.001) as well as

indicators of severity of illness (clinic visits, office visits, prescription for asthma medication, p < 0.001). Using multivariable logistic regression, predictors of frequent ED use were: prescription for asthma meds (OR 2.3, 95%CI 1.4-3.7), having Medicaid or Medical Assistance (OR 1.7, 95%CI 1.1-2.6), having a high school education or less (OR 1.5, 95%CI 1.0-2.3), number of clinic visits (OR 1.1, 95% CI 1.1-1.1), office visits (OR 1.1, 95%CI 1.1-1.1), number of children living in the house (OR 1.2, 95% CI 1.0-1.3), and living in Philadelphia (OR 2.0, 95% CI 1.3-3.1). CONCLUSIONS: Frequent ED use is associated with demographic factors, geographic factors, and markers of severity of illness. While care guidelines recommend prompt referral to a primary care physician to prevent ED visits, given the level of primary care use in this population, frequent primary care attendance alone may not prevent asthma-related ED visits.

Pinkerton C. et al. *Educating children with asthma.* *Nurse Pract.* 2002; 27(3) : 12-4.p

Pinto Pereira L.M. et al. *Understanding and use of inhaler medication by asthmatics in specialty care in Trinidad: a study following development of Caribbean guidelines for asthma management and prevention.* *Chest.* 2002; 121(6) : 1833-40.p **Abstract:** STUDY OBJECTIVES: Following the development of the Caribbean Guidelines for Asthma Care, we examined the utilization of inhaled medications in asthmatic patients in Trinidad, West Indies. SETTING: Chest Clinic, Ministry of Health, Trinidad. PARTICIPANTS: Physician-diagnosed asthmatic patients who attended the Chest Clinic between July 1998 and August 2000. MEASUREMENTS AND RESULTS: A consecutive sample of patients who were > 7 years of age (n = 402) was interviewed about compliance with, understanding of, and use of inhaler medication. The inhaler technique of these patients was directly observed. Inhaled steroid therapy was prescribed in 83% of patients but were prescribed the least in elderly patients (63%) and children (62%). Salbutamol was prescribed in 98% of patients, and ipratropium and sodium cromoglycate were selectively prescribed in elderly men and children, respectively. Only 33% of patients used the inhaler correctly, and children and the elderly were the least efficient in its use. The use of a spacer device was advised in 19% of patients, including only 6% of the elderly patients. Explanations for different inhaler therapies were given to 62% of patients, and 53% of patients could describe these reasons. The reported 40% noncompliance rate among patients in the sample was primarily a result of long waiting periods at the pharmacy (58%) and the personal cost incurred on purchasing the medication (52%). CONCLUSIONS: Educating patients, with a focus on children and the elderly, in inhaler techniques and reinforcing understanding of asthma medications can improve asthma management in Trinidad. Asthma caregivers in the Caribbean should ensure the appropriate dissemination of the guidelines and should outline strategies for their implementation.

Piruzyan L.A. et al. *Laser correlation spectroscopy of macromolecular complexes in blood serum as an effective method of monitoring the progress of bronchial asthma in children.* *Dokl Biochem Biophys.* 2004; 395 : 114-7.p

Pitrez P.M. et al. *[Upper airway cellular pattern in infants with acute bronchiolitis: neutrophils or eosinophils?].* *J Pediatr (Rio J).* 2003; 79(5) : 443-8.p **Abstract:** OBJECTIVE: To analyze the cellular pattern of nasopharyngeal secretions in infants with acute bronchiolitis (AB), focusing on the presence or absence of neutrophils and eosinophils. METHOD: Hospitalized children with AB admitted to Hospital Sao Lucas, Porto Alegre, Brazil, between May and July 2002 were recruited. Nasopharyngeal aspirates were collected during the first 48 hours after admission. Slides were stained with May Grunwald and Giemsa. Total cell count and cellular viability were obtained in all samples. RESULTS: Thirty-

eight infants with AB were enrolled. The mean age was 2.2 months (interquartile range: 1.2-3.5), and 21 subjects were male. Neutrophils were the predominant cells in the nasopharyngeal aspirates (median 95%, interquartile: 94-97). No eosinophils were found in the samples studied. **CONCLUSION:** Our results suggest that eosinophils do not play a significant role in the pathophysiology of AB. Infants with AB present a specific inflammatory response to viral infections, which is distinct from the immune response observed in asthma.

Plaisant I. [The Languedoc-Roussillon Air Quality Regional Plan and pollen]. *Allerg Immunol (Paris)*. 2003; 35(5) : 176-7.p

Plaksina G.V. et al. *Stabilizing effect of milk angiogenin on the crystal structure of biological fluids*. *Bull Exp Biol Med*. 2003; 136(4) : 358-61.p **Abstract:** We revealed a new property of angiogenin to restore the crystal structure of biological fluids (human blood plasma and exudates) impaired in various pathologies.

Pleskow W. et al. *Formoterol delivered via the dry powder Aerolizer inhaler versus albuterol MDI and placebo in mild-to-moderate asthma: a randomized, double-blind, double-dummy trial*. *J Asthma*. 2003; 40(5) : 505-14.p **Abstract:** The objectives of this study were to compare the efficacy and tolerability of twice-daily formoterol dry powder 12 microg and 24 microg (Foradil) delivered via Aerolizer inhaler with four times daily albuterol (salbutamol) 180 microg delivered via metered dose inhaler (MDI) and placebo. A total of 554 adolescents and adults (ages 12-75 years) with mild-to-moderate asthma were randomized to this 12-week, multicenter, double-blind, double-dummy, placebo-controlled, parallel-group study. Twelve-hour spirometry measurements were taken at weeks 0, 4, 8, and 12. A total of 484 patients completed the study (122, 116, 127, and 119 given formoterol 12 microg, formoterol 24 microg, albuterol, and placebo, respectively). For the primary efficacy variable, the forced expiratory volume in 1 second (FEV1), both formoterol 12 microg and 24 microg were statistically superior to placebo at all time points on all test days ($p < 0.017$) and to albuterol at most time points on all test days ($p < 0.001$). The onset of improvement in FEV1 was rapid, with 15% increase within 5 min in 57%, 71%, and 65% of formoterol 12 microg, formoterol 24 microg, and albuterol patients, respectively. Formoterol was also superior to placebo and albuterol in terms of secondary efficacy variables: FEV1 area under the curve, percentage of predicted FEV1, forced vital capacity and forced expiratory flow, asthma symptom scores, and peak expiratory flows. In conclusion, both formoterol doses were superior to placebo in all lung function measurements. Overall, compared with albuterol, both formoterol doses produced superior bronchodilation. Formoterol and albuterol were safe and well-tolerated.

Ploin D. et al. [Risk factors for early bronchiolitis at asthma during childhood: case-control study of asthmatics aged 4 to 12 years]. *Arch Pediatr*. 2002; 9(10) : 1025-30.p **Abstract:** The group of general paediatrics of the French Paediatrics Society conducted a case-control study in order to verify the link between the occurrence of an acute bronchiolitis early during the first year of life, more specifically during the first trimester, and asthma during later childhood. **METHODS:** Parents of 4-to-12-year-old children answered a questionnaire during a general paediatrics visit. Exposition was attested by a diagnosis of bronchiolitis mentioned on the personal health record of the child. Environmental factors and medical history, obtained from the parents and by checking the health record of the child, were studied using multivariate analysis. **RESULTS:** Nineteen paediatricians included 80 children with asthma and 160 controls. Fifty-four per cent of asthmatic children had a medical history of bronchiolitis during the first year of life versus 17% of control children ($P < 0.001$). Mean age of bronchiolitis occurrence was 6.6 months in both groups ($P = 0.98$). Multivariate analysis showed that occurrence of bronchiolitis during the first year

of life was significantly more frequent in asthmatic children ($P < 0.001$, $OR = 5.6$, $IC95 = [2.6-11.6]$) but this effect was not observed during the first trimester of life. **CONCLUSION:** Bronchiolitis during the first year of life was significantly related to later asthma in 4-to-12-year-old children treated by general paediatricians. On the other hand, a very early bronchiolitis during the first trimester of life did not appear, in our set of data, as a contributive factor to explain asthma in later childhood.

Plunkett J. *Resuscitation injuries complicating the interpretation of premortem trauma and natural disease in children*. *J Forensic Sci*. 2006; 51(1) : 127-30.p **Abstract:** Minor soft tissues injuries are common in both adults and children who have had cardiopulmonary resuscitation (CPR). Potentially life-threatening injuries are rare. The pre-arrest history in a resuscitated adult often assists the pathologist to interpret autopsy findings. In contrast, an infant or child may not have a reliable history. In this situation, it may be difficult if not impossible to distinguish resuscitation injuries from pre-existing accidental or inflicted trauma. I describe two children who had significant autopsy-documented injuries initially attributed to abuse. The State filed murder charges against the caretaker in each case. However, further history and review of the medical records suggested that resuscitation rather than pre-arrest trauma caused almost all of the injuries. The State dismissed the charges in the first case. A jury returned a "not guilty" verdict in the second. It is essential to consider the entire history and not just autopsy findings when performing a death investigation.

Polk S. et al. *A prospective study of Fel d1 and Der p1 exposure in infancy and childhood wheezing*. *Am J Respir Crit Care Med*. 2004; 170(3) : 273-8.p **Abstract:** The impact of domestic exposure to cat allergen (Fel d1) and house dust mite (Der p1) on wheezing from birth to the age of 4 years was investigated in a multicenter prospective birth cohort; 1,611 mothers were recruited before delivery in Ashford, England, and Barcelona and Menorca, Spain. Exposures were gathered via dust sample collection at children's home in their first year of life. Families provided complete outcome data (wheezing status in all 4 years) for 1,289 children. Domestic allergen levels varied substantially between centers. Six hundred three (47%) children never wheezed during their first 4 years of life. Der p1 did not correlate with any type of wheezing outcome. Fel d1 significantly increased the risk of wheezing in 3- and 4-year-olds in comparison to 1-year-olds. Distinct risk profiles were found for wheezing at different ages. Multivariate analysis revealed an interaction between Fel d1 and maternal asthma among children who wheeze in Year 4 (relative risk = 2.77; 95% confidence interval = 1.19-6.46). Our data support the idea that several patterns of wheezing with different risk profiles exist among young children. The effect of Fel d1 exposure varied according to age and maternal asthma.

Ponsonby A.L. et al. *The association between synthetic bedding and adverse respiratory outcomes among skin-prick test positive and skin-prick test negative children*. *Allergy*. 2002; 57(3) : 247-53.p **Abstract:** **BACKGROUND:** Synthetic bedding has been associated with increased child wheeze and also higher allergen levels in several studies. We aimed to examine whether the association between synthetic bedding and adverse respiratory outcomes was more evident among skin-prick test (SPT) positive children. **METHODS:** A cross-sectional survey involving a population sample of 758 (81% of eligible) school children aged 8-10 years from randomly selected schools in the Australian Capital Territory in 1999. Parental questionnaires for ISAAC respiratory symptoms and child bedding were obtained. SPT results of 10 common allergens were available on 722 of the subjects (77% of those eligible). Synthetic pillow or quilt use was termed synthetic upper bedding. **RESULTS:** Synthetic quilt use was associated with asthma (Adjusted Odds Ratio 1.67 (1.05, 2.65)), recent wheeze (AOR 1.63 (1.03, 2.59)) and allergic rhinoconjunctivitis (AOR 2.11 (1.33, 3.34)) among SPT-positive

children. However, these associations were not apparent for SPT-negative children. Similarly, increasing synthetic upper bedding use was associated with more than 12 episodes of wheeze among SPT-positive children (AOR 1.69 (1.08, 2.64), $P=0.02$, per category) but not SPT-negative children (AOR 0.77 (0.26, 2.21), $P=0.6$, per category). **CONCLUSION:** The apparent association between synthetic upper bedding and adverse respiratory outcomes was evident among SPT-positive but not SPT-negative children. Prospective intervention studies that aim to examine the effect of upper bedding composition on child asthma among SPT-positive children are required.

Ponsonby A.L. et al. *Asthma and early childhood infectious disease. Critical time for protective effect of large family on asthma may not be during first year of life.* *BMJ.* 2001; 323(7305) : 164-5.p

Poole J.A. et al. *Timing of initial exposure to cereal grains and the risk of wheat allergy.* *Pediatrics.* 2006; 117(6) : 2175-82.p **Abstract:** OBJECTIVE: Early exposure to solid foods in infancy has been associated with the development of allergy. The aim of this study was to examine the association between cereal-grain exposures (wheat, barley, rye, oats) in the infant diet and development of wheat allergy. **METHODS:** A total of 1612 children were enrolled at birth and followed to the mean age of 4.7 years. Questionnaire data and dietary exposures were obtained at 3, 6, 9, 15, and 24 months and annually thereafter. The main outcome measure was parent report of wheat allergy. Children with celiac disease autoimmunity detected by tissue transglutaminase autoantibodies were excluded. Wheat-specific immunoglobulin E levels on children reported to have wheat allergy were obtained. **RESULTS:** Sixteen children (1%) reported wheat allergy. Children who were first exposed to cereals after 6 months of age had an increased risk of wheat allergy compared with children first exposed to cereals before 6 months of age (after controlling for confounders including a family history of allergic disorders and history of food allergy before 6 months of age). All 4 children with detectable wheat-specific immunoglobulin E were first exposed to cereal grains after 6 months. A first-degree relative with asthma, eczema, or hives was also independently associated with an increased risk of wheat-allergy development. **CONCLUSIONS:** Delaying initial exposure to cereal grains until after 6 months may increase the risk of developing wheat allergy. These results do not support delaying introduction of cereal grains for the protection of food allergy.

Poon A.H. et al. *Association of vitamin D receptor genetic variants with susceptibility to asthma and atopy.* *Am J Respir Crit Care Med.* 2004; 170(9) : 967-73.p **Abstract:** Genome scans for asthma have identified suggestive or significant linkages on 17 different chromosomes, including chromosome 12, region q13-23, housing the vitamin D receptor (VDR) gene. Through interaction with VDR, 1,25-dihydroxyvitamin D₃ mediates numerous biological activities, such as regulation of helper T-cell development and subsequent cytokine secretion profiles. Variants of the VDR have been found to be associated with immune-mediated diseases that are characterized by an imbalance in helper T-cell development, such as Crohn's disease and tuberculosis. The VDR, hence, is a good candidate to be investigated for association with asthma, which is characterized by enhanced helper T-cell type 2 activity. Here, we examined VDR genetic variants in an asthma family-based cohort from Quebec. We report six variants to be strongly associated with asthma and four with atopy ($0.0005 < \text{or } = p < \text{or } = 0.05$). Analysis of the linkage disequilibrium pattern and haplotypes also revealed significant association with both phenotypes ($0.0004 < \text{or } = p < \text{or } = 0.01$). The findings have been replicated by another research team in a second but not in a third cohort. These results identify VDR variants as genetic risk factors for asthma/atopy and implicate a non-human leukocyte antigen immunoregulatory molecule in the pathogenesis of asthma and atopy.

Portnoy J. et al. *Pediatric asthma emergencies.* *J Asthma.* 2003; 40 Suppl : 37-45.p

Powell C.V. et al. *A parent completed questionnaire to describe the patterns of wheezing and other respiratory symptoms in infants and preschool children.* *Arch Dis Child.* 2002; 87(5) : 376-9.p **Abstract:** AIM: To develop a standardised and validated respiratory symptom questionnaire for use in epidemiological or follow up studies in infants and preschool children. **METHODOLOGY:** After initial design and development, the questionnaire was administered to two cohorts of subjects, one recruited from a respiratory clinic and the other from a postnatal ward. The two cohorts then repeated the questionnaire, two weeks apart. The qualities of the questionnaire were assessed. **RESULTS:** Response rate to the initial questionnaire was 100% for the clinic based cohort and 64% for postnatally recruited families (total number of subjects 114). Questions showed good to moderate short term reliability (weighted kappa scores 0.47-0.7; average correct classification rates 0.74-0.91). Four domain concept scores showed excellent internal consistency (Cronbach alpha scores 0.87-0.95). Using principal component factor analysis, four new domains were devised showing acceptable construct validity and internal consistency. Criterion validity was assessed using a respiratory physician based diagnosis of asthma (RPBDA) as the gold standard for comparison. All eight scales in the questionnaire could significantly distinguish between infants with RPBDA and well or mildly symptomatic subjects. **CONCLUSION:** We have developed a practical, acceptable questionnaire with eight concept domains for use in infants and preschool children. The questionnaire has strong construct validity and internal consistency with good short term reliability of questions. More detailed study of criterion validity and the responsiveness of the questionnaire is required using a larger population and including children with the different phenotypes of wheezy illness.

Powell K. *Ozone exposure throws monkey wrench into infant lungs.* *Nat Med.* 2003; 9(5) : 490.p

Pradel F.G. et al. *Asthma self-management: the perspective of children.* *Patient Educ Couns.* 2001; 45(3) : 199-209.p **Abstract:** This qualitative study explored the knowledge, perceptions, and autonomy of 7- and 12-year-old children relative to the management of their asthma. A total of 32 children with moderate to severe asthma were interviewed using an open-ended drawing interview and a semi-structured interview. The triangulation of results from these two methods revealed developmental differences. Younger children identified medicines by shape, color, or lay terms, relied on adults to manage their asthma, and did not recognize warning symptoms of an attack. Older children mastered biomedical terminology and used medicines independently, although they sometimes asked for the assistance of an adult. All children perceived benefits and non-monetary costs of asthma medicines. However, they lacked understanding of the categories and role of asthma medicines. This study suggests that long-term control and quick-relief metered dose inhalers should be identifiable by consistent color-coding, and that professionals should tailor asthma education and information to children's stages of cognitive development.

Prasad A. et al. *Exhaled nitric oxide as a screening tool for asthma in school children.* *Respir Med.* 2006; 100(1) : 167-73.p **Abstract:** It is now widely accepted that augmented levels of fractional exhaled nitric oxide (FeNO) reflect airway inflammation and the methodology has been optimised for potential clinical use. We were interested in investigating whether this measurement can be used as a tool to screen and identify school children with asthma. To do this, FeNO was measured using an on-line single exhalation analyser in 368 children aged 8-10 years in six Oxfordshire primary schools, by two investigators blinded to the disease status of the children. The children were then categorised into 'normal', 'atopic asthma', 'non-

atopic asthma' and 'atopy only' groups, according to their responses to the ISAAC questionnaire and perusal of the children's medical records kept by their family practitioners. Increased levels of FeNO were found in 'atopic asthmatic', 'non-atopic asthmatics' and 'atopy only' groups (median values of 24.4, 7.8 and 15.3 ppb, respectively, compared to normal controls' of 6.9 ppb). Levels were increased in atopic children regardless of whether they had asthma and were significantly higher than non-atopic asthmatics. We conclude that FeNO measurement is not a useful tool for identifying children with asthma in the community, as increased levels did not discriminate between those with asthmatic and atopic symptoms.

- Preutthipan A. et al.** *Effect of PM10 pollution in Bangkok on children with and without asthma.* *Pediatr Pulmonol.* 2004; 37(3) : 187-92.p Abstract: This study aimed to investigate the effects of PM10 concentrations exceeding the Thai national standard (24-hr average, >120 microg/m³) on daily reported respiratory symptoms and peak expiratory flow rate (PEFR) of schoolchildren with and without asthma in Bangkok. The 93 asthmatic and 40 nonasthmatic schoolchildren were randomly recruited from a school located in a highly congested traffic area. Daily respiratory symptoms and PEFR of each child were evaluated and recorded in the diary for 31 successive school days. During the study period, 24-hr average PM10 levels ranged between 46-201 microg/m³. PM10 levels exceeded 120 microg/m³ for 14 days. We found that when PM10 levels were >120 microg/m³, the daily reported nasal irritation of asthmatic children was significantly higher than when PM10 levels were < or =120 microg/m³. In addition, when PM10 levels were >120 microg/m³, nonasthmatic children had a significantly higher daily reported combination of any respiratory symptoms. PEFR did not change with different ambient PM10 levels in both groups. This study suggests that elevated levels of PM10 concentrations in Bangkok affect respiratory symptoms of schoolchildren with and without asthma.
- Priftanji A. et al.** *Asthma and allergy in Albania and the UK.* *Lancet.* 2001; 358(9291) : 1426-7.p Abstract: In the first phase of the International Study of Asthma and Allergies in Childhood, a large difference in occurrence of asthma symptoms was seen between children in Albania and the UK. We did skin-prick tests with various allergens and measured peak expiratory flow rate in about 1000 children from each country. A large difference in the proportion of exercise-induced bronchial reactivity was evident between children from Albania and the UK (0.8% vs 5.4%, respectively). However, the frequency of allergic sensitisation was closely similar (15.0% vs 17.8%, respectively). These results suggest that large geographical variations in asthma prevalence can arise without differences in frequency of atopy.
- Primhak R.A.** *Commentary on de Baets et al.: exercise-induced respiratory symptoms are poor predictors of bronchoconstriction.* *Pediatr Pulmonol.* 2005; 39(4) : 299-300.p
- Probst B.** *Patient's perspective on ED asthma education.* *Am J Emerg Med.* 2004; 22(6) : 499.p
- Puccio F.A. et al.** *Importance of including Blomia tropicalis in the routine diagnosis of Venezuelan patients with persistent allergic symptoms.* *Allergy.* 2004; 59(7) : 753-7.p Abstract: BACKGROUND: *Blomia tropicalis* is a common mite found in the house dust of many tropical countries including Venezuela. The prevalence of skin test and specific serum immunoglobulin (Ig)E reactivity to *B. tropicalis* in Venezuela has not been previously evaluated. METHODS: In the present study we evaluated the skin reactivity by skin prick test and specific IgE by a multiple antigen blot assay, against *B. tropicalis* and *Dermatophagoides pteronyssinus*, in a group of 115 subjects who attended the Allergy Clinic of the Institute of Biomedicine, Caracas,

Venezuela, and we studied possible cross reactions between similar proteins of these two mites. RESULTS: One hundred and six patients with persistent allergic respiratory symptoms showed a positive skin prick test to at least one of the mite extracts, with the frequency of positive reactions to *B. tropicalis* being as high as to *D. pteronyssinus*. Twelve patients reacted only to *D. pteronyssinus* and 13 different patients only to *B. tropicalis*. Specific IgE to each of the mite extracts was found with similar frequency, and the results coincided with the skin test reactivity. CONCLUSIONS: The study indicated the importance of including *B. tropicalis* in routine diagnostic testing in tropical and sub-tropical situations.

- Pugia M.J. et al.** *Clinical utility of a rapid test for uristatin.* *Clin Biochem.* 2002; 35(2) : 105-10.p Abstract: OBJECTIVES: Uristatin is a trypsin inhibitor present in urine that is increased in most patients with bacterial or viral infections and in many with inflammatory disorders. We included the assay of uristatin as part of a screening program carried out by pediatricians on 4207 Japanese schoolchildren to judge the ability of uristatin to identify those with an infection and (or) inflammation of any cause. We used urine dipsticks for the assay of uristatin, creatinine, albumin, blood, leukocyte esterase, and protein. We also performed quantitative assays for uristatin and creatinine. Another aim was to estimate the reference range for uristatin in schoolchildren, ages 5 to 14 yr. METHODS: We prepared dipstick pads that were impregnated with a chromogenic substrate for trypsin and measured the uristatin-caused inhibition of trypsin in urine. We measured creatinine so that the ratio of uristatin to creatinine could be calculated to correct for urine concentration. RESULTS: We obtained quantitative uristatin and creatinine results for 4207 children. Of these, 177 had an abnormal urine dipstick for albumin or blood or protein or leukocyte esterase or a combination of these. We used data from 3622 children to establish the reference range for the uristatin dipsticks. The 3622 were diagnosed by their pediatricians as free from an infection or inflammation of any cause and with normal urine dipstick tests. We recommend an upper reference limit for uristatin by dipstick of < or = 7.5 mg uristatin/g creatinine. The leftover 408 children ([4207-3622-177] = 408) fell into two groups: 205 with diagnoses of no infection, possible infection, or possible inflammatory disorders. The remaining 203 children were renal disease follow-up cases. The diagnoses were based on a physical examination, microscopic urinalysis plus urine dipstick tests for albumin, blood, creatinine, protein, leukocyte esterase and a complete blood count. In the 205 children, 46 had an abnormal uristatin dipstick test, 39 had an abnormal uristatin by immunoassay, 41 had an abnormal erythrocyte sedimentation rate (ESR), 27 had an abnormal serum C-reactive protein (CRP), and one had an abnormal urine microscopic exam. For the first 938 children in the study, the agreement was 93% of negative dipstick uristatin results and immunoassays. The agreement of positive uristatin dipsticks with immunoassays was 85%. We assumed that the immunoassay results were correct. In the evaluation of 189 children with fever, 62 also had an abnormal uristatin by dipstick. DISCUSSION: A rapid dipstick test for uristatin read on a reflectance photometer gave values that compared well with a quantitative immunoassay method. The uristatin test is sensitive but not specific for any cause of infection or inflammation. Uristatin is easy to determine and appears to be a better indicator than fever, ESR, or CRP for the diagnosis of an infection or inflammation.
- Pukkala E. et al.** *Increased incidence of cancer and asthma in houses built on a former dump area.* *Environ Health Perspect.* 2001; 109(11) : 1121-5.p Abstract: Twelve blockhouses were built in Helsinki in the 1970s on a former dump area containing industrial and household waste. We investigated whether the exposure to landfill caused cancer or other chronic diseases in the inhabitants of these houses. From the Population Register, we identified 2,000 persons who had ever lived in houses built on the dump area and a similar reference cohort from similar houses elsewhere in Helsinki. We identified their cancer cases from the Cancer Registry, and the other chronic diseases

eligible for free medication from the Finnish Social Insurance Institution. At the end of 1998, 88 cases of cancer had been diagnosed, whereas the expected number based on the incidence rates among all inhabitants of Helsinki was 76.1. The excess cases were entirely attributable to males and to follow-up ≥ 5 years after moving into the dump area [standardized incidence ratio (SIR) in this category, 1.61; 95% confidence interval (CI), 1.11-2.24], and they were distributed evenly over primary sites. The relative risk increased slightly with the number of years lived in the area. The relative risk of cancer between the dump area and reference houses was 1.50 (1.08-2.09), similar in both sexes. Of the other chronic diseases, the SIRs for asthma (1.63; CI, 1.27-2.07) and chronic pancreatitis (19.3; CI, 2.34-69.7) were significantly increased. The possibility of a causal association between dump exposure and incidence of cancer and asthma cannot be fully excluded. The Helsinki City Council decided to demolish the houses in the dump area, and most houses have already been destroyed.

Pumputiene I. et al. *T cell and eosinophil activation in mild and moderate atopic and nonatopic children's asthma in remission.* Allergy. 2006; 61(1) : 43-8.p **Abstract:** BACKGROUND: Inflammation in the pathogenesis of asthma is associated with products of activated T cells and eosinophils. The aim of this study was to determine whether ongoing inflammation persists in children with different phenotypes of asthma despite the disease in remission. METHODS: Serum samples were collected from 68 children with atopic or nonatopic asthma in remission and from 15 healthy children. Soluble interleukin-2 receptor (sIL-2R), IL-2 and IL-4 were examined by using an enzyme-linked immunosorbent assay. Total and specific immunoglobulin E, and eosinophil cationic protein (ECP) were analysed by fluoroimmunoassay (Pharmacia CAP System). RESULTS: In patients with moderate persistent atopic asthma, sIL-2R was increased significantly when compared with mild persistent atopic asthma ($P < 0.05$). No changes of sIL-2R were seen in nonatopic asthmatics compared with atopics and controls. The level of IL-2 was elevated in moderate persistent atopic and nonatopic asthmatic children compared with controls ($P < 0.05$ and $P < 0.05$ respectively) and compared with mild persistent atopic asthmatics and mild persistent nonatopic asthmatics ($P < 0.05$ in both cases). The levels of IL-4 in most patients and controls remained below the sensitivity of the assay. Eosinophil cationic protein levels in moderate persistent atopic and nonatopic asthmatics were significantly higher than in mild persistent asthma severity cases ($P < 0.001$ and $P < 0.01$ respectively) and in healthy children ($P < 0.01$ in both cases). CONCLUSION: Changes in the concentration of sIL-2R, IL-2 and ECP reflect increased T cell and eosinophil activity in relation to the level of severity of asthma in atopic and nonatopic children, thereby proving the presence of persistent inflammation despite the absence of disease symptoms.

Purucker M.E. et al. *Inhaled fluticasone propionate by diskus in the treatment of asthma: a comparison of the efficacy of the same nominal dose given either once or twice a day.* Chest. 2003; 124(4) : 1584-93.p **Abstract:** STUDY OBJECTIVE: In September 2000, the US Food and Drug Administration (FDA) approved the use of Flovent Diskus (FD) [fluticasone propionate; GlaxoSmithKline; Research Triangle Park, NC], which is an orally inhaled, dry-powder corticosteroid, for the maintenance treatment of asthma at dosages of 50 to 1,000 microg administered twice-daily. Once-daily dosage regimens did not receive approval. This article will detail six clinical trials, five of which incorporated comparative once-daily and twice-daily treatment arms of the same nominal dose of FD. DESIGN: Six 12-week, randomized, double-blind, placebo-controlled studies in patients with mild-to-moderate asthma, including two pediatric asthma trials (patient age, 4 to 11 years) of total daily doses of fluticasone propionate (FP) of 100 or 200 microg, and four adult and adolescent studies of total daily doses of FP of 100, 200, or 500 microg. RESULTS: Twice-daily dosing was numerically superior to once-daily dosing at the same nominal dose in all comparative

studies for the primary end point, change in predose FEV₁. In five trials, the results of the once-daily dosage of FP were statistically indistinguishable from those with placebo. One trial demonstrated the superiority of FP, 500 microg once-daily, over placebo; however, the effect size was half that observed with twice-daily dosing. Once-daily FP dosing showed no advantage in safety or in patient adherence to medication. CONCLUSIONS: In the FDA review of once-daily dosing of the FD regimen, 100 or 200 microg once-daily dosing was not shown to be significantly better than placebo. FP 500 microg once-daily was found to be superior to placebo, but at about one half the effect size as the same nominal dose given bid. No advantage in patient safety or adherence was demonstrated for once-daily administration over twice-daily administration, and once-daily administration is not currently recommended.

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Qian Z. et al. *Exposure-response relationships between lifetime exposure to residential coal smoke and respiratory symptoms and illnesses in Chinese children.* J Expo Anal Environ Epidemiol. 2004; 14 Suppl 1 : S78-84.p **Abstract:** Data collected in a large epidemiologic study were analyzed to examine respiratory health effects of residential coal use in 7058 school children living in the four Chinese cities of Chongqing, Guangzhou, Lanzhou, and Wuhan. A Scenario Evaluation Approach was used to develop two exposure variables, heating coal smoke and cooking coal smoke. Estimated lifetime exposures to heating coal smoke and cooking coal smoke were both classified into four-level ordinal scales, as follows: no reported exposure (control); lightly exposed; moderately exposed; and heavily exposed. Zero-one dummy variables were constructed for each exposure level other than the control level (total six variables). These variables were entered into the analytical model. We tested for exposure-response relationships using logistic regression models, while controlling for other relevant covariates, including an indicator variable of ambient air pollution levels. We observed monotonic and positive exposure-response relationships of exposure to heating coal smoke with modeled odds ratios (ORs) of phlegm, cough with phlegm, and bronchitis. Other health outcomes were not associated with such exposure in a monotonic exposure-response pattern. However, ORs for cough, wheeze, and asthma were all higher in the exposed groups than in the control group. We observed no consistent associations between cooking coal smoke and the examined health outcomes. We conclude that exposure to heating coal smoke could have adverse effects on children's respiratory symptoms and illnesses in these four Chinese cities.

Quach C. et al. *Risk factors associated with severe influenza infections in childhood: implication for vaccine strategy.* Pediatrics. 2003; 112(3 Pt 1) : e197-201.p **Abstract:** Infections caused by influenza virus lead to an excess rate of hospitalization of children during winter months. Current recommendations for vaccination target only children >6 months who belong to specific risk groups. OBJECTIVE: To identify possible benefits of universal influenza vaccination, this study aims to determine characteristics of children hospitalized at the Montreal Children's Hospital (MCH) because of an infection attributable to influenza virus as well as risk factors associated with hospitalization. METHODS: We retrospectively reviewed records of all children with a laboratory-proven diagnosis of influenza seen at MCH between April 1, 1999, and April 1, 2002. Data were analyzed using the Student t test and logistic regression. RESULTS: We identified 182 patients hospitalized because of influenza and 114 patients who were not. Admission diagnoses were suspected sepsis (31%), lower respiratory tract infections (27%), and asthma or bronchiolitis (15%). Mean age of hospitalized patients was 26.1 month (median: 12 months), which was similar to that of patients not hospitalized, and 34% were <6 months. Seventy percent

of those hospitalized did not have any underlying medical disorder and only 18% (33) were vaccine candidates according to current recommendations. Of the latter, less than half had been vaccinated. Factors associated with hospitalization were age <12 months (odds ratio [OR]: 2.3; 95% confidence interval [CI]: 1.1-4.8), male gender (OR: 1.9; 95% CI: 1.0-3.7), dehydration (OR: 4.3; 95% CI: 1.2-16.0), and decreased oxygen saturation (OR: 32.1; 95% CI: 4.1-249). CONCLUSIONS: Considering that the majority of children hospitalized for influenza do not belong to the specific risk groups targeted by current recommendations, and that one third are <6 months of age, the target population for vaccination needs to be reexamined. Extending vaccination to all young children, to additional high-risk groups, and to pregnant women has potential to reduce the impact of influenza on children.

Quah B.S. et al. *Prevalence of asthma, eczema and allergic rhinitis: two surveys, 6 years apart, in Kota Bharu, Malaysia.* *Respirology.* 2005; 10(2) : 244-9.p **Abstract:** OBJECTIVE: This study was undertaken to determine the prevalence of asthma, eczema, and allergic rhinitis in school children in Kota Bharu, Malaysia, and in so doing to determine the differences in symptom prevalence rates of asthma, and atopic diseases in Kota Bharu school children between 1995 and 2001. METHODOLOGY: In two studies (1995 and 2001), year one primary school (PS) pupils (6-7 years old) and secondary school (SS) year two pupils (13-14 years old) were randomly selected from the district of Kota Bharu, Kelantan, Malaysia. In 1995, 3939 PS children and 3116 SS children participated, and in 2001 3157 PS children and 3004 SS children participated. The Phase I International Study of Asthma and Allergies in Childhood prevalence written questionnaire and video questionnaire (only shown to SS children) were used in both studies. RESULTS: The written questionnaire showed no significant changes in the prevalence (1995, 2001) of ever wheeze (8.3%, 6.9%P = 0.06), current wheeze (5.4%, 4.3%P = 0.08), exercise-induced wheeze (EIW; 3.9%, 3.7%P = 0.63), and rhinoconjunctivitis (4.6%, 5%P = 0.42) among PS children. The prevalence of flexural itchy rash increased from 14% to 17.6% (P = 0.004) and night cough decreased from 20.4% to 17.5% (P = 0.005). There were also no significant changes in these symptoms among SS children (1995, 2001): ever wheeze (10.7%, 12%P = 0.37), current wheeze (6.8%, 5.7%P = 0.20), EIW (9.9%, 11.6%P = 0.28), night cough (21.6%, 24%P = 0.39), rhinoconjunctivitis (11%, 15%P = 0.11), and flexural itchy rash (12%, 13%P = 0.11). The video questionnaire showed no significant changes in the prevalence of symptoms in the previous 12 months (1995 vs 2001) for wheeze at rest (3.8%, 2.8%P = 0.12), EIW (6.9%, 8.8%P = 0.32), waking with wheeze (1.7%, 1.7%P = 1.0), and severe wheeze (2.1%, 3%P = 0.12). Night cough in the previous 12 months increased significantly from 5.1% to 8.3% (P = 0.007). CONCLUSION: Although asthma and atopic disorders are common in this country, the results revealed no major changes in the prevalence rates of these diseases over a period of 6 years.

Quick J.L. et al. *Cortical bone geometry in asthmatic children.* *Arch Dis Child.* 2006; 91(4) : 346-8.p **Abstract:** At the mid-radius, pre-pubertal asthmatic children had smaller periosteal and endosteal circumferences and thicker cortical shells compared to controls, when assessed by peripheral quantitative computed tomography. Asthmatics had diminished periosteal expansion for muscle size, suggesting that asthma, its treatment, or its effects on physical activity had resulted in impaired adaptation of bone to muscle loading. Alterations in cortical bone geometry might explain the increased fracture risk in asthmatic children.

Raat H. et al. *Reliability and validity of the short form of the child health questionnaire for parents (CHQ-PF28) in large random school based and general population samples.* *J Epidemiol Community Health.* 2005; 59(1) : 75-82.p **Abstract:** STUDY OBJECTIVES: This study assessed the feasibility, reliability, and validity of the 28 item short child health questionnaire parent form (CHQ-PF28) containing the same 13 scales, but only a subset of the items in the widely used 50 item CHQ-PF50. DESIGN: Questionnaires were sent to a random regional sample of 2040 parents of schoolchildren (4-13 years); in a random subgroup test-retest reliability was assessed (n = 234). Additionally, the study assessed CHQ-PF28 score distributions and internal consistencies in a nationwide general population sample of (parents of) children aged 4-11 (n = 2474) from Statistics Netherlands. MAIN RESULTS: Response was 70%. In the school and general population samples seven scales showed ceiling effects. Both CHQ summary measures and one multi-item scale showed adequate internal consistency in both samples (Cronbach's alpha>0.70). One summary measure and one scale showed excellent test-retest reliability (intraclass correlation coefficient >0.70); seven scales showed moderate test-retest reliability (intraclass correlation coefficient 0.50-0.70). The CHQ could discriminate between a subgroup with no parent reported chronic conditions (n = 954) and subgroups with asthma (n = 134), frequent headaches (n = 42), and with problems with hearing (n = 38) (Cohen's effect sizes 0.12-0.92; p<0.05 for 39 of 42 comparisons). CONCLUSIONS: This study showed that the CHQ-PF28 resulted in score distributions, and discriminative validity that are comparable to its longer counterpart, but that the internal consistency of most individual scales was low. In community health applications, the CHQ-PF28 may be an acceptable alternative for the longer CHQ-PF50 if the summary measures suffice and reliable estimates of each separate CHQ scale are not required.

Rabinovitch N. et al. *Particulate levels are associated with early asthma worsening in children with persistent disease.* *Am J Respir Crit Care Med.* 2006; 173(10) : 1098-105.p **Abstract:** RATIONALE: Ambient particulate concentrations have been associated with variable physiologic effects in children with persistent asthma taking controller medications. OBJECTIVE: To determine whether exposure to particulate matter has immediate effects on asthma control in children with persistent disease. METHODS AND MEASUREMENTS: In a school-based cohort, 73 children, primarily with moderate and severe asthma, were followed daily over one or two winters (2001-2002, 2002-2003) in Denver, Colorado. The association among ambient fine particulate, bronchodilator use, and urinary leukotriene E4 levels was assessed. RESULTS: Daily concentrations of fine particulate peaked in the morning hours when children were commuting to school. In a multivariable analysis that controlled for meteorology, time trends, and upper respiratory infections, an increase of one interquartile range in morning maximum fine particulate levels was related to an average increase of 3.8% in bronchodilator usage at school (95% confidence interval [CI], 0.2-7.4; p = 0.04). Children with severe asthma demonstrated significantly stronger associations (8.1% increase; 95% CI, 2.9-13.4; p = 0.003) than those with mild/moderate disease (1.6% increase; 95% CI, -2.2-5.4; p = 0.41; p = 0.03 for difference between groups). Morning maximum fine particulate levels were also associated with urinary leukotriene E4 measured during school hours (average increase of 6.2% per interquartile range increase; 95% CI, 1.9-10.5; p = 0.006). These associations were not discernable when 24-h averaged concentrations were used. CONCLUSIONS: Peak concentrations of ambient fine particulate are associated with early increases in bronchodilator use and urinary leukotriene E4 levels among children with persistent asthma, despite the use of controller medications.

Rabinovitch N. et al. *Effects of wintertime ambient air pollutants on asthma exacerbations in urban minority children with moderate to severe disease.* *J Allergy Clin Immunol.* 2004; 114(5) : 1131-7.p

Abstract: BACKGROUND: Urban minority children with asthma are at higher risk for severe exacerbations leading to hospitalizations and deaths. Because multiple studies have reported associations between air pollution and asthma worsening, elevated levels of air pollution are cited as a possible trigger for increased asthma morbidity in urban areas. Few studies have prospectively followed panels of urban children with asthma to determine whether air pollution levels are associated with clinically relevant outcomes such as asthma exacerbations. OBJECTIVE: To determine the association between levels of ambient air pollutants and asthma exacerbations in urban poor children with moderate to severe asthma. METHODS: A school-based panel of children with difficult-to-control disease was followed over a period of 3 consecutive winters in Denver, Colo. The panel consisted of predominantly urban African American children with moderate to severe asthma. Levels of Environmental Protection Agency criteria air pollutants were measured on a daily basis with concurrent monitoring of lung function, bronchodilator use, symptoms, and asthma exacerbations. RESULTS: After controlling for time-varying factors such as upper respiratory infections and meteorologic factors, a weak association was found between ambient carbon monoxide levels and bronchodilator use. Ozone levels were associated with daytime symptoms only. No association was observed between daily air pollution concentrations and daily levels of FEV₁, peak flow, nighttime symptom scores, or asthma exacerbations over the 3-year period. CONCLUSION: Ambient levels of Environmental Protection Agency criteria air pollutants in Denver do not lead to clinically significant asthma worsening in urban children with moderate to severe asthma during winter months when children are primarily indoors.

Raby B.A. et al. Association of vitamin D receptor gene polymorphisms with childhood and adult asthma. *Am J Respir Crit Care Med.* 2004; 170(10) : 1057-65.p **Abstract:** Vitamin D receptor (VDR) polymorphisms have been associated with several immune-related diseases, and VDR and vitamin D itself modulate T cell differentiation. VDR maps to chromosome 12q, near a region commonly linked to asthma. We evaluated VDR as part of a 12q positional candidate survey, and in response to observations of VDR polymorphism associations with asthma and atopy in a founder population of Quebec. Twenty-eight loci in 7 positional candidates (7 in VDR) were genotyped in 582 families. Whereas other candidates demonstrated no association, the VDR Apal polymorphism demonstrated significant transmission distortion, with undertransmission of the C allele in a ratio of 4:5 ($p = 0.01$). This association was most prominent in girls, in whom distortion was more marked ($p = 0.009$). Sex-specific associations between multiple VDR polymorphisms and immunoglobulin E levels were also observed ($p = 0.006-0.01$). Asthma associations were replicated in a second cohort (517 females with asthma and 519 matched control subjects): 4 of 6 VDR variants demonstrated significant association ($p = 0.02-0.04$). The direction of association in this second cohort was opposite to the effects seen in the trios, but similar to findings in the Quebec study. These results suggest that VDR influences asthma and allergy susceptibility in a complex manner.

Raby B.A. et al. ADAM33 polymorphisms and phenotype associations in childhood asthma. *J Allergy Clin Immunol.* 2004; 113(6) : 1071-8.p **Abstract:** BACKGROUND: A disintegrin and metalloproteinase (ADAM) 33 has been implicated as an asthma susceptibility gene by using a positional cloning approach. However, genetic linkage of asthma phenotypes to chromosome 20p13 (the location of ADAM33) has not been observed in most asthma genome scans, and it is unclear whether these associations with ADAM33 are broadly generalizable. OBJECTIVE: To examine whether ADAM33 is associated with asthma in a North American population of childhood asthmatic patients. METHODS: We performed a family-based association study by using 652 nuclear families ascertained through asthmatic subjects enrolled in a large randomized clinical trial. Seventeen ADAM33 single nucleotide polymorphisms (SNPs; including 9

associated with asthma in the initial report) were genotyped by mass spectrometry. Single-SNP and haplotype association analysis was performed. RESULTS: Among white and African American subjects, no single-SNP association with asthma was observed. However, a common 16-SNP haplotype (frequency, 14.6% in white subjects) was associated with asthma ($P = .006$). Two SNPs in strong linkage disequilibrium (T1 and T+1) were marginally associated with asthma in the Hispanic cohort ($P = .04$). These data provide marginal support for an asthma locus in the ADAM33 genomic region. However, the magnitudes of the observed associations are modest at best and are inconsistent with the original report. CONCLUSIONS: We conclude that either ADAM33 has only modest effects on asthma susceptibility, and the initial reports of association were a result of analysis in a selected population, or the initial findings were a result of chance. It is also possible that the true asthma susceptibility locus in this genomic region is near, but not at, ADAM33.

Raby B.A. et al. Eotaxin polymorphisms and serum total IgE levels in children with asthma. *J Allergy Clin Immunol.* 2006; 117(2) : 298-305.p **Abstract:** BACKGROUND: Eotaxin (chemokine, CC motif, ligand; CCL11) is a potent eosinophil chemoattractant strongly implicated in the pathobiology of asthma. Genetic variation at the CCL11 locus has been correlated with serum total IgE, blood eosinophil counts, and circulating eotaxin protein levels in several case-control asthma studies. Family-based association studies of CCL11 genetic variants have not been reported to date. OBJECTIVE: To evaluate 9 common CCL11 single nucleotide polymorphisms (SNPs) in nuclear families ascertained through patients with asthma participating in the Childhood Asthma Management Program study. METHODS: Single nucleotide polymorphism genotyping was performed by using minisequencing and probe hybridization platforms. Family-based association analysis for asthma and 4 asthma-related intermediate quantitative phenotypes was performed by using FBAT. RESULTS: One SNP, -384A>G, was associated with asthma among African American families ($P = .01$). CCL11 SNPs and haplotypes were not associated with asthma among white or Hispanic families. Two low-frequency alleles in strong pairwise linkage disequilibrium, -426C and IVS2+199A, were associated with lower serum total IgE levels ($P = .0006$ and $P = .009$, respectively) in white families, whereas 2 more common variants, -576C and g.4438C, were associated with higher IgE levels in African American families ($P = .01-.04$). Haplotype analysis in the white cohort provided additional evidence of association with serum total IgE, implicating 2 haplotypes. No single SNP or haplotype associations were observed with blood eosinophil levels, FEV₁, or airway responsiveness. CONCLUSION: These findings provide further evidence that genetic variation at the CCL11 locus is an important determinant of serum total IgE levels among patients with asthma.

Radeos M.S. et al. Predicted peak expiratory flow: differences across formulae in the literature. *Am J Emerg Med.* 2004; 22(7) : 516-21.p **Abstract:** The study objectives were to examine the differences between Peak Expiratory Flow (PEF) formulae in the literature and to assess the potential impact of those differences on the interpretation of clinical guidelines for asthma management. We calculated 100% PEF values for hypothetical patients at the 50(th) percentile for height and weight and classified the percent predicted PEF into severity groups according to national asthma guidelines. Choosing different formulae could give an 18 year old man a 100% predicted PEF as low as 501 L/min and as high as 730 L/min ($\Delta = 229$ L/min); and a 35 year old woman a classification of severe (46%) using one, but moderate (57%) using another. Predicted PEF varied widely across formulae and choice of formula may alter guideline-based care. We propose recently published population-based equations as the reference standard for future asthma guidelines.

Radzik D. et al. *Inhaled steroids in the treatment of mild to moderate persistent asthma in children: once or twice daily administration?* Arch Dis Child. 2002; 87(5) : 415-6.p

Raherison C. et al. *Asthma in exercising children exposed to ozone.* Lancet. 2002; 360(9330) : 411.p

Rahman F. et al. *The magnitude of child injuries in Bangladesh: a major child health problem.* Inj Control Saf Promot. 2004; 11(3) : 153-7.p
Abstract: In recent times, many developing countries including Bangladesh not only have to cope with infectious diseases and malnutrition but also with new health problems, such as asthma, cancer and accidents. The emergence of chronic diseases and injuries has not been seen as an important health issue to date. The work presented here has the objectives of conceptualizing the dynamic changes in child mortality within the framework of the health transition, to provide a basis for projection of future mortality and disability in children in Bangladesh. This paper reviews a number of reports and published articles related to the causes of child deaths in Bangladesh. These include: 1) Year books of Bangladesh Bureau of Statistics; 2) UNICEF reports; 3) Reports of International Centre for Diarrhoeal Disease and Research, Bangladesh; and 4) Reports of Institute of Child and Mother Health. Bangladesh clearly has been progressing along its epidemiological transition. At the current stage, chronic diseases and injuries have overtaken infectious diseases as leading causes of child death. Injury has been identified as a major cause of child death in Bangladesh, and is emerging as the leading cause of child mortality, similar to what is occurring in other developing countries. For these countries, in the advancing stages of their health transition, more research aimed at understanding the dynamic change of child health priorities is urgently needed for appropriate policy and planning.

Raison-Peyron N. et al. *[Connubial contact dermatitis to an inhaled corticosteroid].* Ann Dermatol Venerol. 2005; 132(2) : 143-6.p
Abstract: BACKGROUND: Inhaled corticosteroids are widely used in allergic asthma and rhinitis. They are most often used alone or sometimes in association. Allergic side-effects of inhaled corticosteroids are less frequent than those of topical corticosteroids. We report a case of a connubial dermatitis to a budesonide spray. OBSERVATION: A 3-year old boy was treated for asthma by budesonide (Pulmicort) and terbutaline (Bricanyl) aerosols with an inhalation chamber (Babyhaler). From the fourth day of treatment onwards, his mother had swollen and itchy lesions on the face with conjunctivitis several hours after the administration of the corticosteroids using the inhalation chamber. The last eruptions were marked by extensive lesions. The patient reported a worsening of her eruption when she was treated with a desonide cream (Tridesonit). Prick-tests conducted later on confirmed the contact allergy to budesonide and Pulmicort spray. They were also positive for Tridesonit cream and triamcinolone acetonide. Repeated open application tests with a 17-butyrate hydrocortisone cream (Locoid) for three weeks remained negative. DISCUSSION: Our observation is original: allergic contact dermatitis to inhaled corticosteroids is rare, the clinical presentation mimicked angioedema although it was a delayed-type hypersensitivity, hypersensitivity was limited to group B corticosteroids and it was in fact a connubial contact dermatitis.

Rakes G. et al. *Inhaled budesonide in acute asthma?* J Pediatr . 2001; 139(3) : 346-8.p

Rakusic N. et al. *Physician/patient differences in the perception of asthma: impact on everyday life and level of the asthma control in Croatia.* Coll Antropol. 2001; 25(2) : 475-84.p
Abstract: The aim of the study was to compare physician/patient differences in the perception of asthma. The data were obtained by questionnaires from 156 physicians and 148 asthmatics in four urban regions in Croatia. On a "bad day", 62% of physicians and 16% of patients perceived

respiratory symptoms with statistically significant difference. The patients described asthma impact in terms of reduced daily activities and experienced emotional problems. Asthma was estimated as controlled in 28% of adults and 49% of children, nevertheless, 45% of adults and 22% of children reported respiratory symptoms. The patients seem to be satisfied with asthma control that does not correspond to suppression of symptoms, whereas physicians neglect patients' emotional problems and asthma impact on everyday life. The differences in the perception of asthma may reflect differences in beliefs about health. Physicians see health as an absence of symptoms, whereas patients regard being healthy as "being able".

Ram F.S. et al. *Systematic review of clinical effectiveness of pressurised metered dose inhalers versus other hand held inhaler devices for delivering beta (2) agonists bronchodilators in asthma.* BMJ. 2001; 323(7318) : 901-5.p
Abstract: OBJECTIVES: To determine the clinical effectiveness of pressurised metered dose inhalers compared with other hand held inhaler devices for delivering short acting beta(2) agonists in stable asthma. DESIGN: Systematic review of randomised controlled trials. DATA SOURCES: Cochrane Airways Group specialised trials database (which includes hand searching of 20 relevant journals), Medline, Embase, Cochrane controlled clinical trials register, pharmaceutical companies, and bibliographies of included trials. TRIALS: All trials in children or adults with stable asthma that compared the pressurised metered dose inhaler (with or without a spacer device) against any other hand held inhaler device containing the same beta(2) agonist. RESULTS: 84 randomised controlled trials were included. No differences were found between the pressurised metered dose inhaler and any other hand held inhaler device for lung function, blood pressure, symptoms, bronchial hyperreactivity, systemic bioavailability, inhaled steroid requirement, serum potassium concentration, and use of additional relief bronchodilators. In adults, pulse rate was lower in those using the pressurised metered dose inhaler compared with those using Turbohaler (standardised mean difference 0.44, 95% confidence interval 0.05 to 0.84); patients preferred the pressurised metered dose inhaler to the Rotahaler (relative risk 0.53, 95% confidence interval 0.36 to 0.78); hydrofluoroalkane pressurised metered dose inhalers reduced the requirement for rescue short course oral steroids (relative risk 0.67, 0.49 to 0.91). CONCLUSIONS: No evidence was found to show that alternative inhaler devices are more effective than standard pressurised metered dose inhalers for delivering acting beta(2) agonist bronchodilators in asthma. Pressurised metered dose inhalers remain the most cost effective delivery devices.

Ramadan H.H. *Surgical management of chronic sinusitis in children.* Laryngoscope. 2004; 114(12) : 2103-9.p
Abstract: OBJECTIVES/HYPOTHESIS: The objective was to compare three common surgical modalities in children for the treatment of chronic sinusitis that is refractory to medical management. STUDY DESIGN: Prospective nonrandomized study in a pediatric otolaryngology tertiary service. METHODS: Two hundred two children who satisfied criteria for surgery and were referred over a 10-year period were studied. Children were divided into three surgical groups. Group 1 had both endoscopic sinus surgery and adenoidectomy, group 2 had endoscopic sinus surgery alone, and group 3 had adenoidectomy. After a follow-up period of 12 months, improvement of symptoms was assessed. RESULTS: One hundred eighty-three children had adequate follow-up. Eighty seven percent of children in group 1 had improved symptoms, compared with 75% in group 2 and 52% in group 3 (P < .0001). Multivariate analysis showed that surgical procedure was a predictor of success. Asthma, smoke exposure, and age were independent predictors of success. CONCLUSION: Children who fail medical therapy benefit from surgery. Following certain criteria, one can chose between adenoidectomy alone or endoscopic sinus surgery with adenoidectomy to optimize surgical treatment of these children.

- Ramoutsaki I.A. et al.** *Management of childhood diseases during the Byzantine period: III-- respiratory diseases of childhood.* *Pediatr Int.* 2002; 44(4) : 460-2.p **Abstract:** Evidence on herbal, veterinary and chemical substances used in various forms for respiratory problems of childhood such as acute otitis, acute tonsillitis and parotitis was investigated in the Byzantine medical treatises, from the 4th to the 15th century ad. The problem of asthma in childhood was well known during the Byzantine period. Despite the existent Hippocratic tradition, the physicians of the times developed their own methods of treatment. The texts of Antyllus, Orivasios from Pergamos, Aetius of Amida, Alexander of Tralles, Paulus Aeginitis, Theophanis Nonnos and others, strongly suggest influences from ancient Greek and Roman medicine, but at the same time indicate an original medical thought.
- Rance K. et al.** *Broccoli and pixie stix. Profile of a pediatric asthma program.* *Adv Nurse Pract.* 2004; 12(3) : 47-8.p
- Rance K.S. et al.** *Profile of a primary care practice asthma program: improved patient outcomes in a high-risk population.* *J Pediatr Health Care.* 2005; 19(1) : 25-32.p **Abstract:** Asthma touches all of our lives. Asthma is a disease entity of huge proportions nationally and locally. It is the most common cause of school absences from a chronic disease and a common reason for parents and caregivers to miss work. The purpose of this article is to provide pediatric nurse practitioners with an understanding of the impact of asthma on children, their families, and on clinical practice. It will examine an asthma program created in a pediatric primary care setting to treat a high-risk population that proved very successful. The discussion of these issues incorporates results from a 2-year clinical project that focused on the reduction of asthma-related emergency department visits, asthma-related hospitalizations, and asthma-related missed school days.
- Randolph A.G. et al.** *The IL12B gene is associated with asthma.* *Am J Hum Genet.* 2004; 75(4) : 709-15.p **Abstract:** The IL12B gene on chromosome 5q31-33 encodes the p40 subunit of interleukin 12, an immunomodulatory cytokine. To test the hypothesis that the IL12B gene contains polymorphisms associated with asthma, we genotyped six haplotype-tagging polymorphisms in the IL12B gene, both in 708 children enrolled in the Childhood Asthma Management Program (CAMP) and in their parents. Using the family-based association test (FBAT) program and its haplotype (HBAT) and phenotype (PBAT) options, we tested each polymorphism and haplotype for association with asthma and asthma-related phenotypes. We tested positive associations for replication in a case-control study comparing 177 adult moderate-to-severe asthmatics with 177 nonasthmatic controls. In whites in the CAMP cohort, the A allele of the IL12B G4237A polymorphism was undertransmitted to asthmatic children (P=.0008, recessive model), the global test for haplotypes for affection status was positive (P=.009, multiallelic chi (2)), and two polymorphisms were associated with different atopy phenotypes. In addition, we found a strong association between the IL12B_4237 and IL12B_6402 polymorphisms and an asthma-severity phenotype in whites, which we also found in the independent population of white adult asthmatics. IL12B may be an important asthma gene.
- Randolph A.G. et al.** *Extended haplotype in the tumor necrosis factor gene cluster is associated with asthma and asthma-related phenotypes.* *Am J Respir Crit Care Med.* 2005; 172(6) : 687-92.p **Abstract:** RATIONALE: Tumor necrosis factor is a proinflammatory cytokine found in increased concentrations in asthmatic airways. The TNF-alpha (TNF) and lymphotoxin-alpha (LTA) genes belong to the TNF gene superfamily located within the human major histocompatibility complex on chromosome 6p in a region repeatedly linked to asthma. The TNF position -308 and LTA NcoI polymorphisms are believed to influence TNF transcription and secretion, respectively. OBJECTIVES: This study sought to determine whether polymorphisms in TNF or LTA, or in TNF-LTA haplotypes, are associated with asthma and asthma phenotypes. METHODS: We genotyped the TNF -308 and LTA NcoI polymorphisms, and two other haplotype-tagging polymorphisms in the TNF and LTA genes, in 708 children with mild to moderate asthma enrolled in the Childhood Asthma Management Program and in their parents. Using an extension of the family-based association tests in the PBAT program, each polymorphism was tested for association with asthma, age at onset of asthma, and time series data on baseline FEV(1) % predicted, postbronchodilator FEV(1) % predicted, body mass index, and log of PC(20). MEASUREMENTS AND MAIN RESULTS: Although no associations were found for the individual single-nucleotide polymorphisms, the haplotype analysis found the LTA NcoI_G/LTA 4371T/TNF -308G/TNF 1078G haplotype to be associated with asthma and with all five phenotype groups. Conclusions: We conclude that it is unlikely that the TNF -308 or LTA NcoI polymorphisms influence asthma susceptibility individually, but that this haplotype of variants may be functional or may be in linkage disequilibrium with other functional single-nucleotide polymorphisms.
- Randolph C.** *A review of asthma care guidelines in the United States.* *Minerva Pediatr.* 2003; 55(4) : 297-301.p **Abstract:** This article reviews the guidelines currently in use in the United States for anti-inflammatory and bronchodilator therapy for mild, moderate and severe asthma both intermittent and persistent.
- Rauh V.A. et al.** *Deteriorated housing contributes to high cockroach allergen levels in inner-city households.* *Environ Health Perspect.* 2002; 110 Suppl 2 : 323-7.p **Abstract:** The high prevalence of childhood asthma in low-income, inner-city populations is not fully understood but has been at least partly attributed to the disproportionate exposures associated with socioeconomic disadvantage. The contribution of indoor allergens to asthma is well documented, but links between socioeconomic disadvantage and indoor allergen levels are not clear. We investigated levels of cockroach allergens (Bla g 2) in a sample of 132 Dominican or African American low-income households with young children in northern Manhattan in New York City (40% were receiving public assistance) to determine whether the distribution of allergens is a function of housing deterioration. Deterioration was measured by the presence and number of physical housing problems (holes in the ceilings and walls, water damage, etc.). More than 50% of the sample had two or more types of housing dilapidation, and 67% of the sample reported cockroach sightings in their homes. Samples of dust were collected from kitchen and bedroom surfaces. We hypothesized that the greater the dilapidation, the higher the allergen levels, independent of income, sociocultural factors, and pest-control methods. In addition, we hypothesized that the homes of families characterized by frequent moves (23.5%) would have higher allergen levels than more stable families. Results showed significant positive associations between housing deterioration and allergen levels in kitchens, after adjusting for income and ethnicity, with independent effects of residential stability (p < 0.05). Bedroom allergen levels were associated with housing instability (p < 0.01) and ethnicity (p < 0.01). Findings demonstrated that indoor household allergen levels are related to degree of household disrepair, after adjusting for individual family attributes, suggesting that social-structural aspects of housing may be appropriate targets for public health interventions designed to reduce allergen exposure.
- Reddy D.K. et al.** *Dental caries status of children with bronchial asthma.* *J Clin Pediatr Dent.* 2003; 27(3) : 293-5.p **Abstract:** The purpose of the present study was to determine the dental caries status in children with bronchial asthma and to examine the correlation with the severity of asthma and the form of medication being taken. Two hundred and five asthmatic children of both sexes from three to

eighteen years old participated in this study. Children were divided into groups: primary, mixed and permanent dentitions. They were also grouped depending on the severity of asthma into mild, moderate and severe asthma and depending on the form of medication being used into inhaler, syrup, tablet and combination group. In the primary dentition group, the asthmatic children had a mean deft of 5.02 +/- 3.05 and a caries prevalence of 75.75%, in the mixed dentition group, the mean deft was 3.45 +/- 2.89 and mean DMFT was 4.83 +/- 3.66 with a caries prevalence of 78.31%. In the permanent dentition the mean DMFT was 5.17 +/- 4.54 and a caries prevalence of 83.15%. Asthmatic children had a high caries prevalence and it increased with the severity of bronchial asthma. The caries prevalence was highest in those taking medication in the form of syrup.

Redline S. et al. *Development and validation of school-based asthma and allergy screening questionnaires in a 4-city study.* Ann Allergy Asthma Immunol. 2004; 93(1) : 36-48.p Abstract: BACKGROUND: Asthma and allergies are commonly undiagnosed in children. Schools provide settings for potentially accessing almost all children for asthma and allergy screening. OBJECTIVE: To evaluate the feasibility and validity of using a questionnaire-based screening tool to identify undiagnosed asthma and respiratory allergies in children in kindergarten to grade 6. METHODS: A student questionnaire (SQ) and a parent questionnaire (PQ) were developed, administered in 4 diverse communities, and validated against standardized clinical assessments. Children without diagnosed asthma and representing a range of symptoms participated in a validation study that consisted of independent, standardized, clinical assessments. Sensitivity, specificity, and predictive values for questionnaire items were evaluated against expert consensus designations. RESULTS: A total of 190 children (age range, 7-13 years) completed the validation study. Affirmative responses to individual questions from either the SQ or PQ regarding asthma and allergy were modestly to moderately predictive of the clinical assessments (odds ratios, generally 2.5-5.0). When considering a positive asthma screen as affirmative responses to 3 of the best 7 SQ asthma questions, the odds ratio for asthma was 9.3 (95% confidence interval, 4.1-21.1), with 80% sensitivity and 70% specificity. Considering the allergy screen as positive based on affirmative response to either of the 2 SQ allergy questions yielded 81% sensitivity and 42% specificity. CONCLUSIONS: Either a 9-item SQ or a 10-item PQ can be used in diverse settings to screen for asthma and respiratory allergies. The SQ, obtained by directly screening students, may provide a sensitive approach for detecting children with previously undiagnosed asthma and allergies.

Redline S. et al. *Development and validation of school-based asthma and allergy screening instruments for parents and students.* Ann Allergy Asthma Immunol. 2003; 90(5) : 516-28.p Abstract: BACKGROUND: The increasing morbidity attributable to asthma among school-aged children suggests the potential utility of school-based asthma screening programs. OBJECTIVE: We report our efforts to develop and validate culturally sensitive and clinically useful screening questionnaires (parent and child versions) for asthma and allergies among urban US school children. METHODS: Instrument development was accomplished through literature review, expert medical and child developmental input, focus group feedback, and a rigorous trial of the instruments in a public school setting. Questionnaires were distributed to 2,800 children and their families in an urban public school system (grades kindergarten through 6). Validity was evaluated by blinded comparison of results against a standardized clinical evaluation in 107 children, with final designations determined by an expert panel. RESULTS: Questionnaires pertaining to 2,083 children were returned (participation rate of 74%). A moderate level of agreement was observed between parent and student questionnaire responses (r values = 0.36 to 0.50; P values < 0.001). The highest frequency of asthma-like symptoms was reported for African-American boys and

the lowest for Caucasian girls. The items from the parent questionnaire that best predicted asthma were "breathing problems" (occurring rarely or more; odds ratio 12.8; 95% confidence interval, 4.5 to 36.1) and "problems coughing" (sometimes or more; odds ratio 9.7; 95% confidence interval, 3.6 to 26.5). Considering the presence of cough (sometimes or more) and/or breathing problem (rarely or more) yielded a sensitivity of 80%; a specificity of 75%, a positive predictive value of 50%, and a negative predictive value of 92%. Similar levels of prediction were observed for the items "trouble breathing" and "noisy breathing" as directly reported by the students. Allergic rhinitis was best predicted by report of a runny/stuffy nose (sometimes or more; sensitivity of 83%, specificity of 61%). Allergic conjunctivitis was best predicted by "itchy eyes." CONCLUSIONS: Administration of a school-based questionnaire is feasible, with a high response rate and excellent internal consistency. A high sensitivity and acceptable specificity was achieved by using one to two questions for asthma, allergic rhinitis, and allergic conjunctivitis. Among the children in grades 2 or above, comparable levels of prediction could be achieved with the student or parent version.

Reeves M.J. et al. *Asthma care and management before an emergency department visit in children in western Michigan: how well does care adhere to guidelines?* Pediatrics. 2006; 117(4 Pt 2) : S118-26.p Abstract: OBJECTIVES: Asthma is one of the more common reasons for children's visits to the emergency departments (EDs). Many studies show that the level of asthma care and self-management in children before an ED visit for asthma is often inadequate; however, most of these studies have been conducted in the inner cities of large urban areas. Our objectives were to describe asthma care and management in children treated for asthma in 3 EDs located in an urban, suburban, or rural setting. METHODS: We studied a prospective patient cohort consisting of children aged 2 to 17 years who presented with an acute asthma exacerbation at 3 EDs in western Michigan. An in-person questionnaire was administered to the parent or guardian during the ED visit. Information was collected on demographics; asthma history; usual asthma care; frequency of symptoms during the last 4 weeks; current asthma treatment, management, and control; and past emergency asthma care. A telephone interview conducted 2 weeks after the ED visit obtained follow-up information. The 8 quality indicators of asthma care and management were defined based on recommendations from national guidelines. RESULTS: Of 197 children, 70% were enrolled at the urban site, 18% at the suburban site, and 12% at the rural site. The average age was 7.9 years; 60% were male, and 33% were black. At presentation, nearly half (46%) of the children had mild intermittent asthma, 20% had mild persistent asthma, 15% had moderate persistent asthma, and 19% had severe persistent asthma. One quarter of the children had been hospitalized for asthma, and two thirds had at least 1 previous ED visit in the past year. At least 94% had health insurance coverage and 95% reported having a primary care provider. Less than half of the children had attended at least 2 scheduled asthma appointments with their regular asthma care provider in the past year. Although only 5% of the subjects reported that the ED was their only source of asthma care, at least 30% reported that they always went directly to the ED when they needed urgent asthma care. Only 3 in 5 children possessed either a spacer or a peak-flow meter, whereas approximately 2 in 5 reported having a written asthma action plan. Among those with persistent asthma, there was considerable evidence of undertreatment, with 36% not on either an inhaled corticosteroid or a suitable long-term control medication. Only 20% completed a visit with their regular asthma care provider within 1 week of their ED visit. CONCLUSIONS: Despite very high levels of health care coverage and access to primary care, the overall quality of asthma care and management fell well short of that recommended by national guidelines.

Reich M. et al. *Elevated nonspecific plasma proteins in allergic patients.* J Invest Allergol Clin Immunol. 2003; 13(1) : 60-5.p Abstract: Several allergen-specific plasma proteins, such as IgE and IgG

subclasses, are commonly used for the evaluation of grade of allergy. In the present investigation, we compared the concentration of various nonspecific plasma proteins, mostly known as inflammation markers, in an allergic and a healthy population. Plasma from 130 children with single inhalation allergies to grass pollen, birch pollen, or house dust mites as well as from 42 healthy children was obtained during the symptom-free period. Patients showed symptoms including allergic rhinitis, dermatitis, and asthma with one single radioallergosorbent test (RAST) class 3 or higher. Plasma concentrations of soluble intercellular adhesion molecule-1 (sICAM-1), soluble interleukin-2 receptor (sIL-2R), sE-selectin, and soluble vascular cell adhesion molecule-1 (sVCAM-1) were analyzed by enzyme linked immunosorbent assay (ELISA) technique. Concentrations of sICAM-1 and sE-selectin were significantly increased in all patients compared to controls. In the single allergen groups, sICAM-1 elevation was significant in the grass and mite groups, but not in the birch group; while sE-selection increase was significant in the birch and mite groups, but not in the grass group. The elevation of sIL-2R in the allergic patients was obvious in each single allergen group, but not significant. No difference was observed in sVCAM-1 expression. In two groups of patients with mean age of 9.5 years versus 17.5 years, the analyzed parameters were not age dependent. The increased proteins may be useful as additional markers for efficacy and follow-up investigations of allergy therapies.

Reichenbach J. et al. *Serum ECP levels and methacholine challenge in infants with recurrent wheezing.* Ann Allergy Asthma Immunol. 2002; 89(5) : 498-502.p **Abstract:** BACKGROUND: High levels of serum eosinophil cationic protein (sECP) as a marker of eosinophilic airway inflammation have been described as a predictor of childhood asthma. Bronchial hyperreactivity (BHR) appears to be secondary to the release of inflammatory mediators. OBJECTIVE: We investigated the possible correlation between eosinophilic inflammation and BHR in 72 infants with recurrent wheezing. METHODS: To determine bronchial reactivity, lung function measurements with methacholine challenge were performed in 72 infants, aged 12 to 30 months, and the degree of BHR to methacholine was compared with sECP values. Patients were grouped according to low (group 1, <10 microg/L, n = 22), medium (group 2, 10 to 20 microg/L, n = 23), and high (group 3, >20 microg/L, n = 27) sECP values. RESULTS: In group 1, sECP levels ranged from 3.1 to 9.9 microg/L, mean 6.6 microg/L +/- standard deviation [SD] 2.3, in group 2, from 10.3 to 19.8 microg/L, mean 14.3 microg/L +/- SD 2.8, and in group 3 from 23.0 to 66.7 microg/L, mean 34.5 microg/L +/- SD 9.5. Distribution of provocative methacholine concentration among groups was as follows: group 1, 30 to 976 microg, mean 350.9 microg +/- SD 258.3; group 2, 36 to 752 microg, mean 340.7 microg +/- SD 226.3; group 3, 41 to 848 microg, mean 301.3 microg +/- SD 189.8 methacholine. CONCLUSION: There was no significant correlation between sECP levels and bronchial reactivity in all groups ($r = -0.076$, $P = 0.6$), indicating that these parameters reflect two independent pathogenic mechanisms in the etiology of childhood asthma.

Reina J. et al. [Study of the clinical and epidemiological characteristics of respiratory infections caused by adenovirus in a pediatric population (1997-2003)]. An Pediatr (Barc). 2004; 61(2) : 137-42.p **Abstract:** INTRODUCTION: Infections due to adenoviruses are highly prevalent in pediatric patients. Because the clinical manifestations of the respiratory infections caused by adenoviruses are indistinguishable from those caused by other respiratory viruses, virological methods are required to establish their etiology. We present a retrospective study of the clinical and virological characteristics of patients with isolation of adenovirus in respiratory samples. MATERIAL AND METHODS: From 1997 to 2003 we analyzed 5,746 respiratory samples from pediatric patients (< 15 years old), of which 2,122 (36.9 %) were considered positive. The

adenoviruses were isolated in the Hep-2 cell line culture by the shell vial method. RESULTS: Adenovirus was isolated in 100 clinical samples (4.7 % of all positive samples and 1.7 % of all samples studied) in a group of pediatric patients with a mean age of 14 months. The clinical diagnoses of patients were bronchiolitis (61 %), pneumonia (10 %), pertussis-like syndrome (16 %) and asthmatic crisis (11 %). Adenovirus infections mainly presented between December and March. Seventy-two percent of patients had a history of other viral respiratory tract infections and/or bronchial asthma. None of the patients had clinical conjunctivitis and only five patients had diarrhea due to adenoviruses. Seventy percent of the patients received artificial feeding and 30 % were breast-fed. Ninety percent of the patients were hospitalized and treatment mainly consisted of bronchodilator agents and antibiotics. CONCLUSIONS: Respiratory tract infections caused by adenoviruses mainly affected patients aged less than 14 months, in the first four months of the year, and with clinical manifestations of bronchiolitis or pneumonia without conjunctivitis. Clinically, these infections are difficult to differentiate from other viral respiratory infections.

Rennie D.C. et al. *Differences in respiratory symptoms and pulmonary function in children in 2 Saskatchewan communities.* Ann Allergy Asthma Immunol. 2004; 92(1) : 52-9.p **Abstract:** BACKGROUND: Asthma prevalence is known to vary among different geographical regions both nationally and internationally. However, there is limited understanding of the nature of differences within geographical regions. OBJECTIVE: To evaluate the prevalence of asthma in 2 prairie communities and differences in the patterns of respiratory symptoms between the communities. METHODS: A cross-sectional questionnaire survey was sent through schools in Estevan and Swift Current, Saskatchewan, to parents of 2,231 children in grades 1 to 6. Asthma prevalence was determined by questionnaire report of physician-diagnosed asthma. Pulmonary function tests (PFTs) using spirometry were conducted in children in grades 1 to 4. To evaluate respiratory morbidity without the use of a diagnostic label, similar comparisons were made between communities for respiratory symptoms. RESULTS: The overall response rate to the survey questionnaire was 91.3%. The prevalence of ever asthma in Estevan was 21.4% (95% confidence interval [CI], 20.1%-22.7%) compared with 16.2% (95% CI, 15.1%-17.3%) in Swift Current. A higher proportion of girls in Estevan (19.7%; 95% CI, 17.9%-21.5%) compared with girls in Swift Current (12.5%; 95% CI, 11.1%-13.9%) reported a history of asthma. There was no difference found between towns for boys. These findings were supported by findings for respiratory symptoms, including wheeze and cough. For both boys and girls, the forced expiratory flow at 25% to 75% of forced vital capacity and the ratio of forced expiratory volume in 1 second to forced vital capacity were lower in Estevan compared with Swift Current. CONCLUSIONS: Differences in the distribution of childhood asthma can be found within regions. These results are strengthened by PFTs and cannot be fully explained by diagnostic biases.

Reynaud P. [Medical certificates: medical responsibility in scuba diving]. Rev Mal Respir. 2001; 18(4 Pt 1) : 379-80.p

Reznik M. et al. *Asthma educational videoconferencing for parents: a case-control study.* J Telemed Telecare. 2004; 10 Suppl 1 : 83-5.p **Abstract:** We used a case-control, pre-post study to determine the effectiveness of educational videoconferencing in the delivery of an asthma education programme. The participants were immigrant parents attending scheduled classes on English as a second language. The cases participated in the educational videoconferences, while the controls attended a class on American civics. Knowledge in both groups was assessed with 10 true/false statements. Ninety subjects participated (47 cases and 43 controls). Controls showed no significant post-test improvement in knowledge scores (6.6 for pre-test, 6.4 for post-test). In contrast, cases demonstrated significant knowledge gain after the videoconference (7.3 vs 8.3). Educational

videoconferencing was an effective tool for the delivery of health education in asthma.

Rhodes H.L. et al. *Early life risk factors for adult asthma: a birth cohort study of subjects at risk.* J Allergy Clin Immunol. 2001; 108(5) : 720-5.p **Abstract:** BACKGROUND: Prediction of adult asthma is important, and early prevention strategies should be targeted at those most at risk. Identifying high-risk children at an early age, however, is currently difficult. OBJECTIVE: We sought to determine those factors present in early life that predict an increased risk of adult asthma. METHODS: A prospective cohort study of subjects at risk of asthma and atopy was undertaken in Poole, England. One hundred babies of atopic parents were recruited at birth. During the first 5 years of life, subjects were recalled annually, all respiratory events were reported, and skin prick tests and total serum IgE measurements were performed. At 11 and 22 years, bronchial hyperresponsiveness was also measured. Seventy-three subjects were followed up at 5 years, 67 at 11 years, and 63 at 22 years. RESULTS: Twenty-three (37%) adult subjects reported wheezing within the previous 12 months. Fifteen (25%) of these subjects showed signs of bronchial hyperresponsiveness and were regarded as asthmatic. Wheezing before the age of 2 years occurred in 28% and was not significantly related to adult asthma (odds ratio, 0.3; 95% CI, 0.03-1.7; $P = .19$). A positive skin prick test response to hen's egg, cow's milk, or both in the first year was independently predictive of adult asthma (odds ratio, 10.7; 95% CI, 2.1-55.1; $P = .001$; sensitivity, 57%; specificity, 89%). CONCLUSION: Prediction of adult asthma remains difficult. In this study of subjects at risk of atopy, skin sensitivity to hen's egg or cow's milk in the first year was predictive of adult asthma.

Ribeiro J.D. [Aerosols and spacers for acute asthma in children. Evolution and time to change the routine]. J Pediatr (Rio J). 2005; 81(4) : 274-6.p

Riccio A.M. et al. *Cytokine pattern in allergic and non-allergic chronic rhinosinusitis in asthmatic children.* Clin Exp Allergy. 2002; 32(3) : 422-6.p **Abstract:** BACKGROUND: Rhinosinusitis represents one of the most common chronic diseases. The association of rhinosinusitis with asthma has been frequently reported. Eosinophils and Th2 cells play a pathogenic mechanism in asthma. OBJECTIVE: The aims of the study were to evaluate the cytokine pattern in chronic rhinosinusitis in asthmatic children and to compare the findings in allergic vs. non-allergic asthmatics. METHODS: Thirty-five asthmatic children were evaluated, 19 males and 16 females, with an average age of 8.7 years. All children were asthmatic and suffered from chronic rhinosinusitis. Twenty were allergic and 15 were non-allergic. Ten healthy children were studied as normal controls. Evaluated parameters were the levels of the following cytokines: IL-1beta, IL-4, IL-6, IL-8, IL-12, IFN-gamma and TNF-alpha. Cytokines were recovered from rhinosinusal lavage and measured by immunoassays. Nasal cytology was also performed in all subjects and inflammatory cells were counted by conventional staining. RESULTS: Allergic subjects showed a significant increase of IL-4 ($P < 0.01$) and TNF-alpha ($P < 0.05$) and a significant decrease of IL-12 ($P < 0.05$) and of IFN-gamma ($P < 0.0001$), whereas IL-1beta, IL-6 and IL-8 were not significantly increased. Non-allergic children showed a significant increase of IL-4 ($P < 0.05$) and a significant decrease of IFN-gamma ($P < 0.0001$), IL-12 was not significantly decreased, and IL-1beta, IL-6 and IL-8 were not significantly increased. A significant inflammatory infiltrate was present in all asthmatic children. Significant correlations were demonstrated between IL-4 and IL-12 ($P < 0.001$), IL-12 and IFN-gamma ($P < 0.001$), IL-8 and neutrophils ($P < 0.01$), and TNF-alpha and monocytes/macrophages ($P < 0.05$), in allergic asthmatics. IL-4 and IL-12 were significantly correlated ($P < 0.05$) as well as IL-8 and neutrophils ($P < 0.01$) in non-allergic asthmatics. CONCLUSION: This study shows that allergic asthmatic children with chronic rhinosinusitis have a typical Th2 cytokine pattern, but also non-allergic asthmatic children share a similar pattern. These findings

would suggest the existence of a common pathophysiological mechanism shared by upper and lower airways and are consistent with the concept of united airways disease.

Richardson C.R. *Educational interventions improve outcomes for children with asthma.* J Fam Pract. 2003; 52(10) : 764-6.p

Richardson J.L. et al. *Knowledge of skin test results among parents of asthmatic children.* J Asthma. 2004; 41(2) : 199-204.p **Abstract:** BACKGROUND: The control of asthma in children depends upon several factors, among which is the ability of parents to minimize the exposure of their children to specific allergens. If parents are ill-informed of the specific allergen sensitivity of their children, they may be unable to take the necessary steps to minimize exposure. OBJECTIVES: This study seeks to determine the ability of parents to recall accurately the skin test results for their children. Parents were low income, multicultural, urban residents. METHODS: One hundred eligible children with persistent asthma, between 6 and 14 years old, who were skin test positive to dust mite or cockroach allergen, were recruited from a mobile asthma clinic in Los Angeles. Caretakers were interviewed in English or Spanish. From skin test results, sensitivity and specificity of parental recall of test results were computed. The sensitivity and specificity were further stratified on demographic and exposure characteristics. RESULTS: The sensitivity was lowest for dogs (65%), but higher for all other allergens: cat 93%, roach 91%, dust mites 88%, and mold 81%. The range of specificity was from 40% to 83%. Thus, parents were more aware of positive than of negative test results. Stratification did not appreciably change the sensitivity or specificity results. CONCLUSIONS: We conclude that the sensitivity and specificity of parental response concerning skin test results is high regardless of cultural, demographic, or exposure levels of the child.

Richter-Reichhelm H.B. et al. *Workshop report. Children as a special subpopulation: focus on immunotoxicity. Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV), 15-16 November 2001, Berlin, Germany.* Arch Toxicol. 2002; 76(7) : 377-82.p **Abstract:** An international symposium on the impact of environmental hazards, chemicals and drugs on the developing immune system of children was held in Berlin (Germany) organized by the BgVV. Epidemiological evidence indicates that an immature immune system challenged early in life by bacterial antigens may prevent, to some extent, allergic reactions including asthma bronchiale triggered by environmental pollutants. However, the prevalence for infectious disease is increased in childhood, especially when exposure to contaminants takes place in the period of pregnancy and breast-feeding. The effects of chlorinated biphenyls, dioxin, endotoxins, hexachlorobenzene, and direct and indirect in utero tobacco smoke exposure are examples. All participants recommend comparative and follow-up epidemiological studies and clinical examination of infants and children at risk during upbringing. There is ample evidence from experimental studies that indicates adverse effects on the developing immune system after in utero and postnatal exposure to chemicals and drugs. The adverse reactions of aciclovir, benzodiazepines, hexachlorobenzene, organotins (di-n-octyltin dichloride, tributyltin oxide), pesticides (methoxychlor, heptachlor) and polyhalogenated aromatic hydrocarbons (2,3,7,8-tetrachlorodibenzo-p-dioxin) are presented and reviewed. To determine the predictive value of test data in risk assessment for neonates and children, development, differentiation and maturation of the immune system in humans and laboratory rodents is compared in their pre- and postnatal stages. Considering some differences in immunocompetence at birth and after lactation, and differences in the time frame for maturation of the immune system, reaction types are thought to be common, comparable and similar in human childhood and early adolescence and the postnatal lifetime of laboratory rodents. The participants of the symposium felt strongly that regulatory steps urgently need to be initiated to incorporate some relevant aspects into existing test guidelines for testing

developmental immunotoxicity. In this context, it is recommended that animals culled otherwise in one- and two-generation studies be examined for developmental immunotoxicity according to the valid methods and parameters discussed. The majority of participants agreed that a safety factor of 10 is too low in risk assessment and management to protect a sensitive subpopulation of children against man-made environmental pollutants.

Riechelmann H. et al. *Comparison of conjunctival and nasal provocation test in allergic rhinitis to house dust mite.* Int Arch Allergy Immunol. 2003; 130(1) : 51-9.p **Abstract:** BACKGROUND: Nasal allergen provocation tests (NPTs) are useful in confirming the diagnosis of allergic rhinitis, if data obtained by clinical history, skin tests and specific IgE determinations are not conclusive. Since NPTs are laborious, conjunctival provocation tests (CPTs) appear as an attractive alternative. The concordance of CPTs and NPTs with house dust mite allergen extract in sensitized and nonsensitized subjects should be evaluated. METHODS: 50 otherwise healthy subjects with self-reported house dust mite allergy and positive skin prick tests and serum specific IgE to Dermatophagoides pteronyssinus and 45 sex- and age-matched healthy controls without allergic symptoms were included. For NPTs, 100 microl allergen extract [10,000 allergy units (AU/ml)] were applied to the less congested nasal cavity. A clinical symptom score and active anterior rhinomanometry were employed to assess the response. For CPTs, 50 microl low-concentrated D. pteronyssinus extract (1,000 AU/ml), and if negative, 50 microl normally concentrated extract (10,000 AU/ml) were applied to the lower conjunctival sac. The response was assessed employing clinical symptom scores. RESULTS: NPTs and CPTs yielded concordant results in 90% of the subjects successfully tested (Cohen's kappa = 0.78, $p < 0.0001$). The diagnostic efficacy of the CPT, with the NPT as the reference method, was 89%, whether or not conjunctival symptoms had been reported in addition to rhinitis symptoms. Both techniques were judged almost equally uncomfortable. CONCLUSION: CPTs are an acceptable alternative to NPTs in patients with allergic rhinitis to house dust mite, even if they have no conjunctival symptoms.

Rietveld S. et al. *The relationship between specific anxiety syndromes and somatic symptoms in adolescents with asthma and other chronic diseases.* J Asthma. 2005; 42(9) : 725-30.p **Abstract:** BACKGROUND: The impact of a chronic disease on the emotional well-being of children and adolescents is controversial in the literature. This study tested the hypotheses that 1) a specific approach is required to assess emotional deviations in adolescents with chronic diseases and 2) specific anxiety symptoms are predictive of excessive somatic symptoms. METHODS: Emotional and somatic symptoms were measured in four groups, selected from a community sample of 897 adolescents: 32 with asthma, 20 with other severe chronic diseases, 30 with median scores (the true comparison group), and 29 with minimal scores on common measures of trait anxiety and depression. RESULTS: The asthma and chronic disease groups scored not significantly higher than the true comparison group on trait anxiety, depression, negative affectivity, five anxiety syndromes, anxiety-related physical, and miscellaneous somatic symptoms. The asthma and chronic disease groups scored only higher than the true comparison group on panic attacks and respiration symptoms. Regression analyses showed that severity of asthma was no significant factor, and the minimal group scored consistently lower than the other groups, except on physical injury fears. There were no group differences in positive affect. Girls scored higher than boys on specific anxiety syndromes (except on obsessive-compulsive disorder) and also on respiration symptoms. CONCLUSION: Adolescents with severe chronic diseases deviated from a true comparison control group on panic attacks, but not on other negative and positive emotions.

Rijssenbeek-Nouwens L.H. et al. *Clinical evaluation of the effect of anti-allergic mattress covers in patients with moderate to severe asthma and house dust mite allergy: a randomised double blind placebo controlled study.* Thorax. 2002; 57(9) : 784-90.p **Abstract:** BACKGROUND: The use of anti-allergic mattress covers in patients with asthma can result in a large reduction in the level of house dust mite allergen in dust samples. Apart from a reduction in histamine induced bronchial hyperresponsiveness, there are few data on the effect of mattress covers on clinical efficacy and quality of life in patients with moderate to severe asthma. METHODS: Thirty patients with asthma and house dust mite allergy were studied in a randomised, double blind, placebo controlled study. Before and after using anti-allergic covers for 1 year, dust was collected from the mattresses to determine concentrations of Dermatophagoides pteronyssinus (Der p 1), and bronchial hyperresponsiveness and quality of life were measured. The patients scored their symptoms (lungs and nose), morning and evening peak flow values, and rescue medication for 14 days before and after the intervention period. RESULTS: There was a significant reduction in the concentration of Der p 1 in the dust collected from the mattresses in the actively treated group after 1 year compared with before treatment; no change was found in the placebo group. In both the actively treated and placebo groups there was no significant improvement in PC(20) histamine. Quality of life improved similarly in both groups. The symptom score of the lower airways did not significantly change in either group. A significant decrease in nasal symptom score was seen in the actively treated group compared with before treatment, but there was no significant difference between the groups. No changes in morning and evening peak flow values, peak flow variability, nor in the use of rescue medication were found in either group. CONCLUSION: The use of anti-allergic mattress covers results in significant reductions in Der p 1 concentrations in carpet-free bedrooms. However, in patients with moderate to severe asthma, airways hyperresponsiveness and clinical parameters are not affected by this effective allergen avoidance.

Rio E.M. et al. *[Asthma mortality in the Municipality of Sao Paulo (1993-1995): analysis by multiple cause of death].* Cad Saude Publica. 2003; 19(5) : 1541-4.p **Abstract:** This article aims to quantify the asthma mortality rate using the multiple causality analytical method in comparison to the underlying cause of death. Data were obtained from all death certificates (224,854) of individuals from 5 to 34 years of age issued in 1993, 1994, and 1995 in the Municipality of S o Paulo, in which mention of the word asthma was considered valid information (code 493/ICD-9). First, the underlying cause of death was studied. The same data were then used, but submitted to the multiple causality method. The comparative study of basic and multiple causes of death increased the diagnosis of asthma by a ratio of 1.165. The over-20-year age group remained the most affected by the problem. The age range of individuals most affected by this disease did not change with the analytical method (20 to 34 years). Although asthma was present more frequently when the multiple causality method was used, the increase in the number of asthma diagnoses highlights that the disease can be considered underreported in Brazil in the chain of events leading to death.

Rio E.M. et al. *[Asthma mortality in the city of Sao Paulo, Brazil].* Rev Saude Publica. 2002; 36(2) : 149-54.p **Abstract:** OBJECTIVE: To quantify and compare asthma mortality rates as the main cause of death, taking into consideration the following variables: sex, age and seasonality. METHODS: Data was collected from all death certificates coded 493 of people aged 5 to 34 years in the periods of 1983-5 and 1993-5 in the city of Sao Paulo, SP, Brazil. Data analysis was performed by directly comparing death rates and identifying the odds ratio trend and directly comparing the numbers of asthma deaths. RESULTS: There was no increase in asthma mortality rates for the study periods. There was no difference between men and women. A greater number of deaths in the age group 20 to 34 years were observed. Seasonality was more evident in the first period

studied. CONCLUSIONS: Differing from reports in other countries, the results did not show any increase in asthma mortality rates, The variable sex didn't seem to interfere with mortality. Deaths are more frequent among young adults, and their risk may be 9 times greater than that of young children. Deterioration of social and economic issues and health care services and even climatic changes may have been implicated in the absence of seasonality as a risk factor for asthma mortality. The disease by itself is not considered by many health professionals as critical in order to explain the chain of events that lead to death.

Rivera M.L. et al. *Albuterol nebulized in heliox in the initial ED treatment of pediatric asthma: a blinded, randomized controlled trial.* Am J Emerg Med. 2006; 24(1) : 38-42.p Abstract: OBJECTIVE: A prospective blinded, randomized controlled trial was undertaken to compare the initial response of albuterol nebulized in heliox or control in the treatment of moderately severe asthma in children presenting to a pediatric ED. METHODS: Patients were randomized to receive heliox (n = 20) or control (n = 21). The primary outcome was to compare a modified dyspnea index score at 10 and 20 minutes after randomization. Secondary outcomes were to determine if heliox decreased admission rates or endotracheal intubation. RESULTS: There was no statistically significant difference found at 10 or 20 minutes after randomization with heliox (P = .169 and P = .062, respectively). No statistical difference in admission rate was found, and no patients required endotracheal intubation in either group. CONCLUSIONS: Our results demonstrate that albuterol nebulized with heliox offered no clinical benefit over standard therapy in the initial treatment of moderately severe asthma in the ED.

Rivera-Matos I.R. et al. *A multicenter hospital surveillance of invasive Streptococcus pneumoniae, Puerto Rico, 2001.* P R Health Sci J. 2005; 24(3) : 185-9.p Abstract: Although antimicrobial resistance to Streptococcus pneumoniae has been increased dramatically worldwide, there is limited information of pattern of susceptibility for this pathogen in Puerto Rico. Hospital-based surveillance for invasive pneumococcal infections was begun among 38 hospitals island-wide in Puerto Rico from January to December, 2001. One hundred ninety-two cases of invasive pneumococcal disease were identified. Of the 177 isolates available for susceptibility testing, 50.3% were susceptible to penicillin and 49.7% were nonsusceptible (intermediate (I) and resistance (R)) (19.2% I, 30.5% R). Resistance was documented for expanded spectrum cephalosporins and macrolides. All isolates were susceptible to vancomycin. Diabetes, cardiovascular disease, smoking and bronchial asthma were the most common risk factors associated with invasive pneumococcal disease of the adult population. Bronchial asthma was the most common disease in the pediatric population with a fatality rate of 21%. There was no increased mortality detected among patients infected with penicillin resistant strains. Most of the isolates serotypes are represented in the 23-valent polysaccharide vaccine (78%) and 7-valent conjugate vaccine (62%). Penicillin-resistant isolates (47%) were 14, 19F, 6B, 6A, 9V, 23F, 19A and 35B serotype. Our data indicated a high prevalence for drug-resistant strains of S. pneumoniae in Puerto Rico. Continue surveillance for this common but serious pathogen is needed. Asthma is an important risk factor for pneumococcal disease. The pneumococcal vaccine should be recommended for all age groups with this risk factor.

Robert J. et al. [Contribution of salmeterol in ambulatory practice to the improvement of asthma and quality of life in childhood]. Allerg Immunol (Paris). 2002; 34(8) : 287-92.p Abstract: International guidelines on asthma recommend to add inhaled long-acting b2-agonists in patients insufficiently controlled with an inhaled corticosteroid alone. A multicentre prospective study was carried out in 250 children (age 8.4 +/- 2.7 years) whose asthma remained symptomatic with impaired lung function despite a treatment with

400-1000 micrograms/day of beclomethasone or equivalent. Salmeterol 100 micrograms/day was added to the previous dose of inhaled corticosteroid for 2 months. PEFR was improved as soon as the first month of treatment (67.2 +/- 44.4 L/min, p < 0.001) and at month 2 (75.0 +/- 44.1 L/min, p < 0.001). The percentage of symptomatic patients, the number of days and nights with symptoms, the number of days with prn bronchodilator use were significantly reduced (p < 0.001). The decrease in the distress and severity scores of the Childhood Asthma Questionnaire indicated an improvement in quality of life due to better asthma control. This study showed that lung function and symptoms were significantly improved as soon as the first month of treatment, improvement maintained thereafter, with a better quality of life and a good tolerability.

Roberts G. et al. *Development of a quality-of-life assessment for the allergic child or teenager with multisystem allergic disease.* J Allergy Clin Immunol. 2003; 111(3) : 491-7.p Abstract: BACKGROUND: Health-related quality of life (HRQOL) questionnaires currently being used to evaluate allergic disease are organ-specific. They therefore fail to take account of the systemic aspects of allergic disease. OBJECTIVE: To develop and validate a pediatric HRQOL questionnaire for allergic disease (Pediatric Allergic Disease Quality of Life Questionnaire, PADQLQ) that encapsulates problems related to the eyes, ears, nose, lungs, skin, emotions, and everyday activities. METHODS: In the development phase, 77 subjects (6 to 16 years of age), with seasonal or perennial allergic problems, were asked how much they were bothered by each different area of HRQOL impairment. The highest scoring areas were used to construct the PADQLQ. In the validation phase of the study, 36 subjects (8 to 16 years of age) with seasonal allergic rhinoconjunctivitis, seasonal allergic asthma, and/or cutaneous manifestations of grass pollen allergy were assessed before and during the pollen season. RESULTS: The PADQLQ contains 26 questions. In addition to standard symptoms (eg, rhinitis), it incorporates multiorgan symptoms that are usually overlooked (eg, hearing problems). The PADQLQ demonstrated good cross-sectional and longitudinal validity, showing a high degree of correlation with symptom scores and quality of life as measured by a visual analogue scale and two-organ specific questionnaires. The PADQLQ showed good within-subject reliability and a small minimal important difference (0.33; 95% CI, 0.11 to 0.54 on a 7-point scale). CONCLUSIONS: The PADQLQ has good cross-sectional and longitudinal validity, making it a potentially useful outcome measure in the evaluation of systemic treatments such as antihistamine medications and immunotherapy in children with multisystem allergic disease.

Roberts K. et al. *A review of emergency equipment carried and procedures performed by UK front line paramedics on paediatric patients.* Emerg Med J. 2005; 22(8) : 572-6.p Abstract: OBJECTIVES: In 1997 a review of paramedic practice upon adult patients in the UK found many inconsistencies and deficiencies in basic care. A follow up review in 2002 identified widespread improvement in provision of equipment and skills to provide basic and advanced life support. Paediatric care was not assessed in either review. The authors conducted this study to identify current standards of care in paediatric paramedic practice and areas of potential improvement. METHOD: A questionnaire designed to determine what equipment and skills were available to paramedics for the management of common or serious paediatric emergencies was sent to chief executives of the 32 NHS Ambulance Trusts in England and Wales. RESULTS: The trend of expanding and standardising practice among adult patients has not extended to paediatric practice despite national guidelines from the Joint Royal Colleges Ambulance Liaison Committee (JRCALC). Furthermore there are some serious failings in the provision of care and skills. Many Trusts have not adopted JRCALC guidelines for the management of life threatening paediatric emergencies such as asthma, meningitis, and fluid replacement in hypovolaemia.

CONCLUSIONS: Ambulance Trusts not meeting standards set out in the JRCALC guidelines must address their areas of deficiency. Failure to do so endangers children's lives and leaves Trusts open to criticism.

Robroeks C.M. et al. *Cytokines in exhaled breath condensate of children with asthma and cystic fibrosis.* *Ann Allergy Asthma Immunol.* 2006; 96(2) : 349-55.p **Abstract:** BACKGROUND: Inflammatory mediators in exhaled breath condensate (EBC) indicate ongoing inflammation in the lungs and might differentiate between asthma and cystic fibrosis (CF). OBJECTIVES: To evaluate the presence, concentration, and short-term variability of TH1- and TH2-mediated cytokines (interferon-gamma [IFN-gamma], tumor necrosis factor alpha [TNF-alpha], interleukin 10 [IL-10], IL-5, IL-4, and IL-2) in EBC of children with asthma or CF and in controls and to analyze the discriminating ability of inflammatory markers in EBC between children with asthma or CF and controls. METHODS: Expired air was conducted through a double-jacketed glass tube cooled by circulating ice water. In 33 asthmatic children, 12 children with CF, and 35 control children, EBC was collected during tidal breathing. Cytokines were measured using flow cytometry. RESULTS: Interleukin 2, IL-4, IFN-gamma, and IL-10 were detected in 16%, 16%, 11%, and 9%, respectively, of all samples in asthma and CF. Interleukin 5 and TNF-alpha were not detected in children with CF. Cytokine concentrations did not differ significantly in children with asthma vs CF. In controls, IFN-gamma, TNF-alpha, and IL-10 were detected in 9%, 14%, and 3%, respectively; IL-2, IL-4, and IL-5 were not detected in controls. CONCLUSIONS: Cytokines such as IFN-gamma, TNF-alpha, IL-10, IL-5, IL-4, and IL-2 can be detected in EBC of children with asthma or CF. However, the concentrations found are close to the detection limits of the assay used. These findings emphasize the importance of developing more sensitive techniques for the analysis of EBC and of standardizing the EBC collection method.

Rodehorst T.K. *Rural elementary school teachers' intent to manage children with asthma symptoms.* *Pediatr Nurs.* 2003; 29(3) : 184-92.p **Abstract:** A study of 212 rural elementary school teachers sought to determine the relationships among the variables of their general knowledge about asthma, attitude toward asthma, self-efficacy in helping children with asthma manage their asthma, and social support for initial management of children's asthma with the teachers' intent to manage children who present with signs and symptoms of asthma in the classroom. The situational variables of number of years teaching experience, number of children with asthma that teachers have had in their classroom during their teaching profession, and whether or not the teacher had asthma or knew of someone with asthma also were explored in relation to intent to manage asthma. Results indicate that although teachers had a favorable attitude toward asthma and were tolerant of students with asthma, their knowledge about asthma was low. Because asthma can be life-threatening, it is essential to assist those involved in monitoring and managing children with asthma to provide timely, appropriate care. In this way, the goal of having a child with asthma live as normal a life as possible, including all school activities, can be realized.

Roder I. et al. *Psychosocial functioning and stress-processing of children with asthma in the school context: differences and similarities with children without asthma.* *J Asthma.* 2003; 40(7) : 777-87.p **Abstract:** OBJECTIVE: To characterize children with asthma by their stress processing at school and their psychosocial functioning. To establish similarities and differences between children with and without asthma. METHODS: Participants were 79 children with asthma and 359 children without asthma (ages 8-12). Children completed questionnaires on stress processing and their well-being at school. Parents filled in a questionnaire on behavior problems, and teachers provided data on school performance and absence rate.

RESULTS: Children with asthma had higher scores on absence rates, teacher-rated well-being, internalizing behavior problems, occurrence of "rejection by peers," and use of aggression when coping with "problems with school work." However, using discriminant analyses, the groups could not reliably be distinguished from one another by these variables. CONCLUSIONS: Children with asthma are similar to other children with regard to their stress processing at school and their psychosocial functioning. The value of conducting multivariate analysis over several univariate tests is underscored.

Roel E. et al. *Clinically diagnosed childhood asthma and follow-up of symptoms in a Swedish case control study.* *BMC Fam Pract.* 2005; 6(1) : 16.p **Abstract:** BACKGROUND: Childhood asthma has risen dramatically not only in the western societies and now forms a major and still increasing public health problem. The aims of this study were to follow up at the age of ten the patterns of asthma symptoms and associations among children with a clinically diagnosed asthma in a sizeable urban-rural community and to compare them with demographic controls using a standardised questionnaire. METHODS: In a defined region in Sweden with a population of about 150,000 inhabitants, all children (n = 2,104) born in 1990 were recorded. At the age of seven all primary care and hospital records of the 1,752 children still living in the community were examined, and a group of children (n = 191) was defined with a well-documented and medically confirmed asthma diagnosis. At the age of ten, 86 % of these cases (n = 158) and controls (n = 171) completed an ISAAC questionnaire concerning asthma history, symptoms and related conditions. RESULTS: Different types of asthma symptoms were highly and significantly over-represented in the cases. Reported asthma heredity was significantly higher among the cases. No significant difference in reported allergic rhinitis or eczema as a child was found between cases and controls. No significant difference concerning social factors or environmental exposure was found between case and controls. Among the control group 4.7 % of the parents reported that their child actually had asthma. These are likely to be new asthma cases between the age of seven and ten and give an estimated asthma prevalence rate at the age of ten of 15.1 % in the studied cohort. CONCLUSION: A combination of medical verified asthma diagnosis through medical records and the use of self-reported symptom through the ISAAC questionnaire seem to be valid and reliable measures to follow-up childhood asthma in the local community. The asthma prevalence at the age of ten in the studied birth cohort is considerably higher than previous reports for Sweden. Both the high prevalence figure and allowing the three-year lag phase for further settling of events in the community point at the complementary roles of both hospital and primary care in the comprehensive coverage and control of childhood asthma in the community.

Rollins G. *Inhaled corticosteroids are safe even for young asthma patients.* *Rep Med Guidel Outcomes Res.* 2002; 13(13) : 5-8.p

Rollins G. *Study demonstrates effectiveness of new model of pediatric asthma care.* *Rep Med Guidel Outcomes Res.* 2004; 15(20) : 1, 6-7.p

Romans S. et al. *Childhood abuse and later medical disorders in women. An epidemiological study.* *Psychother Psychosom.* 2002; 71(3) : 141-50.p **Abstract:** BACKGROUND: There have been many studies documenting adverse psychiatric consequences for people who have experienced childhood and adult sexual and physical abuse. These include posttraumatic stress disorder, anxiety, depression, substance abuse, eating disorders and probably some personality disorders or trait abnormalities. Much less is known about the links between abuse and physical/psychosomatic conditions in adult life. Hints of causal links are evident in the literature discussing headache, lower back pain, pelvic pain and

irritable bowel syndrome. These studies are not definitive as they use clinic-based samples. **METHODS:** This study used interview data with a random community sample of New Zealand women, half of whom reported childhood sexual abuse and half who did not. Details about childhood physical abuse and adult abuse were also collected in a two-phase study. **RESULTS:** Complex relationships were found, as abuses tended to co-occur. Seven of 18 potentially relevant medical conditions emerged as significantly increased in women with one or more types of abuse. These were chronic fatigue, bladder problems, headache including migraine, asthma, diabetes and heart problems. Several of these associations with abuse are previously unreported. **CONCLUSIONS:** In this random community sample, a number of chronic physical conditions were found more often in women who reported different types of sexual and physical abuse, both in childhood and in adult life. The causal relationships cannot be studied in a cross-sectional retrospective design, but immature coping strategies and increased rates of dissociation appeared important only in chronic fatigue and headache, suggesting that these are not part of the causal pathway between abuse experiences and the other later physical health problems. This finding and the low co-occurrence of the identified physical conditions suggest relative specificity rather than a general vulnerability to psychosomatic conditions in women who have suffered abuses. Each condition may require separate further study.

Romero-Placeres M. et al. [Air pollution, bronchial asthma, and acute respiratory infections in minors, Havana City]. *Salud Publica Mex.* 2004; 46(3) : 222-33.p **Abstract:** **OBJECTIVE:** To identify the relationship between emergency visits for acute respiratory illnesses, acute bronchial asthma crisis (ABAC) and acute respiratory infections (ARI), in children less than 14 years of age, and the daily changes of air pollutant levels, in two central hospitals of Havana City, between October 1st 1996 and March 16 1998. **MATERIAL AND METHODS:** An ecological time series study was conducted. We assessed the relationship between the presence of acute respiratory illnesses, ABAC, and IRA, and exposure to levels of particles less than 10 microg/m³ (PM10), smoke, and sulfur dioxide (SO₂); negative binomial regression models were used to assess latency periods of one to five days as well as the cumulative effect of seven days before the emergency visit. **RESULTS:** The levels of atmospheric pollutants were low, in general. The 24-hour mean values for PM10 levels, smoke, and SO₂, were 59.2 microg/m³ (SD=29.2), 27.7 microg/m³ (SD=21.2), and 21.1 microg/m³ (SD=20.1), respectively. An increase of 20 microg/m³ in the daily average of black smoke was associated with a 2.2% increase (95% CI 0.9-3.6) in the number of emergency visits for ABAC. A 20 microg/m³ increase in the daily average of black smoke and SO was associated with an increase in ARI of 2.4% (95% CI 1.2-3.6), and 5% (95% CI 1.3-5.3), respectively, with a 5-day lag. We also observed a cumulative effect for all the contaminants studied. **CONCLUSIONS:** These results suggest that air pollution levels in Havana City affect children's respiratory health; therefore implementation of control measures is necessary, especially those aimed at decreasing motor vehicle exhaust fumes. The English version of this paper is available at: <http://www.insp.mx/salud/index.html>.

Rona R.J. et al. *The early origins hypothesis with an emphasis on growth rate in the first year of life and asthma: a prospective study in Chile.* *Thorax.* 2005; 60(7) : 549-54.p **Abstract:** **BACKGROUND:** There is uncertainty about the impact of the programming hypothesis in terms of nutritional status at birth, rate of growth in the first year of life, length of gestation, breast feeding, and episodes of illness on asthma. An analysis was therefore carried out to test this hypothesis. **METHODS:** Data were collected on 1232 children born between 1974 and 1978 in a semi-rural area of Chile. Measurements at birth and growth in the first year of life were obtained from a birth registry and clinical notes. Information on asthma was collected using the European Community Respiratory Health Survey questionnaire. Sensitisation to eight allergens and bronchial hyperresponsiveness

(BHR) to methacholine were determined. All other information was obtained using a questionnaire. Polytomous logistic analyses were carried out to explore the association of factors at birth and during the first year of life with asthma symptoms, atopy, and BHR. **RESULTS:** Weight and length gain in the first year were positively associated with wheeze (odds ratio (OR) 1.004, 95% CI 1.001 to 1.007 and OR 1.11, 95% CI 0.98 to 1.25, respectively). A higher body mass index (BMI) at birth was protective in subjects reporting both wheeze and waking with breathlessness (OR 0.54, 95% CI 0.35 to 0.84). Length rate in tertiles divided by length at birth in tertiles was related to asthma symptoms (OR 1.68, 95% CI 1.19 to 2.37). Most other assessments were not associated with asthma. **CONCLUSION:** These results show promising but inconclusive evidence that a rapid rate of growth in length, especially in newborn infants of low length, might be involved in the aetiology of asthma.

Ronchetti F. et al. *Detection of Chlamydia pneumoniae in cholesteatoma tissue: any pathogenetic role?* *Otol Neurotol.* 2003; 24(3) : 353-7.p **Abstract:** **BACKGROUND:** Acquired cholesteatoma is a complication of chronic otitis media that is usually associated with an intense local inflammatory reaction. Cholesteatoma probably arises from epithelial migration close to an ongoing host inflammatory response attributable to a chronic bacterial infection. Chlamydia pneumoniae is an intracellular microorganism associated with several pathologic conditions originally considered noninflammatory, including asthma, atherosclerosis, and Alzheimer disease. To investigate a possible relationship between C. pneumoniae and the development of cholesteatoma, tissue was studied in three different layers by polymerase chain reaction analysis. The results were compared with those relative to other two common middle-ear pathogens, Mycoplasma pneumoniae and Haemophilus influenzae. **METHODS:** Cholesteatoma specimens were collected from 32 patients undergoing middle ear surgery. A series of 5 microm-thick specimens were obtained at three different tissue levels, internal (matrix), intermediate (perimatrix), and external (granulation tissue), and processed by polymerase chain reaction for detection of C. pneumoniae, H. influenzae, and M. pneumoniae. Fragmentation and polymerase chain reaction amplification were carried out using two substantially different techniques. **RESULTS:** C. pneumoniae was detected with either polymerase chain reaction techniques in the internal layers in 16 of the 32 cholesteatomas (50%), associated with a positive finding in the intermediate layer in two cases and in the external layer in one case. Four specimens contained H. influenzae, always in the external layer, whereas none contained M. pneumoniae. **CONCLUSIONS:** The close relationship between cholesteatoma and C. pneumoniae demonstrated by the findings of this study could suggest a direct cause and effect link between the pathogen action and the clinical manifestations. Otherwise, a facilitated colonization by C. pneumoniae and chronic pathology of the ear could both take origin from a peculiar immunologic background of the host.

Ronchetti R. et al. *Association of asthma with extra-respiratory symptoms in schoolchildren: two cross-sectional studies 6 years apart.* *Pediatr Allergy Immunol.* 2002; 13(2) : 113-8.p **Abstract:** Epidemiological information on symptoms affecting extra-respiratory organs and apparatuses in asthmatic children is scarce. The aim of this study therefore was to evaluate, at a population level, if and what extra-respiratory symptoms are associated with asthma. Two questionnaire-based, cross-sectional surveys were carried out on 1,262 students (651 males; mean age 9.57 years, age-range 6-14 years) in 1992 and on 1,210 students (639 males; mean age 9.02 years, age-range 6-14 years) in 1998, from two elementary and two junior high schools in Rome, Italy. Questionnaires included queries about asthma and its risk factors and extra-respiratory symptoms (headache, restlessness, sleep disturbances, urticaria, itching, and abdominal pain). Of responders, 11.9% (279/2,342) had a history of asthma. After adjustment for gender, family history of atopic disease, low birth weight, early respiratory problems, and damp house, asthma was significantly associated with recurrent abdominal pain

(odds ratio [OR] 1.90; 95% confidence interval [CI]: 1.04, 3.16), itching (OR 3.15; 95% CI: 1.75, 5.68), and urticaria (OR 2.52; 95% CI: 1.02, 6.20). Asthma was reported by 10.2% (201/1,962) of children unaffected by this triad, by 20.1% (56/279; OR 2.20) with one of the symptoms, and by 31.6% (12/38; OR 4.04) with two or more symptoms. An emerging characteristic of pediatric asthma in our setting appears to be its association with certain extra-respiratory symptoms (abdominal pain, itching, and urticaria). A global, internistic approach to asthmatic children is increasingly required both in the clinical setting and in future epidemiological studies.

Ronmark E. et al. *Different sensitization profile for asthma, rhinitis, and eczema among 7-8-year-old children: report from the Obstructive Lung Disease in Northern Sweden studies.* *Pediatr Allergy Immunol.* 2003; 14(2) : 91-9.p **Abstract:** Sensitization to different airborne allergens in relation to asthma, rhinitis, and eczema has been studied. A cross-sectional study was performed among 7-8-year-old children living in northern Sweden. The ISAAC-questionnaire with additional questions were sent to the parents, and 3431 (97%) participated. Two-thirds of the children were invited to undergo a skin test with 10 common airborne allergens, and 2148 (88%) participated. The prevalence rates of all three diseases were significantly higher among the children who were sensitized to any of the tested allergens. Among asthmatics, 40% were sensitized to cat, 34% to dog, 28% to horse, 23% to birch and 16% to timothy. The corresponding figures for rhinitis were: cat 49%, dog 33%, horse 37%, birch 46%, timothy 32%; and for eczema: cat 29%, dog 21%, horse 15%, birch 20%, and timothy 11%. Only a few children were sensitized to mites or moulds. The main risk factors for all three diseases were type-1 allergy and a family history of the disease. Independently from other risk factors, sensitization to dog (OR 2.4) and horse (OR 2.2) were significant risk factors for asthma. Sensitization to birch (OR 6.0), horse (OR 4.1), and timothy (OR 2.8) were significant risk factors for rhinitis, while birch (OR 2.4), dog (OR 2.0) and cat (OR 1.6) were significant risk factors for eczema. Despite a large over-lapping of the diseases the pattern of sensitization was different for asthma, rhinitis and eczema. Sensitization to cat was most common among all children, but sensitization to dog and horse was associated with the highest risk for asthma, and sensitization to birch showed the highest risk for rhinitis and eczema. The different risk factor pattern for the often coexisting diseases; asthma, rhinitis, and eczema, may indicate differences in the etiology.

Ronmark E. et al. *Incidence rates and risk factors for asthma among school children: a 2-year follow-up report from the obstructive lung disease in Northern Sweden (OLIN) studies.* *Respir Med.* 2002; 96(12) : 1006-13.p **Abstract:** Studies of incidence of asthma are still limited. A longitudinal study of asthma in school children was started in 1996 in Northern Sweden. The incidence of asthma and the associated risk factors have been studied over a 2 years period. The study started with a parental questionnaire, the ISAAC questionnaire with additional questions, and a skin-prick test. The cohort, 3,525 children, 7 and 8 years old at start, was followed after 1 and 2 years by using the same questions. Each year responded 97%. The cumulative incidence of physician-diagnosed asthma was 1.7%, 0.9/1,000/year the first year, and 0.8/1,000/year the second year. The cumulative incidence of wheezing was 6.3%, and of frequent or daily users of asthma medicines 2.1%. Significant risk factors for incident asthma were a positive skin test, OR 5.64 (3.10-10.25); rhinitis, OR 3.53 (1.80-6.90); eczema, OR 2.19 (1.26-3.82); a family history of asthma, OR 2.83 (1.75-4.56); low birth weight, OR 3.38 (1.61-7.54); respiratory infections, OR 2.12 (1.24-3.63); male gender, OR 1.71 (1.06-2.81); and a smoking mother OR 2.00 (1.07-3.73). In summary the incidence of asthma during 2 years after age 7 was high, almost 1/100/year. Allergy was the most important risk factor, but other factors were influential.

Rosas Vargas M.A. et al. *[Changes in lung function after a bronchial provocation test with cockroach antigens].* *Rev Alerg Mex.* 2003; 50(1) : 13-6.p **Abstract:** BACKGROUND: Cockroach allergens sensitized patients at a very young age and can predispose to severe asthma on atopic children. OBJECTIVE: To evaluate the FEV₁ changes induced after bronchoprovocation with *Blattella germanica* (Bg) or placebo on allergic respiratory children. MATERIAL AND METHODS: A prospective transversal study was performed in 25 children from 8 to 16 yr with allergic rhinitis and/or asthma diagnosis with sensibility only to Bg (Bayer Corp allergens) by Prick skin test, with a 1:20 weight/volume dilution. After previous training on spirometry, they assisted for a double blind bronchial challenge with 10, 25, 50, 75, 100, 150, 200, 300, 400, 500 until 750 proteic nitrogen units of Bg or 0.9% NaCl solution in a nebulized open circuit, with a 5 litter flow for 3 min. A week after, they returned for the crossover double blind bronchial challenge. At the beginning of the study a basal spirometry was performed and subsequent spirometrics at 1.5 and 3 min after each challenge with a 10 min rest between the challenges. The test was interrupted if cough, dyspnea, wheezing and/or a 15% or more FEV₁ fall appeared. RESULTS: Twelve patients showed a FEV₁ fall with the antigen challenge, all with specific IgE for Bg. All they had positive skin test to Bg, 9 had asthma and rhinitis and 3 only asthma. When placebo was used 6 patients showed a FEV₁ fall. When comparing the average basal and final FEV₁ values after the challenges, the fall was statistical significant in both groups with a p = 0.0015 when Bg was used, and p = 0.046 with placebo. CONCLUSION: These results show that two times fold number of patients challenged with Bg had a FEV₁ fall than placebo, and the t Student test showed that antigen challenge was more significant than placebo. We demonstrated that respiratory allergic patients sensitised with Bg after a bronchial challenge with these allergens show a FEV₁ fall. This suggests that cockroach allergen sensitisation can be on account of children's asthma.

Rose D. et al. *Urban American Indian family caregivers' perceptions of barriers to management of childhood asthma.* *J Pediatr Nurs.* 2003; 18(1) : 2-11.p **Abstract:** American Indian family caregivers of children with asthma face numerous barriers to effective management of the illness. The purpose of this qualitative, community-based study is to identify those barriers as perceived by family caregivers in a large Midwestern city. An ecological perspective and principles of family-centered care provided the theoretical orientation for the study. Interviews were conducted with 16 urban Ojibwe family caregivers of children with asthma. Five categories of barriers characterize the families' experiences: provider (individual and system), condition-related, family caregiver, socioeconomic, and environmental. Examination of these findings suggests directions for improving care to American Indian children with asthma and their families.

Rosenthal M. *Differential diagnosis of asthma.* *Paediatr Respir Rev.* 2002; 3(2) : 148-53.p **Abstract:** Asthma tends to be diagnosed too easily by clinicians without sufficient consideration being given to alternative possibilities. Most asthma is obvious, mild and easy to treat. Deviations from this typical picture should be a signal to consider carefully other diagnoses. Age of onset, pattern of symptoms, sputum production, diurnal variations or the lack thereof, associated upper respiratory symptoms, abnormal physical signs, poor control on standard inhaler therapy and unusual flow volume loops are all pointers to non-asthma diagnoses.

Rosias P.P. et al. *Childhood asthma: exhaled markers of airway inflammation, asthma control score, and lung function tests.* *Pediatr Pulmonol.* 2004; 38(2) : 107-14.p **Abstract:** Exhaled markers of airway inflammation become increasingly important in the management of childhood asthma. The aims of the present study are: 1) to compare exhaled markers of inflammation (nitric oxide, carbon monoxide, and acidity of breath condensate) with conventional

asthma measures (lung function tests and asthma control score) in childhood asthma; and 2) to investigate the detectability of albumin, CRP, IL-6, IL-8, TNF-alpha, sICAM-1, and sTNF-R75 in the exhaled breath condensate (EBC) of asthmatic children. Thirty-two children with mild to moderate persistent asthma and healthy controls aged 6-12 years were studied. We measured exhaled NO and CO, and subsequently EBC was collected. Inflammatory mediators in EBC were measured using an enzyme-linked immunosorbent assay. Respiratory symptoms and asthma control were assessed using the asthma control questionnaire (ACQ) of Juniper et al. (Eur Respir J 1999;14:902-907). Exhaled NO showed a significant correlation with exhaled CO ($r = 0.59, P < 0.05$) and FEV1 ($r = -0.59, P < 0.05$), but not with ACQ score ($r = 0.48, P = 0.06$). Exhaled CO was correlated with prebronchodilator FEV1 ($r = -0.45, P < 0.05$), but not with asthma control ($r = 0.18, P = 0.35$). Acidity of EBC was significantly lower in asthmatic children than in healthy controls ($P < 0.05$), but did not correlate with any of the conventional asthma measures. We were not able to demonstrate the presence of CRP, IL-6, IL-8, TNF-alpha, sICAM-1, and sTNF-R75 in EBC. Albumin was found in two EBC samples of asthmatic children. We conclude that exhaled NO had a better correlation with lung function parameters and asthma control than exhaled CO and acidity of EBC, in mild to moderate persistent childhood asthma. However, exhaled NO, CO, and deaerated pH of EBC did not differ between asthmatic children and controls, possibly because of a too homogeneous and well-controlled study population. To further evaluate the clinical utility of exhaled markers in monitoring childhood asthma, more studies are required on a wider range of asthma severity, and preferably with repeated measurements of markers and of asthma control.

Rossi G.A. *Airway remodeling: structure and physiology.* *Pediatr Pulmonol Suppl.* 2004; 26 : 100-2.p

Rossi R.E. et al. *Prevalence of serum IgE antibodies to the Staphylococcus aureus enterotoxins (SAE, SEB, SEC, SED, TSST-1) in patients with persistent allergic rhinitis.* *Int Arch Allergy Immunol.* 2004; 133(3) : 261-6.p **Abstract:** BACKGROUND: Enterotoxins produced by Staphylococcus aureus and their specific IgE antibodies were thought to be important in worsening atopic dermatitis. However, few studies have documented an association between S. aureus or its exotoxins and exacerbations of upper airway/nasal disease. In the current study, we determined the prevalence of serum-specific IgE towards staphylococcal enterotoxin A, B, C, D (SEA, SEB, SEC, SED) and toxic shock syndrome toxin 1 (TSST-1) in patients suffering from rhinitis and/or asthma due to allergy. Therefore, we examined whether SEA, SEB, SEC, SED and TSST-1 were important in worsening the clinical status of patients allergic to house dust mites by means of assessing serum eosinophil cationic protein (ECP), which is thought to be a reliable marker of asthma and rhinitis severity. METHODS: 198 patients with persistent allergic rhinitis and/or asthma due to house dust mites were evaluated. Specific IgE towards SEA, SEB, SEC, SED, TSST-1, timothy grass and birch pollen recombinant allergens, and other aeroallergen extracts from common allergen sources were evaluated by the Pharmacia CAP System. Serum ECP was assessed, too. RESULTS: The percentages of sensitization to staphylococcal enterotoxins of 198 house dust mite-allergic patients were as follows: TSST-1-specific IgE 24.7% (n=49), SEC-specific IgE 22.2% (n=44), SEB-specific IgE 15.1% (n=30), SEA-specific IgE 9.1% (n=18), and SED-specific IgE 5.5% (n=11). Out of 198 individuals allergic to house dust mites 136 patients suffering from persistent rhinitis were subdivided into two subgroups: 53 patients with serum-specific IgE to at least one staphylococcal enterotoxin and 83 patients without specific IgE towards staphylococcal enterotoxins. Patients sensitive to staphylococcal enterotoxins had higher serum ECP levels than patients lacking specific IgE to SEA, SEB, SEC, SED and TSST-1 (geometric mean 24.3 vs. 16.6 microg/100 ml; $p=0.029$), as well as total IgE levels (geometric mean 564 vs. 161 kU/l, $p=0.00063$) and specific IgE to Dermatophagoides pteronyssinus (geometric mean 16.7 vs. 6.6 kU/l; $p=0.0235$) and Dermatophagoides farinae

(geometric mean 18.6 vs. 7.8 kU/l; $p=0.0246$). CONCLUSION: A status of sensitization to staphylococcal enterotoxins seems to be a factor increasing serum ECP, which is thought to be a reliable marker of clinical severity of allergic disease. Therefore, the evaluation of SEA, SEB, SEC, SED and TSST-1-specific IgE antibodies may have additional significance for the prognosis of persistent allergic diseases of the upper airway.

Rothenbacher D. et al. *Breastfeeding, soluble CD14 concentration in breast milk and risk of atopic dermatitis and asthma in early childhood: birth cohort study.* *Clin Exp Allergy.* 2005; 35(8) : 1014-21.p **Abstract:** BACKGROUND: Breast milk contains a variety of bioactive substances, among them, soluble CD14 (sCD14), which plays an important role in innate immunity. OBJECTIVE: We analysed data of a large prospective birth cohort study to examine the determinants of sCD14 in breast milk, and investigated whether breastfeeding practice and sCD14 concentrations in breast milk are determinants of the risk of atopic dermatitis (AD) and asthma in children. METHODS: Eight hundred and three mothers and their newborns were included in this analysis. We measured sCD14 concentrations in breast milk samples collected 6 weeks post-partum. During a 2-year follow-up the cumulative incidences of AD and asthma were recorded. RESULTS: Overall, AD was reported for 20.6% of the 2-year-olds and asthma was reported for 19.6%. We found the lowest incidence of physician-reported AD in children of mothers without a history of atopic diseases if breastfed for 6 to less than 9 months. Furthermore, we found an inverse association between duration of breastfeeding and risk of asthma, which was especially evident in children with mothers without a history of atopic disease ($P=0.01$). These patterns persisted after control for other factors by multivariate analysis methods. The protective effect of breastfeeding seemed to be synergistic with sCD14 concentrations in breast milk (P for trend 0.0005). CONCLUSIONS: The results of this prospective birth cohort study suggest that a longer duration of breastfeeding does decrease the risk for asthma in early childhood, especially in children of mothers without a history of atopic disease. The beneficial effects of breastfeeding might be further supported by high levels of sCD14 in breast milk.

Rottem M. et al. *Hospital admission trends for pediatric asthma: results of a 10 year survey in Israel.* *Isr Med Assoc J.* 2005; 7(12) : 785-9.p **Abstract:** BACKGROUND: In the last decade there has been an increase in asthma morbidity. Hospital admission rates for childhood asthma are influenced by the prevalence of asthma and the quality of asthma care. OBJECTIVES: To assess trends in hospital admission and readmission rates for childhood asthma in the Jezreel Valley in Israel in the last decade, and to evaluate the possible effect of changes in asthma treatment on hospitalization for acute asthma during this period. METHODS: All records of pediatric patients from the central hospital in the Jezreel Valley in northeastern Israel over a 10 year period from 1990 through 1999 who were diagnosed as having asthma were thoroughly reviewed and analyzed for admissions, re-admissions, and treatment before and during admissions. RESULTS: There were 1584 admissions, 1208 were first-time admissions and 376 were re-admissions. The number of first-time admissions increased significantly over time ($P < 0.0001$), with a significant decrease in re-admissions ($P < 0.005$); this finding was more significant in children under the age of 8 years ($P < 0.005$). The length of hospital stay decreased significantly from 3.3 days to 2.7 days ($P < 0.002$). Significant changes in the use of medications included an increase in inhaled glucocorticoids and a decrease in the use of sodium cromoglycate and theophylline. Controller medication use was concomitant with a significant decrease in the re-admission rates. CONCLUSIONS: The increase in the admission rate and the decrease in the rate of re-admissions and the length of hospital stay probably reflect the increase in the prevalence of asthma and changes in its treatment, respectively. It is essential that asthma be recognized as a significant cause of morbidity and that controller medications be

administered to decrease its severity, morbidity, and resultant hospital admissions.

Roy S.R. et al. *Bacterial DNA in house and farm barn dust.* J Allergy Clin Immunol. 2003; 112(3) : 571-8.p Abstract: BACKGROUND: Early in life, natural exposure to microbial components (eg, endotoxin) may mitigate allergy and asthma development in childhood. Bacterial DNA is a potent stimulus for the innate immune system; its immune stimulatory potential in dust is unknown. OBJECTIVES: We sought to quantify bacterial DNA and endotoxin content in dust from urban homes, rural homes, farm homes, and farm barns and to determine if dust DNA is immune-stimulatory. METHODS: Total DNA, bacterial DNA, and endotoxin were measured in 32 dust samples. To measure bacterial DNA content, a quantitative polymerase chain reaction assay specific for bacterial ribosomal DNA was developed. Peripheral blood mononuclear cells from 5 adults were stimulated with endotoxin-free dust DNA with/without lipopolysaccharide (LPS) from selected dust samples. IL-12p40, IL-10, and tumor necrosis factor-alpha were measured in cell supernatants by enzyme-linked immunosorbent assay. RESULTS: Bacterial DNA in dust correlated with endotoxin ($r = 0.56$, $P < .001$) and total DNA content ($r = 0.51$, $P = .003$). The highest bacterial DNA levels were measured in farm barns (mean, 22.1 microg/g dust; range, 1.3 to 56.2), followed by rural homes (6.3 microg/g; 0.2 to 20), farm homes (2.2 microg/g; 0.1 to 9.1), and urban homes (0.6 microg/g; 0.1 to 1.2). Farm barn DNA significantly potentiated ($P < \text{or} = .05$) LPS-induced IL-10 and IL-12 p40 but not tumor necrosis factor-alpha release (13-fold, 3-fold, and 1.5-fold increases, respectively). DNA from 6 urban homes did not demonstrate this LPS-potentiating effect. CONCLUSIONS: Endotoxin is a marker for bacterial DNA, which is also higher in locales of lower asthma and allergy prevalence. DNA from farm barn dust augments the immune modulatory effects of endotoxin and may combine with exposure to other such naturally occurring microbial components to mitigate allergy and asthma development.

Rubin B.K. *Inhaled corticosteroids: devices and deposition.* Paediatr Respir Rev. 2004; 5 Suppl A : S103-6.p

Rubin R.N. et al. *Relationship of serum antioxidants to asthma prevalence in youth.* Am J Respir Crit Care Med. 2004; 169(3) : 393-8.p Abstract: The relationship of serum vitamin E, beta-carotene, vitamin C, and selenium to asthma was investigated among 7,505 youth (4-16 years old) in the Third National Health and Nutrition Examination Survey. Logistic regression models adjusted for potentially confounding variables, which generally had no effect on the coefficients for the antioxidants. Serum vitamin E had little or no association with asthma. In separate models, a SD increase in beta-carotene (odds ratio [OR], 0.9; 95% confidence interval [CI], 0.7, 1.0), vitamin C (OR, 0.8; 95% CI, 0.7, 0.9), and selenium (OR, 0.9; 95% CI, 0.7, 1.1) was associated with a 10-20% reduction in asthma prevalence. Serum cotinine was used to identify youth with no cigarette smoke exposure and passive exposure (7%): Active smokers were too few to be studied further. The selenium-asthma association was stronger in youth who were smoke exposed ($p = 0.075$). A SD increase in selenium was associated with a 50% reduction in asthma prevalence (OR, 0.5; 95% CI, 0.2, 1.4) in youth with passive smoke exposure compared with a 10% reduction in youth with no smoke exposure. The findings support an association of antioxidants with prevalent asthma, which for some antioxidants is stronger among children exposed to cigarette smoke.

Ruiz-Charles M.G. et al. *[Risk factors associated with bronchiolitis in children under 2 years of age].* Rev Invest Clin. 2002; 54(2) : 125-32.p Abstract: INTRODUCTION: The objective of this study was to determine the risk factors associated to bronchiolitis in infants less than two years of age. MATERIALS AND METHODS: Prospective

case-control study was performed in a hospital of second level of attention. The sample size was calculated for a level of confidence of 95%, a power of 90%, and a difference of exposure of 15% between cases and controls. For each case, there was one control matched for age and sex. The cases were obtained in the pediatric emergency room and the controls were healthy infants who came to the preventive medicine service of the same hospital. The diagnosis of bronchiolitis was established by direct observation in accordance to clinical criteria and chest X-ray. All the patients were weighed to the moment to be included in the study, and through structured interview the following variables were investigated: family history of bronchial asthma and atopy in immediate family members, prematurity, mechanical ventilation, bronchopulmonary dysplasia, present-day breast-feeding, length of time of breast feeding, early weaning, passive tobacco smoke exposure, maternal smoking, housing and living with domestic animals. The global significance of the study was probed by multiple logistic regression. RESULTS: Were studied 110 pairs with a range of age of 10 days to 23 months (average of 7.1 +/- 4.7 months), 49 pairs were female and 61 male (ratio 1:1.2) The variables significantly associated ($P < \text{or} = 0.05$) to bronchiolitis were family history of bronchial asthma in immediate family members (OR: 2.9, IC 95% 1.29-6.34) and prematurity (OR: 3.0, IC 95% 1.04-8.87). The early weaning (OR: 0.44, IC 95% 0.24-0.79) and present-day breast-feeding (OR: 0.53, IC 95% 0.30-0.95) revealed a significant negative association. The other studied variables didn't show statistically significant association with bronchiolitis. CONCLUSIONS: Factors that increase the risk of bronchiolitis are a history of prematurity, and family history of bronchial asthma. Factors that have a protective effect are early weaning, and present-day breast-feeding.

Rumchev K.B. et al. *Domestic exposure to formaldehyde significantly increases the risk of asthma in young children.* Eur Respir J. 2002; 20(2) : 403-8.p Abstract: Concern has arisen in recent years about indoor air pollution as a risk factor for asthma. Formaldehyde exposure was examined in relation to asthma among young children (between 6 months and 3 yrs old) in a population-based control study carried out in Perth, Western Australia, between 1997-1999. An association between exposure to formaldehyde and asthma in young children has been suggested. Cases ($n=88$), whose parents were recruited at Princess Margaret Hospital Accident and Emergency Dept (Perth, Western Australia), were children discharged with asthma as the primary diagnosis. Controls ($n=104$), who were children in the same age group without asthma diagnosed by a doctor, were identified from birth records through the Health Dept of Western Australia (Perth, Western Australia). Health outcomes for the children were studied using a respiratory questionnaire and skin-prick tests. Formaldehyde, average temperature and relative humidity were measured on two occasions, winter (July-September 1998) and summer (December 1998-March 1999) in the child's bedroom and in the living room. The study found seasonal differences in formaldehyde levels in the children's bedrooms and living rooms with significantly greater formaldehyde exposure during the summer period for case and control subjects. The generalised estimating equation model showed that children exposed to formaldehyde levels of $> \text{or} = 60$ microg x m(-3) are at increased risk of having asthma. The results suggest that domestic exposure to formaldehyde increases the risk of childhood asthma.

Runge C. et al. *Outcomes of a Web-based patient education program for asthmatic children and adolescents.* Chest. 2006; 129(3) : 581-93.p Abstract: BACKGROUND: Asthma is the most common chronic disease among children in Germany. Approaches to reduce the burden of asthma include patient education to improve self-management skills. STUDY OBJECTIVES: We determined whether a continuous Internet-based education program (IEP) as an add-on to a standardized patient management program (SPMP) improves health outcomes of asthma patients at a favorable benefit-cost ratio. PATIENTS AND METHODS: A total of 438 asthmatic patients

aged 8 to 16 years in 36 study centers were enrolled during a 6-month period. We performed a prospective cost-benefit analysis alongside a nonrandomized trial. At baseline and at 6 months and 12 months, health service utilization data were collected. INTERVENTIONS: Study participants were assigned to a control group and two intervention groups. Patients in both intervention groups participated in an SPMP. Additionally, patients in one intervention group received the IEP. RESULTS: Utilization of various health-care services decreased significantly in both intervention groups. From a payer perspective, the benefit-cost ratio of the traditional education program was 0.55. Adding the IEP improved the ratio (0.79). For patients with moderate or severe asthma, the benefit-cost ratios were 1.07 and 1.42 (with IEP), respectively. CONCLUSIONS: The IEP offers the potential to decrease the burden of disease and to realize incremental morbidity cost savings. Subgroup analysis demonstrated that within 1 year, the savings exceed the intervention costs in patients with moderate or severe asthma.

Runton N. *Update on asthma medications.* Nurse Pract. 2002; Suppl : 13-6.p

Russell G. *The use of inhaled corticosteroids during childhood: plus ça change..* Arch Dis Child. 2004; 89(10) : 893-5.p

Ryttilä P. et al. *Induced sputum in children with newly diagnosed mild asthma: the effect of 6 months of treatment with budesonide or disodium cromoglycate.* Allergy. 2004; 59(8) : 839-44.p **Abstract:** BACKGROUND: There are few controlled studies on the effects of anti-inflammatory treatment on airway inflammation in newly diagnosed childhood asthma. METHODS: Sixty children with newly diagnosed mild persistent asthma, 5-10 years of age, and 17 healthy control subjects were studied. Asthmatic children were randomized into an open study with two treatment groups: (1) budesonide 400 microg twice daily for 1 month, 200 microg twice daily for 5 months and (2) disodium cromoglycate (DSCG) 10 mg three-times daily for 6 months. All exacerbations were treated with budesonide 400 microg twice daily for 2 weeks. Symptoms and lung function were recorded throughout the study. RESULTS: Sputum induction was safe and the overall success rate was 71%. This improved with age and decreased after treatment. At baseline, the asthmatic children had more eosinophils in blood (0.26 vs 0.18 x 10⁹/l, P = 0.03) and sputum (1.1 vs 0.0 %, P = 0.0001) than the control subjects. The numbers of sputum eosinophils correlated with bronchial responsiveness (R = -0.58, P = 0.0002). Eosinophils were higher in children with atopic asthma than with nonatopic asthma (P < 0.0001), and in children with a history wheezing than in children without wheezing (P = 0.02). Six months of budesonide treatment, but not of DSCG, improved lung function (P = 0.007), decreased symptoms (P = 0.007) and sputum eosinophils (P = 0.003). The effects of budesonide were pronounced in children with intense sputum eosinophilia (>3%). CONCLUSION: Sputum eosinophilia is present in children with newly diagnosed mild persistent asthma. Treatment with inhaled budesonide, but not with DSCG, decreases sputum eosinophils along with clinical and functional improvement.

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Sacco O. et al. *Epithelial cells and fibroblasts: structural repair and remodelling in the airways.* Paediatr Respir Rev. 2004; 5 Suppl A : S35-40.p **Abstract:** Extensive lesions and changes in the architecture of the airway walls are commonly described in patients with respiratory infections, asthma, chronic bronchitis and interstitial lung diseases. Current knowledge identifies in airway epithelial cells and in fibroblasts the two cell types mainly involved in tissue repair after injury. During inflammatory respiratory disorders, extensive

injury of airway epithelium may occur, with shedding of a large sheet of damaged cells in the bronchial and alveolar lumen but also with activation of the surviving epithelial cells and of the underlying fibroblasts. Indeed, besides acting as a physical and functional barrier to external agents, the epithelial surface of the bronchi has the capability to modulate the repair processes through the secretion of extracellular matrix proteins and the interaction with interstitial fibroblasts. Besides releasing pro-inflammatory cytokines and chemokines, the surviving epithelial cells and the underlying fibroblasts secrete factors contributing to airway repair, including the formation of the provisional extracellular matrix. This is indeed the substrate to which the epithelial cells at the edge of the lesion can attach to migrate in order to reconstitute the surface layer. In these processes airway epithelial cells receive the support of bronchial wall fibroblasts which actively release cytokines stimulating epithelial cell functions.

Sachdev H.P. et al. *Improving antibiotic and bronchodilator prescription in children presenting with difficult breathing: experience from an urban hospital in India.* Indian Pediatr. 2001; 38(8) : 827-38.p **Abstract:** OBJECTIVE: To evaluate the relative frequency of other conditions that share a clinical overlap with pneumonia as defined by the WHO case management algorithm and to determine the possibility of refining the antibiotic and bronchodilator prescription on the basis of simple clinical features. DESIGN: Prospective observational. SETTING: Urban tertiary care center. METHODS: Two hundred children, between the ages of 6 months to 5 years, presenting with difficult breathing (as defined by WHO algorithm) were prospectively evaluated for the diagnosis and the need for bronchodilator and antibiotic therapy (clinician's diagnosis). An additional independent blinded evaluation of the chest X-rays was done by a radiologist after the study (radiologist-aided diagnosis). On the basis of reliable predictors (sensitivity > 70% and specificity > 70%) of antibiotic and bronchodilator prescription, irrespective of the exact diagnostic category, two viable modifications of WHO case management algorithm emerged, which were compared by paired proportion test. RESULTS: Acute asthma was the predominant condition (46% or 54%), pneumonia alone was rare (10%), co-existence of pneumonia with wheeze (bronchospasm) was more frequent (22% or 15%) and often diagnoses not related to the respiratory system were documented (18% or 17%). All the subjects in whom a preceding history of cough was not elicited had non-respiratory illnesses. An audible wheeze was appreciated in only 44 of the 150 cases (29.3%) with an auscultable wheeze. The two alternatives represented a significant (p < 0.0001) improvement over the WHO algorithm preventing inappropriate usage of both antibiotics and bronchodilators, primarily by restricting over-prescription of the former (14% and 26.5% for proposed algorithms 1 and 2, respectively) and under-utilization of the latter (40%). The performance of the alternative algorithms for the radiologist-aided diagnosis was marginally better for over-prescription of antibiotics (16.2% and 30.9% for proposed algorithms 1 and 2, respectively). CONCLUSION: It is feasible to amalgamate simple clinical features (history of: (i) previous similar episode of cough and difficult breathing, and (ii) fever) in the WHO case management algorithm to significantly refine the antibiotic (95% CI range 7% to 33%) and bronchodilator (35%; 95% CI 27% to 43%) prescription.

Sackesen C. et al. *The effect of polymorphisms at the CD14 promoter and the TLR4 gene on asthma phenotypes in Turkish children with asthma.* Allergy. 2005; 60(12) : 1485-92.p **Abstract:** BACKGROUND: Endotoxin, with its potential to enhance type 1 immunity, is a significant player in the hygiene hypothesis. The combined effects of the genetic variants of various molecules in the endotoxin response pathway on asthma related phenotypes are largely unknown. OBJECTIVE: To investigate the effects of the genetic variants of CD14 and TLR4 genes on asthma phenotypes in a large number of asthmatic children. METHODS: 613 asthmatic children were genotyped at the CD14-C159T, TLR4-A896G and

TLR4-C1196T loci. IgE, eosinophil numbers and FEV1 were compared in 327 children who were not on any controller medications and were symptom free. Multivariate logistic regression was used to determine the factors associated with total IgE. RESULTS: Among children with atopic asthma, total IgE levels were significantly different among the three genotypes in the co-dominant model [CC: 435 kU/l (interquartile range: 146-820); CT: 361 (140-710); TT 204 (98-435), P = 0.035]. TT genotype was significantly and independently associated with lower IgE levels (OR: 0.5 95%; CI = 0.28-0.90, P = 0.021). Both TLR4-A896G and TLR4-C1196T polymorphisms were more frequent in the mild asthma group with atopy (P = 0.032, 0.018, respectively). The combined effects of the genetic variants in CD14 and TLR4 genes did not improve the observed associations. CONCLUSION: Our study demonstrates that the CD14-C159T promoter variant influences total IgE levels and also indicates that the T allele has a more profound effect on total IgE in children with atopic asthma. Polymorphisms in the TLR4 gene may be associated with milder forms of disease in atopic asthmatics in the population studied.

Sackesen C. et al. *Use of polymerase chain reaction for detection of adenovirus in children with or without wheezing.* Turk J Pediatr. 2005; 47(3) : 227-31.p **Abstract:** Eighty percent of asthma attacks in children are accompanied by an upper respiratory tract viral infection. Adenovirus is one of the major viral causes of childhood bronchiolitis. As the polymerase chain reaction (PCR) is the most sensitive technique for documenting viral respiratory infections, the PCR method was performed on the throat swab samples of asthmatic children with and without wheezing to investigate the presence of the adenovirus genome in the upper respiratory tract. The frequencies of adenovirus in asymptomatic and symptomatic asthmatic patients, healthy controls and wheezy children were as follows: 33.3%, 71.4%, 37% and 62.96%, respectively. The adenovirus was detected in a significantly higher percentage in the upper airways of patients with asthma exacerbation and in children with wheezing than in patients without asthma exacerbation and in the healthy controls (p < 0.05). The frequency of adenovirus was not different between asthmatic patients receiving or not receiving inhaled corticosteroid. Adenovirus has the potential to precipitate asthma exacerbations in asthmatic patients; its frequency was not affected by the treatment of inhaled corticosteroid.

Sadeghnejad A. et al. *Raised cord serum immunoglobulin E increases the risk of allergic sensitisation at ages 4 and 10 and asthma at age 10.* Thorax. 2004; 59(11) : 936-42.p **Abstract:** BACKGROUND: Evidence suggests that a raised level of cord serum IgE (CS-IgE) is a risk factor for allergic sensitisation. However, whether CS-IgE is a risk for asthma is controversial. A study was undertaken to investigate the association between CS-IgE levels and allergic sensitisation at 4 and 10 years of age and asthma at ages 1-2, 4 and 10. METHODS: CS-IgE was available for 1358 of 1456 children born between 1989 and 1990. The cohort was evaluated for allergic diseases at ages 1, 2, 4 and 10 years. Skin prick tests for six allergens were performed on 981 children at age 4 and 1036 at age 10. Asthma was defined based on a physician's diagnosis. Using logistic regression analysis, the risk of asthma and allergic sensitisation for raised levels of CS-IgE (> or =0.5 kU/l) was estimated. RESULTS: At ages 4 and 10 years 20.2% and 27.0% of children, respectively, had allergic sensitisation. The risk of allergic sensitisation was significantly associated with raised CS-IgE levels at ages 4 (OR 2.29) and 10 years (OR 1.73). The prevalence of asthma was 10.3% at age 1-2, 15.2% at age 4, and 12.8% at age 10. CS-IgE was not associated with asthma at age 1-2 and 4 but showed an increased relative risk at age 10 (OR 1.66, 95% CI 1.05 to 2.62). The association was stronger in children who did not develop allergic sensitisation at age 4 or 10 (OR 3.35, 95% CI 1.41 to 7.93). CONCLUSIONS: Raised cord serum IgE is a risk factor for allergic sensitisation at ages 4 and 10 years. This is the second study suggesting that CS-IgE is also a risk factor for asthma at age 10,

probably related to the late onset of asthma. This association is not necessarily mediated by allergic sensitisation.

Safronova O.G. et al. *Relationship between glutathione S-transferase P1 polymorphism and bronchial asthma and atopic dermatitis.* Bull Exp Biol Med. 2003; 136(1) : 73-5.p **Abstract:** We determined the prevalence of GSTP1-Ile105 and GSTP1-Val105 alleles in patients with bronchial asthma and atopic dermatitis and healthy children of 2 groups (randomized and nonatopic control). The GSTP1-Ile105/Val105 genotype determines the resistance to atopic dermatitis (odds ratio=0.51; 95% confidence interval: 0.28-0.92; p=0.023). However, both homozygotes are at high risk of developing atopic dermatitis (near-significant differences).

Saha C. et al. *Individual and neighborhood-level factors in predicting asthma.* Arch Pediatr Adolesc Med. 2005; 159(8) : 759-63.p **Abstract:** OBJECTIVE: To identify the neighborhood socioeconomic and housing factors at the census-block level and the sociodemographic factors at the individual level that are associated with the risk of asthma. DESIGN: Cross-sectional study of children aged between 5 and 18 years seen in a network of urban primary care clinics. SETTING: A network of urban primary care clinics (Indiana University Medical Group) in Marion County, Indiana, in the calendar year 2000. PARTICIPANTS: A total of 2544 subjects with 1541 black children (947 girls, 594 boys) and 1003 white children (568 girls, 435 boys). MAIN OUTCOME MEASURE: Whether a subject ever had asthma. RESULTS: The prevalence rate of ever having asthma was 21% with the lowest (14.6%) in white girls and the highest (27.4%) in black boys. None of the census-block characteristics were significant in predicting ever having asthma. The significant predictors for childhood asthma were age, race, sex, and body mass index. Boys who were overweight had 3.1 times higher odds and girls who were overweight had 1.8 times higher odds of having asthma than girls who were normal weight. There was a stronger association between asthma and being overweight in female subjects than in male subjects. Black children had 1.3-fold higher odds of ever having asthma than white children. The highest likelihood of having asthma is among boys who were young, black, and overweight and the lowest among girls who were older, white, and normal weight. CONCLUSION: Increased efforts at prevention, screening, and treatment may need to be directed at certain subpopulations such as children living in socially and physically at-risk families and neighborhoods.

Salam M.T. et al. *Early-life environmental risk factors for asthma: findings from the Children's Health Study.* Environ Health Perspect. 2004; 112(6) : 760-5.p **Abstract:** Early-life experiences and environmental exposures have been associated with childhood asthma. To investigate further whether the timing of such experiences and exposures is associated with the occurrence of asthma by 5 years of age, we conducted a prevalence case-control study nested within the Children's Health Study, a population-based study of > 4,000 school-aged children in 12 southern California communities. Cases were defined as physician-diagnosed asthma by age 5, and controls were asthma-free at study entry, frequency-matched on age, sex, and community of residence and counter-matched on in utero exposure to maternal smoking. Telephone interviews were conducted with mothers to collect additional exposure and asthma histories. Conditional logistic regression models were fitted to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Asthma diagnosis before 5 years of age was associated with exposures in the first year of life to wood or oil smoke, soot, or exhaust (OR = 1.74; 95% CI, 1.02-2.96), cockroaches (OR = 2.03; 95% CI, 1.03-4.02), herbicides (OR = 4.58; 95% CI, 1.36-15.43), pesticides (OR = 2.39; 95% CI, 1.17-4.89), and farm crops, farm dust, or farm animals (OR = 1.88; 95% CI, 1.07-3.28). The ORs for herbicide, pesticide, farm animal, and crops were largest among children with early-onset persistent asthma. The risk

of asthma decreased with an increasing number of siblings (ptrend = 0.01). Day care attendance within the first 4 months of life was positively associated with early-onset transient wheezing (OR = 2.42; 95% CI, 1.28-4.59). In conclusion, environmental exposures during the first year of life are associated with childhood asthma risk.

Salameh P.R. et al. *Respiratory symptoms in children and exposure to pesticides.* Eur Respir J. 2003; 22(3) : 507-12.p **Abstract:** In Lebanon, childhood asthma is an important disease and pesticides are commonly used. The objective of this study was to evaluate whether exposure to pesticides has chronic effects on the respiratory health of Lebanese children. A cross-sectional study was performed on children from a randomly selected sample of Lebanese public schools. Exposure to pesticides was evaluated by a standardised questionnaire and a residential exposure score, and respiratory symptoms were assessed by using the American Thoracic Society standardised questionnaire. A chronic respiratory disease was reported in 407 (12.4%) out of 3,291 children. The baseline difference in mean age was small but statistically significant. Any exposure to pesticides, including residential, para-occupational and domestic, was associated with respiratory disease and chronic respiratory symptoms (chronic phlegm, chronic wheezing, ever wheezing), except for chronic cough. Exposure to pesticides was associated with chronic respiratory symptoms and disease among Lebanese children.

Salamzadeh J. et al. *The relationship between the quality of prescribing and practice appointment rates with asthma management data in those admitted to hospital due to an acute exacerbation.* Respir Med. 2005; 99(6) : 735-41.p **Abstract:** Specific targeting of patients with a previous asthma hospitalisation could be more focused if predictors could be identified. This study was an observational retrospective analysis using ridge and linear multivariate regression analysis. Patient asthma management data were extracted from the hospital and general practice notes of those that had been admitted with an acute exacerbation of their asthma over a 5-year period. From the prescribing data, the annual doses of preventer (P) and reliever (R) medication were converted to defined daily doses then divided to give a P:R ratio. Preliminary statistical analysis was used to identify any association between either the P:R ratio or for the number of general practitioner (GP) practice appointments (PA) and their asthma management data. Multivariate regression analysis was applied to the P:R ratio and to PA to determine a model between each of these and asthma management data/events. GPs gave consent to access the data of 115 (out of 440) asthmatics, age >5 years, admitted to a district general hospital for asthma exacerbations between 1994 and 1998. The multivariate analysis revealed that PA was associated with oral prednisolone rescue courses (PRCs) and age whilst the P:R ratio was associated to PRCs and more reliever usage but not preventers. Patients with low preventer usage with respect to their reliever medication should be targeted for medication review as these were the patients prescribed more prednisolone courses and their increased PAs reflect this. This could decrease visits to the doctor and acute exacerbations.

Salari K. et al. *Genetic admixture and asthma-related phenotypes in Mexican American and Puerto Rican asthmatics.* Genet Epidemiol. 2005; 29(1) : 76-86.p **Abstract:** Genetic association studies in admixed populations may be biased if individual ancestry varies within the population and the phenotype of interest is associated with ancestry. However, recently admixed populations also offer potential benefits in association studies since markers informative for ancestry may be in linkage disequilibrium across large distances. In particular, the enhanced LD in admixed populations may be used to identify alleles that underlie a genetically determined difference in a phenotype between two ancestral populations. Asthma is known to have different prevalence and severity among ancestrally distinct populations. We investigated several asthma-related phenotypes in

two ancestrally admixed populations: Mexican Americans and Puerto Ricans. We used ancestry informative markers to estimate the individual ancestry of 181 Mexican American asthmatics and 181 Puerto Rican asthmatics and tested whether individual ancestry is associated with any of these phenotypes independently of known environmental factors. We found an association between higher European ancestry and more severe asthma as measured by both forced expiratory volume at 1 second ($r = -0.21$, $p = 0.005$) and by a clinical assessment of severity among Mexican Americans (OR: 1.55; 95% CI 1.25 to 1.93). We found no significant associations between ancestry and severity or drug responsiveness among Puerto Ricans. These results suggest that asthma severity may be influenced by genetic factors differentiating Europeans and Native Americans in Mexican Americans, although differing results for Puerto Ricans require further investigation.

Samet J.M. et al. *Commentary: nitrogen dioxide and asthma redux.* Int J Epidemiol. 2004; 33(1) : 215-6.p

Sanchez-Borges M. et al. *Tolerance of nonsteroidal anti-inflammatory drug-sensitive patients to the highly specific cyclooxygenase 2 inhibitors rofecoxib and valdecoxib.* Ann Allergy Asthma Immunol. 2005; 94(1) : 34-8.p **Abstract:** BACKGROUND: Selective inhibitors of cyclooxygenase 2 (COX-2) are generally tolerated by patients sensitive to nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit COX-1. Valdecoxib is a new sulfonamide-containing COX-2-specific inhibitor indicated for the treatment of acute pain, osteoarthritis, and rheumatoid arthritis. OBJECTIVE: To compare the clinical tolerance to rofecoxib and valdecoxib in patients who previously developed urticaria and angioedema while taking classic NSAIDs. METHODS: Patients with challenge-proven NSAID cutaneous sensitivity were submitted to single-blinded controlled oral challenges with rofecoxib, 50 mg, and valdecoxib, 40 mg. RESULTS: Twenty-eight patients (19 females and 9 males; mean +/- SD age, 28.6 +/- 15.0 years; age range, 10-61 years) participated in this study. Twenty-two (85%) of 26 patients who underwent skin tests were atopic, as demonstrated by a clinical history of rhinitis and/or asthma plus positive immediate-type skin hypersensitivity test results. A previous exclusive cutaneous reaction pattern (urticaria and/or angioedema) had occurred in 10 patients (36%), whereas a mixed pattern of skin and respiratory symptoms had occurred in 18 patients (64%). Twenty patients (71%) were multiple reactors, and 8 patients (28%) were single reactors. In this current study, 2 patients (7%) taking rofecoxib experienced angioedema, and 1 patient (4%) taking valdecoxib experienced urticaria. CONCLUSIONS: Rofecoxib and valdecoxib can be safely used by most NSAID-sensitive patients with cutaneous reactions. Our findings suggest that isolated cross-reactions may occur in these patients, and for this reason, controlled oral provocation may be prudent when prescribing valdecoxib or rofecoxib for patients who have previously had urticaria or angioedema triggered by NSAIDs.

Sander N. *Making the grade with asthma, allergies, and anaphylaxis.* Pediatr Nurs. 2002; 28(6) : 593-5, 598.p **Abstract:** For some students with asthma, allergies, or anaphylaxis, school attendance can be risky. School administrators and educators are ill prepared to address medical challenges of students with chronic illness. Yet, the number of school nurses employed in the United States and the nurse-student ratio is uncertain. An unknown number of schools restrict children's rights to carry prescribed lifesaving medications while at or traveling to and from school or on field trips. Additionally, school indoor air quality is often poor and adversely affects students' health. Nurses are natural educators and advocates. Both of these roles are instrumental in empowering families to ensure the health of their children with asthma and allergies while in school.

Sandford A. et al. *Homing in on the asthma gene.* Lancet. 2002; 360(9331) : 422-3.p

Sandford A.J. et al. *Candidate genetic polymorphisms for asthma in Chinese schoolchildren from Hong Kong.* Int J Tuberc Lung Dis. 2004; 8(5) : 519-27.p **Abstract:** BACKGROUND: Polymorphisms in several genes have been associated with asthma, atopy and bronchial hyperresponsiveness in white and Japanese populations. In this study we tested for associations of 11 polymorphisms with wheeze and asthma in 10-year-old Chinese schoolchildren. METHODS: The subjects were 107 children who had wheeze in the last 12 months and 118 without wheeze in the last 12 months. They were randomly selected from 3110 children who took part in Phase II of the International Study of Asthma and Allergies in Childhood. These schoolchildren underwent questionnaire, spirometry and methacholine challenge testing. RESULTS: The A allele of the tumor necrosis factor-alpha (TNFA) G-308A polymorphism was significantly associated with wheeze in the last 12 months (odds ratio [OR] 2.1, P = 0.04) and current asthma (OR 2.6, P = 0.006). When stratified by gender, these associations were only seen in the female study participants. In girls, the OR for the TNFA-308A allele and wheeze in the last 12 months was 3.6 (P = 0.01) and for current asthma it was 6.0 (P = 0.0006). CONCLUSION: The A allele of the TNFA G-308A polymorphism was a risk factor for asthma-related phenotypes in girls but not boys.

Sandin A. et al. *Development of atopy and wheezing symptoms in relation to heredity and early pet keeping in a Swedish birth cohort.* Pediatr Allergy Immunol. 2004; 15(4) : 316-22.p **Abstract:** The role of pet keeping during infancy for the development of allergy and asthma is still controversial. The objective of this population-based birth cohort study was to assess the development of atopy and different wheezing phenotypes during the first 4 yr of life in relation to heredity and early pet keeping. The cohort comprised all 1228 infants living in a Swedish county who were born over a 1-yr period. The parents replied to repeated questionnaires and 817 of the children were skin prick tested both at 1 and 4 yr. Cat keeping during the first year of life was associated with an increased risk of a positive skin prick test to cat at 1 yr of age [odds ratio (OR) 2.2, 95% confidence interval (CI) 0.9-5.6], but neither with sensitivity nor clinical symptoms of allergy at 4 yr. Dog keeping during the first year of life was associated with an increased risk of early-onset transient wheezing, but only in children with parental asthma (adjusted OR 4.3, 95% CI 1.5-12.1). In contrast, early dog keeping had an inverse association with sensitivity to pollen allergen at 4 yr (adjusted OR 0.3, 95% CI 0.1-0.9) and late-onset wheezing (adjusted OR 0.4, 95% CI 0.2-1.0). Thus, pet keeping during the first year of life was not associated with an increased risk of atopy at 4 yr, although a positive SPT to cat was more common at 1 yr. Our findings may even suggest that dog keeping during the first year of life might provide some protection from pollen allergy and late-onset wheezing and increase the risk of early-onset transient wheezing in children with heredity for asthma.

Santic Z. et al. *The relationships between the asthma and weather.* Med Arh. 2002; 56(3) : 155-7.p **Abstract:** In this study there has been investigated the effect of climatic factors on the occurrence of the bronchial asthma. The study was performed among 129 patients aged 5-67 years in the region of west Herzegovina (Bosnia and Herzegovina) with mild climate. The attacks of the asthma were checked on each individual patient by questionnaire as well as by reporting at polyclinical's investigation in several centres according to the months (year when attack polyclinic occur). From meteorological services there were obtained the monthly values of temperature, relative humidity of air and the number of hours of sunshine per month. The highest number of the asthmatic attacks were during the period from XI-I month of highest humidity and the lowest temperature. In this period individuals over 35 years were ill more frequently while younger than 34 have more asthmatic attacks during the period III-V months. The coefficient of multiple

correlation R express connection among the asthmatic attacks with each meteorological factors. The coefficient was high R = 0.494 which means that in 90% of cases of the attacks of the asthma bronchial the climatic factors have also participated.

Santos M.C. et al. *A brief questionnaire for screening asthma among children and adolescents in Rio de Janeiro, Brazil.* Allergol Immunopathol (Madr). 2005; 33(1) : 20-6.p **Abstract:** BACKGROUND: Asthma is the most common chronic disease in childhood with recognition and detection still unsatisfactory. Questionnaires focusing on reported symptoms are a very promising and useful tool. OBJECTIVE: To determine the diagnostic accuracy of a basic questionnaire (BQ) as a screening test for asthma in children and adolescents who sought medical assistance in a pediatric hospital in Duque de Caxias County, Rio de Janeiro State, Brazil. METHODS AND RESULTS: A cross-sectional, observational, prospective study was carried out. A BQ with four questions was used to screen for asthma. The gold standard for a diagnosis of asthma was a minimum increase of 12 % in the first second of forced expiratory volume after a bronchodilatation test. Two hundred eleven patients, aged 5 to 15 years, who presented to the emergency department for various reasons were evaluated. The prevalence of asthma was 22 %. In 67 % of the families the annual income was less than USD 3600 and 60 % of support providers were illiterate or had less than 4 years of education. The test showed better performance when the answer to question 1 was considered separately: sensitivity = 74.50 % (95 % CI: 60.50-84.70), specificity = 64 % (95 % CI: 56.40-71.10), positive likelihood ratio = 2.07 (95 % CI: 1.59-2.70), positive predictive value = 37.20 % (95 % CI: 28.10-47.30), negative predictive value = 89.70 % (95 % CI: 82.90-94) and accuracy = 66.40 % (95 % CI: 55.80-78.30). CONCLUSIONS: The BQ has high sensitivity and negative predictive values. It is easy to use and implement and is convenient for both the doctor and patient. It is useful for excluding a diagnosis of asthma in populations with a high or low prevalence of this disease, so long as there has been no wheezing in the previous 12 months.

Santuz P. et al. *Transient phrenic nerve paralysis associated with status asthmaticus.* Pediatr Pulmonol. 2004; 38(3) : 269-71.p **Abstract:** Phrenic nerve paralysis is a condition typically occurring after invasive procedures in the chest and neck. Here we describe a case of transient unilateral diaphragmatic paralysis in a child with status asthmaticus complicated by complete right lung atelectasis. Common causes of this disorder and possible implications for our case are discussed.

Sapien R.E. et al. *Teaching school teachers to recognize respiratory distress in asthmatic children.* J Asthma. 2004; 41(7) : 739-43.p **Abstract:** OBJECTIVE: To demonstrate that school teachers can be taught to recognize respiratory distress in asthmatic children. METHODOLOGY: Forty-five school teachers received a one-hour educational session on childhood asthma. Each education session consisted of two portions, video footage of asthmatic children exhibiting respiratory distress and didactic. Pre- and posttests on general asthma knowledge, signs of respiratory distress on video footage and comfort level with asthma knowledge and medications were administered. RESULTS: General asthma knowledge median scores increased significantly, pre = 60% correct, post = 70% (p < 0.0001). The ability to visually recognize respiratory distress also significantly improved (pre-median = 66.7% correct, post = 88.9% [p < 0.0001]). Teachers' comfort level with asthma knowledge and medications improved. CONCLUSIONS: Using video footage, school teachers can be taught to visually recognize respiratory distress in asthmatic children. Improvement in visual recognition of respiratory distress was greater than improvement in didactic asthma information.

- Saraiva-Romanholo B.M. et al.** *Comparison of three methods for differential cell count in induced sputum.* Chest. 2003; 124(3) : 1060-6.p **Abstract:** BACKGROUND: Induced sputum (IS) using the cytopsin technique has been extensively employed to characterize inflammatory airway diseases; however, procedures of cell enrichment based on cytopsin increase the analytical costs and require slide processing within a short period of time after sampling. STUDY OBJECTIVES: To compare three different techniques for cytologic analysis of IS, and to determine the time required by each method and the costs involved. DESIGN: Cross-sectional study. SETTING: Tertiary-care university hospital. PATIENTS AND MEASUREMENTS: Eighty-nine patients with asthma and 11 subjects without asthma were submitted to increasing hypertonic saline solution concentrations of 2, 3, 4, and 5% for 7 min for sputum induction. Samples were smeared without treatment with 0.1% dithiothreitol (DTT) [technique A], after treatment with DTT (technique B), and after treatment with DTT and cytopsin (technique C). All slides were air-dried and stained with Leishman stain. Two independent observers counted at least 200 inflammatory cells on each slide. RESULTS: Eighty percent of the slides processed by techniques A and B and 65% of the slides processed by technique C represented sputum samples of acceptable quality. The eosinophil percentages in sputum obtained by techniques A and C were closely correlated, as also were those obtained by techniques B and C ($r = 0.64$ and $r = 0.63$, respectively; $p < 0.01$). There was a positive correlation for eosinophils when we compared techniques A and B ($r = 0.57$, $p < 0.01$). The neutrophil correlation was significant when the three techniques were compared (technique A vs technique B, $r = 0.66$; technique A vs technique C, $r = 0.51$; and technique B vs technique C, $r = 0.57$; $p < 0.01$). Bland-Altman analysis showed a good agreement for eosinophil and neutrophil counts when techniques A and B were compared to technique C. CONCLUSIONS: The three techniques are good indicators of lung inflammation. Techniques A and B are less time consuming and are of lower cost.
- Savilahti E. et al.** *Mothers of very low birth weight infants have less atopy than mothers of full-term infants.* Clin Exp Allergy. 2004; 34(12) : 1851-4.p **Abstract:** BACKGROUND: Studies on the pregnancy outcome of asthmatic mothers have suggested an increased rate of preterm deliveries. In contrast, our earlier study suggests that mothers of very low birth weight (VLBW) (<1500 g) infants less frequently had atopy than did mothers of full-term infants. METHODS: We inquired about symptoms of atopy and doctor-diagnosed atopy in parents of 370 infants of VLBW (<1500 g) and 544 parents of full-term infants. Odds ratios for atopic symptoms and diagnosed atopy were calculated, and groups were compared with a trend test. RESULTS: Mothers of preterm infants of birth weight (BW) <1000 g significantly less often had physician-diagnosed allergic rhinitis (AR) ($P=0.02$). Among all the mothers, a trend test showed that maternal AR was significantly ($P=0.03$) higher in parallel with a higher infant BW. Fathers of infants with different BWs showed no differences in prevalence of atopic symptoms. CONCLUSION: We thus infer that maternal balance between T-helper type 1 (Th1) and Th2 cells, shifted towards Th2 in those with AR, may have a favourable effect on maintenance of pregnancy before gestational week 30.
- Sawyer M.G. et al.** *A two-year prospective study of the health-related quality of life of children with chronic illness--the parents' perspective.* Qual Life Res. 2005; 14(2) : 395-405.p **Abstract:** The aim of this study was to assess prospectively changes in the health-related quality of life (HRQL) of children and adolescents with diabetes, asthma or cystic fibrosis (CF). One hundred and twenty-two parents of children aged 10-16 years with asthma, diabetes, or CF were recruited from specialist paediatric clinics. Parents described their children's HRQL using the Child Health Questionnaire (PF98) at baseline, 6, 12, 18 and 24 months post-baseline. They reported that the general health of children with CF was significantly worse than that of children with asthma and diabetes at baseline. In other domains there were few differences between the HRQL of children in the three groups. In several domains, the HRQL of children with asthma or diabetes improved over the 2 years of the study. This improvement was less evident for children with CF.
- Sawyer S.M. et al.** *Sticky issue of adherence.* J Paediatr Child Health. 2003; 39(1) : 2-5.p **Abstract:** The phenomenon of adherence, also known as compliance, is the vital link that allows effective medications to have the desired clinical effect when self-administered. It is often assumed that the population is generally adherent, but more than 50% of people with chronic illness do not take their medication as prescribed. We highlight how the terminology and language of non-adherence act to conceptualize adherence as a patient problem in a manner that is inadvertently judgmental, narrowly focused and clinically unhelpful. In contrast, knowledge of the dynamic nature of adherence promotes the conceptualization of adherence as the common problem that it is, where the responsibility for improving it lies primarily with the health professional. The example of asthma is used to highlight how individually focused clinical strategies can fit within a population perspective that, in its entirety, can be conceptualized as a framework of adherence-promoting strategies.
- Sawyer S.M. et al.** *Bridging the gap between doctors' and patients' expectations of asthma management.* J Asthma. 2003; 40(2) : 131-8.p **Abstract:** OBJECTIVES: To assess the prevalence of asthma symptoms, their impact on daily activities, and perceptions of disease severity among people with asthma. METHODS: A telephone survey of 699 people with asthma was conducted in 1999 in metropolitan and nonmetropolitan New South Wales, Victoria, and Queensland, Australia. RESULTS: Forty-two percent of adults and 26% of children reported experiencing asthma symptoms at least every 2-3 days. Thirty-seven percent of adults and 26% of children reported using a reliever more than four times in the previous week. Of those for whom preventer therapy had been prescribed (61% of respondents), 30% of children and 45% of adults did not use their preventer as instructed. A high proportion of respondents reported avoiding physical and social activities because of their asthma, while 75% said asthma generally made them feel tired. Many respondents attributed frustration (61%), irritability (57%), fear (38%), and worry (43%) to their asthma. Only 50% of respondents had been reviewed by a general practitioner for asthma in the past year. Respondents generally underestimated the severity of their asthma, compared with symptom frequencies reported. CONCLUSIONS: The Living with Asthma Survey suggests that national asthma management goals are not being achieved in a high proportion of patients, with evidence for both underprescribing and underusage of preventer medication. Achieving closer alignment between medical and patient perspectives is an important goal of asthma education and management in order to help bridge the gap between current concepts of best practice and the reality of persistently poor asthma outcomes.
- Saxena S. et al.** *Socioeconomic and ethnic group differences in self reported health status and use of health services by children and young people in England: cross sectional study.* BMJ. 2002; 325(7363) : 520.p **Abstract:** OBJECTIVES: To examine whether self reported health status and use of health services varies in children of different social class and ethnic group. DESIGN: Cross sectional study from the 1999 health survey for England. SUBJECTS: 6648 children and young adults aged 2-20 years. SETTING: Private households in England. MAIN OUTCOME MEASURES: Proportion of children (or their parents) reporting episodes of acute illness in the preceding fortnight and prevalence of self reported longstanding illness. Proportion reporting specific illnesses. Proportion reporting that they had consulted a general practitioner in the preceding fortnight, attended hospital outpatient departments in the three preceding months, or been admitted to

hospital in the preceding year. **RESULTS:** Large socioeconomic differences were observed between ethnic subgroups; a higher proportion of Afro-Caribbean, Indian, Pakistani, and Bangladeshi children belonged to lower social classes than the general population. The proportion of children and young adults reporting acute illnesses in the preceding two weeks was lower in Bangladeshi and Chinese subgroups (odds ratio 0.41, 95% confidence interval 0.27 to 0.61 and 0.46, 0.28 to 0.77, respectively) than in the general population. Longstanding illnesses was less common in Bangladeshi and Pakistani children (0.52, 0.40 to 0.67 and 0.57, 0.46 to 0.70) than in the general population. Irish and Afro-Caribbean children reported the highest prevalence of asthma (19.5% and 17.7%) and Bangladeshi children the lowest (8.2%). A higher proportion of Afro-Caribbean children reported major injuries than the general population (11.0% v 10.0%), and children from all Asian subgroups reported fewer major and minor injuries than the general population. Indian and Pakistani children were more likely to have consulted their general practitioner in the preceding fortnight than the general population (1.86, 1.35 to 2.57 and 1.51, 1.13 to 2.01, respectively). Indian, Pakistani, Bangladeshi, and Chinese children were less likely to have attended outpatient departments in the preceding three months. No significant differences were found between ethnic groups in the admission of inpatients to hospitals. Acute and chronic illness were the best predictors of children's use of health services. Social classes did not differ in self reported prevalence of treated infections, major injuries, or minor injuries, and no socioeconomic differences were seen in the use of primary and secondary healthcare services. **CONCLUSIONS:** Children's use of health services reflected health status rather than ethnic group or socioeconomic status, implying that equity of access has been partly achieved, although reasons why children from ethnic minority groups are able to access primary care but receive less secondary care need to be investigated.

Sayers I. et al. *Allelic association and functional studies of promoter polymorphism in the leukotriene C4 synthase gene (LTC4S) in asthma.* Thorax. 2003; 58(5) : 417-24.p **Abstract:** **BACKGROUND:** LTC4 synthase is essential for the production of cysteinyl leukotrienes (Cys-LT), critical mediators in asthma. We have identified a novel promoter polymorphism at position -1072 (G/A) and a -444 (A/C) polymorphism has previously been reported. The role of these polymorphisms in the genetic susceptibility to asthma was examined. **METHODS:** To test for genetic association with asthma phenotypes, 341 white families (two asthmatic siblings) and 184 non-asthmatic control subjects were genotyped. Genetic association was assessed using case control and transmission disequilibrium test (TDT) analyses. LTC4S promoter luciferase constructs and transiently transfected human HeLa and KU812F cells were generated to determine the functional role of these polymorphisms on basal transcription. **RESULTS:** No associations were observed in case control analyses (-1072 A, $q=0.09$; -444 C, $q=0.29$); the TDT identified a borderline association between the -444 C allele and bronchial responsiveness to methacholine ($p=0.065$). Asthmatic children with the -444 C allele had a lower mean basal forced expiratory volume in 1 second (97.4 v 92.7% predicted, $p=0.005$). LTC4S promoter luciferase analyses provided no evidence for a functional role of either polymorphism in determining basal transcription. **CONCLUSION:** This study does not support a role for these polymorphisms in genetic susceptibility to asthma but provides evidence to suggest a role in determining lung function parameters.

Sayers I. et al. *Promoter polymorphism in the 5-lipoxygenase (ALOX5) and 5-lipoxygenase-activating protein (ALOX5AP) genes and asthma susceptibility in a Caucasian population.* Clin Exp Allergy. 2003; 33(8) : 1103-10.p **Abstract:** **BACKGROUND:** 5-Lipoxygenase (5-LO) and 5-lipoxygenase-activating protein (FLAP) are essential for cysteinyl-leukotriene (cys-LT) production, critical mediators in asthma. **OBJECTIVE:** We sought to identify novel promoter polymorphisms within the FLAP (ALOX5AP) gene promoter and

test the role of these and the previously identified 5-LO (ALOX5) Sp1 promoter polymorphism in asthma susceptibility. **METHODS:** To assess genetic association with asthma phenotypes, we genotyped 341 Caucasian families (containing two asthmatic siblings) and non-asthmatic control subjects ($n=184$). Genetic association was determined by case-control and transmission disequilibrium test (TDT) analyses. To determine the functional role of polymorphisms on basal transcription, we generated ALOX5AP-promoter-luciferase constructs and transiently transfected human HeLa cells. **RESULTS:** A novel G/A substitution at -336 bp and a poly(A) repeat ($n=19$ or 23) at position -169 to -146 bp were identified in the ALOX5AP promoter. Genotyping found the -336 A and poly(A19) alleles at frequencies of $q=0.06$ and 0.12, respectively. No ALOX5AP allele was associated with asthma or asthma-related phenotypes in case-control or TDT analyses. ALOX5AP-promoter-luciferase analyses did not support a functional role of the -336 or poly(A) polymorphism in determining basal transcription. The ALOX5 Sp1 polymorphism was predominantly homozygous wild-type 5/5 (frequency $q=0.70$) and heterozygous 4/5 ($q=0.23$) genotypes and no allele was associated with asthma or asthma-related phenotypes. **CONCLUSION:** Taken together, these data do not support a significant role for these polymorphisms in genetic susceptibility to asthma in the Caucasian population.

Scadding G.K. *Recent advances in the treatment of rhinitis and rhinosinusitis.* Int J Pediatr Otorhinolaryngol. 2003; 67 Suppl 1 : S201-4.p **Abstract:** Current rhinitis treatment is unsatisfactory for many patients, possibly because monotherapy is employed, without regard to the major presenting symptom. Recognition of the impact of rhinitis on quality of life and on associated disorders such as asthma has led to the development of guidelines, use of which has been shown to improve symptom control and quality of life compared to unguided therapy. The role of antihistamines, topical corticosteroids and anti-leukotrienes is discussed.

Scafaro P. et al. *Salbutamol prevents the increase of respiratory resistance caused by tracheal intubation during sevoflurane anesthesia in asthmatic children.* Anesth Analg. 2001; 93(4) : 898-902.p **Abstract:** Asthmatic children having their tracheas intubated with sevoflurane often have an increase in respiratory system resistance (Rrs). In this randomized, placebo-controlled, double-blinded study, we investigated the protective effect of an inhaled beta2-adrenergic agonist. Either salbutamol or placebo was administered 30 to 60 min before anesthesia to 30 mildly to moderately asthmatic children scheduled for elective surgery. Induction was performed with sevoflurane in a mixture of 50% nitrous oxide in oxygen and maintained at 3%, with children breathing spontaneously via a face mask and Jackson-Rees modification of the T-piece. Airway opening pressure and flow were measured before and after insertion of an oral endotracheal tube. Rrs and respiratory system compliance were calculated with multilinear regression analysis. The groups were comparable with respect to age, weight, asthma history, and breathing pattern. Intubation induced a different Rrs response in the two groups: children treated with salbutamol showed a 6.0% (-25.2% to +13.2%) decrease (mean, 95% confidence interval), whereas in the Placebo group there was a 17.7% (+4.4% to +30.9%) increase ($P = 0.04$). Neither asthma history nor the serum inflammation marker eosinophilic cationic protein was predictive for this response. We conclude that when using sevoflurane in mildly to moderately asthmatic children, a preanesthetic treatment with inhaled salbutamol is protective of an increase in Rrs. **IMPLICATIONS:** Tracheal intubation with sevoflurane as the sole anesthetic is now often performed in children. It can induce an increase in respiratory system resistance in children with asthma. This study shows that in children with mild to moderate asthma, a preanesthetic treatment with inhaled salbutamol can prevent the increase of respiratory system resistance.

Scanlon D.M. *Throat clearing in asthma.* N Engl J Med. 2003; 349(2) : 194-5; author reply 194-5.p

Scarfone R.J. et al. *Emergency physicians' prescribing of asthma controller medications.* Pediatrics. 2006; 117(3) : 821-7.p **Abstract:** **OBJECTIVES:** To determine the frequency with which emergency department (ED) physicians prescribe long-term controller medications (LTCMs) for children with asthma, to assess ED physicians' awareness of and level of agreement with national guidelines for LTCM use, and to identify criteria ED physicians use to prescribe LTCMs and barriers to the use of LTCMs. **METHODS:** A survey of all physician members of the American Academy of Pediatrics Section on Emergency Medicine who provide care for children in an ED was performed. **RESULTS:** Surveys were returned by 391 (50%) of 782 physicians. The majority (80%) indicated that fewer than one half of children with persistent asthma were using LTCMs on ED arrival. Although 99% believe that children with persistent asthma should be treated with LTCMs, <20% provide LTCMs for the majority of such children at ED discharge. For 49%, the main reason for not prescribing these medications was the belief that this was the role of the primary care provider or asthma specialist. Practice setting, prior training, and annual patient volume were not associated significantly with prescribing LTCM. Patient's age and likelihood of compliance and physician's belief in efficacy and concerns about adverse effects were not important criteria in the decision to begin LTCM. **CONCLUSIONS:** ED physicians often encounter children with persistent asthma who are not receiving LTCMs, they believe in the efficacy and safety of LTCMs, and they think that children with persistent disease should be treated with LTCMs, but they prescribe LTCMs infrequently.

Schachter L.M. et al. *Asthma and atopy in overweight children.* Thorax. 2003; 58(12) : 1031-5.p **Abstract:** **BACKGROUND:** Obesity may be associated with an increase in asthma and atopy in children. If so, the effect could be due to an effect of obesity on lung volume and thus airway hyperresponsiveness. **METHODS:** Data from 5993 caucasian children aged 7-12 years from seven epidemiological studies performed in NSW were analysed. Subjects were included if data were available for height, weight, age, skin prick test results to a common panel of aeroallergens, and a measure of airway responsiveness. History of doctor diagnosed asthma, wheeze, cough, and medication use was obtained by questionnaire. Recent asthma was defined as a doctor diagnosis of asthma ever and wheeze in the last 12 months. Body mass index (BMI) percentiles, divided into quintiles per year age, were used as a measure of standardised weight. Dose response ratio (DRR) was used as a measure of airway responsiveness. Airway hyperresponsiveness was defined as a DRR of ≥ 8.1 . Adjusted odds ratios were obtained by logistic regression. **RESULTS:** After adjusting for atopy, sex, age, smoking and family history, BMI was a significant risk factor for wheeze ever (OR = 1.06, $p = 0.007$) and cough (OR = 1.08, $p = 0.001$), but not for recent asthma (OR = 1.02, $p = 0.43$) or airway hyperresponsiveness (OR = 0.97 $p = 0.17$). In girls a higher BMI was significantly associated with higher prevalence of atopy (χ^2 trend 7.9, $p = 0.005$), wheeze ever (χ^2 trend 10.4, $p = 0.001$), and cough (χ^2 trend 12.3, $p < 0.001$). These were not significant in boys. **CONCLUSIONS:** Higher BMI is a risk factor for atopy, wheeze ever, and cough in girls only. Higher BMI is not a risk factor for asthma or airway hyperresponsiveness in either boys or girls.

Schatz M. et al. *Sex differences in the presentation and course of asthma hospitalizations.* Chest. 2006; 129(1) : 50-5.p **Abstract:** **OBJECTIVE:** To distinguish between differences in prevalence, asthma severity, and treatment to explain sex-related differences in hospitalized asthma patients. **DESIGN:** Medical record review. **SETTING:** Thirty US hospitals as part of the University HealthSystem Consortium Asthma Clinical Benchmarking Project. **PATIENTS:** A random sample of patients aged 2 to 54 years and admitted to the hospital for acute asthma from 1999 to 2000.

MEASUREMENTS: Demographics, medical history, initial oxygen saturation, initial peak expiratory flow (adults), initial pulmonary index (children), emergency department course, length of hospital stay, and discharge plans. **RESULTS:** The cohort included 606 pediatric (aged 2 to 17 years) and 680 adult (aged 18 to 54 years) inpatients. The sex ratio varied significantly by age: 40% were girls 2 to 17 years of age, and 68% were women 18 to 54 years of age $p < 0.001$. Among children, girls did not differ from boys according to asthma history, pulmonary index scores, or hospital length of stay. Among adults, women were more likely to have a primary care provider (90% vs 73%, $p < 0.001$) but did not differ according to asthma history or recent medication use. Women had a higher mean initial PEF compared to men (43% of predicted vs 36% of predicted, $p < 0.001$) and higher median initial oxygen saturation (95% vs 93%, $p = 0.002$) but did not differ by hospital length of stay. No sex differences in discharge regimens were identified in children or adults. **CONCLUSIONS:** Among US inpatients with acute asthma, male children are more common than female children, while women are more common in adults. The results in children are probably explained by prevalence differences, since no sex differences were seen in markers of asthma severity or treatment. In adults, increased symptoms in response to a given level of airway obstruction in women may contribute to the female predominance in asthma hospitalizations.

Schatz M. et al. *Sex differences among children 2-13 years of age presenting at the emergency department with acute asthma.* Pediatr Pulmonol. 2004; 37(6) : 523-9.p **Abstract:** Hospitalization rates for asthma have been reported to be higher in males than females in children under age 15, but it is not clear whether this disparity reflects gender differences in prevalence, severity, or treatment. We performed a prospective cohort study as part of the Emergency Medicine Network. Patients aged 2-13 years who presented to the emergency department (ED) with acute asthma underwent a structured interview in the ED and another by telephone 2 weeks later. Of 1,602 patients, 61% (95% CI, 59-64%) were boys. Girls were slightly older than boys, although no material differences existed in acute presentation, chronic asthma characteristics, ED treatment, or ED course. There was no difference in admission rates for boys or girls (20% vs. 22%; $P = 0.48$). This finding persisted when adjusting for other factors in a multivariate logistic regression model. No sex differences were observed for relapse or ongoing exacerbation on univariate or multivariate analysis. These data suggest that asthma is not inherently more severe in boys with asthma compared to girls, and that the increased rate of hospitalizations in boys under age 13 is due to differences in prevalence, not severity.

Schatz M. et al. *Risk factors for asthma hospitalizations in a managed care organization: development of a clinical prediction rule.* Am J Manag Care. 2003; 9(8) : 538-47.p **Abstract:** **OBJECTIVE:** To use a computerized administrative database to develop and validate a clinical prediction rule for the occurrence of asthma hospitalizations. **STUDY DESIGN:** Retrospective cohort. **METHODS:** Subjects included asthmatic patients ages 3 to 64 who were continuously enrolled in the Southern California Kaiser Permanent managed care organization in both 1998 and 1999. Data were based on linkage of a hospital discharge database, diagnosis and procedures database, membership database, and prescription database. The outcome was any 1999 hospitalization with a primary diagnosis of asthma. The outcome was evaluated and modeled separately for children (ages 3-17) and adults (ages 18-64). **RESULTS:** Univariate analyses showed that hospitalized children were younger than nonhospitalized children. Adults and children hospitalized in 1999 had lower mean household incomes, were more likely to have required an emergency department visit or hospitalization in 1998, used more beta-agonists and oral corticosteroids in 1998, and had more 1998 prescribers than nonhospitalized patients. In multivariable analysis, independent predictors of 1999 hospitalization in children included age and 1998

hospitalizations, beta-agonist dispensings, total anti-inflammatory dispensings, and number of prescribers. Among adults, 1998 hospitalizations and oral steroid dispensings as well as income were independent predictors of hospitalization in 1999. The prediction rules developed in this study identified the 11% to 13% of adults or children with an approximately 6-fold higher likelihood for being hospitalized in the following year. CONCLUSION: These models can be used to identify high-risk asthmatic patients in whom targeted intervention might reduce asthma morbidity and cost of care.

Schatz M. et al. *Inhaled corticosteroids and allergy specialty care reduce emergency hospital use for asthma.* J Allergy Clin Immunol. 2003; 111(3): 503-8.p **Abstract:** BACKGROUND: The interrelationships between optimal inhaled corticosteroid (IC) therapy, allergy specialist care, and reduced emergency hospital care for asthma have not been well defined. OBJECTIVE: We sought to evaluate the independent effectiveness of various levels of IC dispensing and allergy specialist care in reducing subsequent emergency asthma hospital use. METHODS: Asthmatic patients (n = 9608) aged 3 to 64 years were identified from an electronic database of a large health maintenance organization. The outcome was any year 2000 asthma hospitalization or emergency department visit. The main predictors were at least one allergy department visit and the number of IC canisters dispensed in 1999. Analyses were adjusted for age, sex, insurance type, and asthma severity (1999 emergency asthma hospital use, beta-agonist use, and oral corticosteroid use). RESULTS: Dispensing of 7 or more canisters of ICs (odds ratio [OR], 0.64; 95% CI, 0.43-0.94) and allergy care (OR, 0.73; 95% CI, 0.55-0.97) were associated with reduced subsequent emergency asthma hospital use. More patients with allergy specialist care than those without such care received 7 or more dispensations of ICs (24.7% vs 8.3%, P < .001). When 7 or more dispensations of ICs and allergy specialist care were simultaneously included in an adjusted model, both ICs (OR, 0.68; 95% CI, 0.46-1.00) and allergy care (OR, 0.77; 95% CI, 0.58-1.02) were independently associated with a lower risk of year 2000 emergency asthma hospital care, although significance was borderline. CONCLUSION: Allergy care reduces emergency hospital use for asthma by increasing use of ICs but probably also has an independent effect.

Schatz M. et al. *Asthma quality-of-care markers using administrative data.* Chest. 2005; 128(4): 1968-73.p **Abstract:** STUDY OBJECTIVE: To evaluate the relationship of potential asthma quality-of-care markers to subsequent emergency hospital care. DESIGN: Retrospective administrative database analysis. SETTING: Managed care organization. PATIENTS: Asthmatic patients aged 5 to 56 years of age. INTERVENTIONS: None. MEASUREMENTS AND RESULTS: Candidate quality measures included one or more or four or more controller medication canisters, a controller/total asthma medication ratio of > or = 0.3 or > or = 0.5, and the dispensing of fewer than six beta-agonist canisters in 2002. Outcome was a 2003 asthma emergency department visit or hospitalization. Multivariable analyses adjusted for age, sex, and year 2002 severity (based on utilization). In the total sample (n = 109,774), one or more controllers (odds ratio, 1.35) and four or more controllers (odds ratio, 1.98) were associated with an increased risk of emergency hospital care, whereas a controller/total asthma medication ratio of > or = 0.5 (odds ratio, 0.73) and the dispensing of fewer than six beta-agonist canisters (odds ratio 0.30) were associated with a decreased risk. After adjustment for baseline severity in the total asthma sample, the controller/total asthma medication ratio (odds ratio, 0.62 to 0.78) and beta-agonist measure (odds ratio, 0.42) were associated with decreased risk, whereas the dispensing of four or more canisters of controller medication was associated with increased risk (odds ratio, 1.33). After stratification by year 2002 beta-agonist use, all of the measures were associated with decreased risk in those who received fewer than six beta-agonist canisters, whereas all of the measures except the medication ratio of > or = 0.5 were associated with increased risk in the cohort who received six or more beta-agonist

canisters. CONCLUSION: Controller use and beta-agonist use may function as severity indicators in large populations rather than as asthma quality-of-care markers. A medication ratio of > or = 0.5 appeared to function as the best quality-of-care marker in this study.

Schatz M. et al. *Asthma population management: development and validation of a practical 3-level risk stratification scheme.* Am J Manag Care. 2004; 10(1): 25-32.p **Abstract:** OBJECTIVE: To define and validate a practical risk stratification scheme based on administrative data for use in identifying patients at high, medium, and low risk of requiring emergency hospital care for asthma. STUDY DESIGN: Retrospective cohort. PATIENTS AND METHODS: Predictors in 1999 were evaluated in relation to 2000 asthma emergency hospital care (any asthma hospitalization or emergency department visit) in a training set (n = 8789, 2000 emergency hospital care = 5.5%) and a testing set (n = 6104, 2000 emergency hospital care = 7.9%). Logistic regression was used to assign risk points in the training set, and positive and negative predictive values, sensitivities, and specificities were calculated in the training and testing sets. RESULTS: High risk was defined as asthma emergency hospital care in the previous year or use of >14 beta-agonist canisters and oral corticosteroid use; medium risk was defined as no emergency hospital care but use of either >14 beta-agonist canisters or oral corticosteroids; and low risk was defined as none of the above. For the high-risk groups in the training and testing sets, positive predictive values were 12.9% and 22.0%, sensitivities were 24.8% and 25.4%, specificities were 90.3% and 92.0%, and negative predictive values were 95.4% and 93.2%, respectively. The medium-risk groups identified another 32.6% of patients in the training set and 28.3% in the testing set requiring subsequent asthma emergency hospital care. CONCLUSION: This simple risk stratification scheme is useful for identifying patients from administrative data who are at increased risk of experiencing emergency hospital care for asthma.

Schatz M. et al. *Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists.* J Allergy Clin Immunol. 2006; 117(3): 549-56.p **Abstract:** BACKGROUND: The development of the Asthma Control Test (ACT), a short, simple, patient-based tool for identifying patients with poorly controlled asthma, was recently described in patients under the routine care of an asthma specialist. OBJECTIVES: We sought to evaluate the reliability and validity of the ACT in a longitudinal study of asthmatic patients new to the care of an asthma specialist. METHODS: Patients (n=313) completed the ACT and the Asthma Control Questionnaire (ACQ) at 2 physician visits (4-12 weeks apart). Pulmonary function was measured, and asthma specialists rated asthma control. RESULTS: Internal consistency reliability of the ACT was 0.85 (baseline) and 0.79 (follow-up). Test-retest reliability was 0.77. Criterion validity was demonstrated by significant correlations between baseline ACT scores and baseline specialists' ratings of asthma control (r=0.52, P<.001) and ACQ scores (r=-0.89, P<.001). Discriminant validity was demonstrated, with significant (P<.001) differences in mean ACT scores across patients differing in asthma control, pulmonary function, and treatment recommendation. Responsiveness of the ACT to changes in asthma control and lung function was demonstrated with significant correlations between changes in ACT scores and changes in specialists' ratings (r=0.44, P<.001), ACQ scores (r=-0.69, P<.001), and percent predicted FEV1 values (r=0.29, P<.001). An ACT score of 19 or less provided optimum balance of sensitivity (71%) and specificity (71%) for detecting uncontrolled asthma. CONCLUSIONS: The ACT is reliable, valid, and responsive to changes in asthma control over time in patients new to the care of asthma specialists. A cutoff score of 19 or less identifies patients with poorly controlled asthma. CLINICAL IMPLICATIONS: In a clinical setting the ACT should be a useful tool to help physicians identify patients with uncontrolled asthma and facilitate their ability to follow patients' progress with treatment.

- Schedel M. et al.** *A signal transducer and activator of transcription 6 haplotype influences the regulation of serum IgE levels.* J Allergy Clin Immunol. 2004; 114(5) : 1100-5.p **Abstract:** BACKGROUND: Because of its central role in the IL-4/IL-13 pathway, the intracellular signaling molecule signal transducer and activator of transcription 6 (STAT6) may be crucial for IgE production in asthma and allergy. OBJECTIVE: We analyzed the association between polymorphisms in the STAT6 gene and the regulation of serum IgE levels. Methods In a population of 1120 German schoolchildren (age 9-11 years), we genotyped 6 previously identified polymorphisms spanning the STAT6 gene by using the matrix-assisted laser desorption ionization-time of flight mass spectrometry method. Haplotypes were estimated and population-derived IgE percentiles (50% IgE > 60 IU/mL, 66% IgE > 115 IU/mL, and 90% IgE > 457 IU/mL) were modeled as outcome variables in haplotype-trend regression analysis. RESULTS: Polymorphisms located in intron 2 (C2892T) and the 3' untranslated region (T12888C) significantly and consistently contributed to elevated total serum IgE levels. One STAT6 haplotype showed increased odds ratios of 1.58 (95% CI, 1.08-2.32; P = .020), 1.82 (95% CI, 1.19-2.77; P = .006), and 3.92 (95% CI, 1.93-7.96; P = .0002) for elevated IgE levels at percentiles 50%, 66%, and 90%, respectively. Because C2892T is located within a nuclear factor kappaB transcription factor binding site, a functional role of this polymorphism is very likely. CONCLUSION: The data indicate that within the IL-4/IL-13 pathway, genetic variants in the STAT6 gene significantly contribute to the regulation of serum IgE levels.
- Scheinmann P. et al.** *Immunotherapy in young children.* Clin Allergy Immunol. 2004; 18 : 567-83.p
- Schenker M.B.** *Farming and asthma.* Occup Environ Med. 2005; 62(4) : 211-2.p
- Schirm E. et al.** *Anti-asthmatic drugs and dosage forms in children: a cross-sectional study.* Pharm World Sci. 2002; 24(4) : 162-5.p **Abstract:** OBJECTIVE: To describe the choice of drugs as well as the dosage forms of anti-asthmatic drugs in children with regard to different age groups. METHODS: Cross-sectional study based on computerized pharmacy dispensing records of 1999 for children aged 0-16 years in the north of the Netherlands. All children were selected and divided in the following age groups: 0-1, 2-5, 6-11 and 12-16-year-olds. RESULTS: Inhaled beta 2-agonists and inhaled corticosteroids were the most widely used anti-asthmatic drugs in all age groups (respectively 59 and 58 users per 100 anti-asthmatic using 0-16 year-olds). Cromones were rarely used. Up to four years of age the use of treatment with aerosol inhalers increased simultaneously with a decrease of oral dosage forms. The use of dry powder inhalers started at the age of approximately 4 years old and increased to about 85% of the users at the age of 11, with the strongest increase around the age of 6 and 7. CONCLUSION: The choice of drugs and dosage forms corresponds with what might be expected based on guidelines for the treatment of asthma in children, except for the high use of deproprine in the youngest age group. Anti-asthmatic drugs for preventive treatment are used so frequently without beta 2-agonists that questions about possible overtreatment need to be raised.
- Schmeling H. et al.** *Pulmonary function in children with juvenile idiopathic arthritis and effects of methotrexate therapy.* Z Rheumatol. 2002; 61(2) : 168-72.p **Abstract:** OBJECTIVE: To evaluate impairment of lung function as an adverse effect associated with methotrexate therapy in patients with juvenile idiopathic arthritis (JIA). METHODS: We performed pulmonary function testing including diffusion capacity for carbon monoxide as measured by the single breath method (DLCO-SB) in 89 children with juvenile idiopathic arthritis. Forty (45%) were treated with methotrexate for a median of 24 months (range 3 to 120 months). Except for the presence of asthma in two children, there was no clinical or radiological evidence of pulmonary disease. RESULTS: Pulmonary function testing demonstrated moderate airway obstruction in two children with known bronchial asthma. Neither obstructive nor restrictive alteration of ventilation was found in any other patient. Two juvenile idiopathic arthritis patients showed a reduced CO diffusion capacity of 64 and 67%. One of them was treated with methotrexate. CONCLUSIONS: With regard to lung function impairment treatment with low dose methotrexate appears to be safe even when performed for several years reaching a total amount of up to 3.5 g. In contrast to studies performed in adult rheumatoid arthritis patients, in children with juvenile idiopathic arthritis impairment of lung function is a rare event.
- Schmidt C.K.** *Comparison of three teaching methods on 4- through 7-year-old children's understanding of the lungs in relation to a peak flow meter in the management of asthma: a pilot study.* J Asthma. 2002; 39(7) : 641-8.p **Abstract:** This pilot study of 19 children compared three methods of teaching 4- through 7-year-old children about their lungs in relation to a peakflow meter. One group saw a doll with three-dimensional lungs, another group saw a puppet with inflatable lungs, and a comparison group received usual Asthma Clinic education. Knowledge of the lungs was measured pre- and post-teaching through two body knowledge assessment instruments. Four children in the Puppet Group improved their posttest scores, compared to three in the Doll Group and two in the Usual Care Group. Continued psychometric studies of the instruments and similar studies with larger sample sizes need to be conducted.
- Schmidt J.R. et al.** *Web-based distributed data management in the childhood asthma research and education (CARE) network.* Clin Trials. 2005; 2(1) : 50-60.p **Abstract:** A well-designed distributed data management application provides an efficient, effective process to collect quality data in multicenter clinical trials. This paper describes the web-based clinical center data management application that was developed by the Data Coordinating Center of the Childhood Asthma Research and Education (CARE) Network. A series of modules was designed to allow the clinical staff at the remote clinical centers to enter clinical trial data, correct entry errors, respond to queries from the Data Coordinating Center, and submit data corrections for previously entered data to ultimately provide a clean and accurate dataset for analysis.
- Schmidt W.P.** *Model of the epidemic of childhood atopy.* Med Sci Monit. 2004; 10(2) : HY5-9.p **Abstract:** The reasons for the steep rise in the prevalence of atopic diseases such as asthma, atopic eczema and allergic rhinitis are unexplained. Studies have shown that immune regulation in the intestinal mucosa-associated lymphoid tissue (MALT) plays an important role in atopic sensitization and is influenced by the intestinal microflora. The hypothesis presented here is based on the following assumptions: 1. Mothers transfer some of their intestinal microflora to their children at birth and by close contact. 2. The intestinal microflora has the properties of an ecosystem that may react unexpectedly to changing conditions. 3. Modern lifestyle and diets negatively influence the intestinal ecosystem during the lifespan. Thus, from one generation to the next, there may be cumulative degradation of the intestinal microflora. Children inherit a non-physiological gut flora that is further degraded in later life and contributes to atopic sensitization in the following generation. Linear changes in environmental conditions and lifestyle may lead to non-linear changes in the gut flora and, possibly, to an increasing susceptibility to atopic diseases. Clinical studies using probiotics and dietary intervention should be the focus of future research.

- Schneider D. et al.** *Asthma and respiratory dysfunction among urban, primarily Hispanic school children.* Arch Environ Health. 2004; 59(1) : 4-13.p **Abstract:** A screening program identified children with poorly managed asthma or respiratory dysfunction. Children in grades 2-5 in all Passaic, New Jersey, schools were eligible for screening with questionnaires and a biometric test. Those with risk factors or failed biometric screening were referred to primary care providers. Of the 6,579 eligible children, 3,657 (56%) had parental questionnaires returned and 3,834 (58%) were biometrically screened. Over the 4-yr study period, 6-22% of children were previously diagnosed with asthma. Approximately 20% of children demonstrated peak flow measures <75% of predicted values. Predictors of a prior diagnosis of asthma and a medical treatment plan for asthma management were health care coverage and ethnicity. Predictors of peak flow test failure were the presence of roaches and mold in the home, pesticide use, and a family member with asthma.
- Schock B.C. et al.** *Antioxidants and oxidative stress in BAL fluid of atopic asthmatic children.* Pediatr Res. 2003; 53(3) : 375-81.p **Abstract:** Earlier studies in adults have indicated that increased oxidative stress may occur in the blood and airways of asthmatic subjects. Therefore the aim of this study was to compare the concentrations of antioxidants and protein carbonyls in bronchoalveolar lavage fluid of clinically stable atopic asthmatic children (AA, n = 78) with our recently published reference intervals for nonasthmatic children (C, n = 124). Additionally, lipid peroxidation products (malondialdehyde) in bronchoalveolar lavage fluid and several antioxidants in plasma were determined. Bronchoalveolar lavage concentrations (median and interquartile range) of ascorbate [AA: 0.433 (0.294-0.678) versus C: 0.418 (0.253-0.646) micromol/L], urate [AA: 0.585 (0.412-0.996) versus C: 0.511 (0.372-0.687) micromol/L], alpha-tocopherol [AA: 0.025 (0.014-0.031) versus C: 0.017 (0.017-0.260) micromol/L], and oxidized proteins as reflected by protein carbonyls [AA: 1.222 (0.970-1.635) versus C: 1.243 (0.813-1.685) nmol/mg protein] were similar in both groups (p > 0.05 in all cases). The concentration of protein carbonyls correlated significantly with the number of eosinophils, mast cells, and macrophages in AA children only. Concentrations of oxidized proteins and lipid peroxidation products (malondialdehyde) correlated significantly in AA children (r = 0.614, n = 11, p = 0.044). Serum concentrations of ascorbate, urate, retinol, alpha-tocopherol, beta-carotene, and lycopene were similar in both groups whereas alpha-carotene was significantly reduced in asthmatics. Overall, increased bronchoalveolar lavage eosinophils indicate ongoing airway inflammation, which may increase oxidatively modified proteins as reflected by increased protein carbonyl concentrations.
- Schou A.J. et al.** *Does vitamin D administered to children with asthma treated with inhaled glucocorticoids affect short-term growth or bone turnover?* Pediatr Pulmonol. 2003; 36(5) : 399-404.p **Abstract:** Our objective was to assess whether administration of 25-OH-vitamin D to children with asthma treated with inhaled dry-powder budesonide 400 microg daily affects short-term growth or markers of bone turnover. We utilized a randomized, double-blind, two-period crossover trial with run-in and washout periods of 2 weeks and treatment periods of 4 weeks duration. The setting was an Outpatient clinic in a secondary referral center. Subjects included 14 boys and 3 girls with a mean age of 11.7 (range, 6.1-14.4) years. Interventions included 15 microg (600 IU) 25-OH-vitamin D (cholecalciferol) in one tablet ABCDin(R) once daily in the morning. Primary outcome measures were: lower leg growth rate, serum osteocalcin, and serum markers of type I collagen turnover, i.e., the amino terminal propeptide of type I procollagen (PINP), the carboxy terminal propeptide of type I procollagen (PICP) (formation markers), and the carboxy terminal pyridinoline cross-linked telopeptide of type I collagen (ICTP) (degradation markers). Secondary outcome measures were parameters of asthma control and serum 25-OH-vitamin D. Lower leg growth rate was 0.22 mm/week during vitamin D and 0.25 mm/week during placebo treatment (NS). Osteocalcin was 59.9 and 57.8 microg/l during vitamin D and placebo treatment, respectively, PINP 574 and 565 microg/l, PICP 381 and 382 microg/l, and ICTP 11.5 and 11.1 microg/l, respectively (NS). Serum 25-OH-vitamin D was 76.3 nmol/l and 48.2 nmol/l, respectively (P < 0.001). There were no statistically significant differences in measures of pulmonary function. In conclusion, administration of 25-OH-vitamin D does not affect short-term growth or markers of bone turnover in children with asthma treated with inhaled dry-powder budesonide 400 microg daily.
- Schou A.J. et al.** *Ultrasound of skin in prednisolone-induced short-term growth suppression.* J Pediatr Endocrinol Metab. 2003; 16(7) : 973-80.p **Abstract:** OBJECTIVE: To assess the thickness of the cutis and subcutis in children with prednisolone-induced knemometric growth suppression. DESIGN: A double blind, placebo-controlled crossover trial with two 7-day treatment periods. PATIENTS: Twenty children with asthma aged 7.7 to 13.8 (mean 10.4) years. INTERVENTIONS: 5 mg prednisolone/day. OUTCOME MEASURES: Lower leg growth rate, thickness of cutis and subcutis and the fraction of low echogenic pixels determined by ultrasound. RESULTS: Mean lower leg growth rate was -0.23 during prednisolone, 0.58 mm/week during placebo treatment (p < 0.01). Mean total thickness of cutis and subcutis over the knee was reduced by 0.28 during prednisolone, increased by 0.07 mm/week during placebo treatment (p = 0.04). Lower leg growth rate was positively correlated to changes in thickness of cutis and subcutis (p = 0.04; r = 0.31). CONCLUSIONS: Reductions in thickness of cutis and subcutis may account for some of the lower leg growth suppression caused by systemic glucocorticoids.
- Schramm B. et al.** *Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study.* Eur Respir J. 2003; 21(1) : 116-22.p **Abstract:** The purpose of this study was to evaluate the cost of illness of moderate-to-severe atopic asthma and/or seasonal allergic rhinitis (SAR) in Germany from the perspective of third-party payers (TPP) and patients. Five-hundred patients (276 children/adolescents) with moderate-to-severe asthma and/or SAR were included in this cross-sectional study. Information was collected using a specific patient questionnaire and the abstraction of patient records. Overall, annual costs per patient increased with the severity of atopic asthma and if it was associated with SAR. The average annual cost of SAR was Euro1,089 per child/adolescent and Euro1,543 per adult. Annual costs of severe asthma plus SAR increased to Euro7,928 per child/adolescent and to Euro9,287 per adult. For TPPs, the main cost drivers were medication, hospitalisation, and rehabilitation. The most significant costs for patients were household modifications. For children/adolescents, 60-78% of the expenditures were direct costs, while in adults, 58% of expenditures were indirect costs. It was also observed that patients with moderate and severe asthma used inhaled corticosteroids less frequently than recommended by treatment guidelines. In summary, the total cost for patients increases with the severity of atopic asthma and/or seasonal allergic rhinitis and indirect costs represent a large proportion of the total cost.
- Schubert M.S. et al.** *HLA-DQB1 *03 in allergic fungal sinusitis and other chronic hypertrophic rhinosinusitis disorders.* J Allergy Clin Immunol. 2004; 114(6) : 1376-83.p **Abstract:** BACKGROUND: Many common chronic inflammatory disorders have strong HLA gene associations, particularly with MHC class II. Allergic fungal rhinosinusitis (AFS) and hypertrophic sinus disease (HSD) are chronic sinonasal mucosal inflammatory disorders. Allergic bronchopulmonary aspergillosis, a disorder analogous to AFS, was recently reported to have HLA-MHC class II associations. OBJECTIVE: We sought to determine whether MHC class II is also associated with AFS and HSD. METHODS: HLA DNA genotyping was obtained on 44 patients with AFS and 30 patients with HSD (of

which 21 were atopic). RESULTS: Sixty-six percent of patients with AFS carried at least one HLA-DQB1 *03 allele; DQB1 *0301 and DQB1 *0302 were the most frequent allelic variants (odds ratio [OR] vs healthy subjects = 8.22; 95% CI, 4.30-15.73; $P < .001$; OR vs all patients with HSD = 1.93; 95% CI, 1.09-3.41; $P < .01$; OR vs atopic patients with HSD = 2.57; 95% CI, 1.46-4.53; $P < .001$). Of the 31 patients with AFS and positive Bipolaris spicifera cultures, 68% had DQB1 *03, with DQB1 *0301 and DQB1 *0302 being most frequent (OR vs healthy subjects = 8.93; 95% CI, 4.65-17.15; $P < .001$; OR vs patients with HSD = 2.10; 95% CI, 1.18-3.73; $P < .001$). Of the 30 patients with HSD, 50% carried DQB1 *03 (OR vs healthy subjects = 4.25; 95% CI, 2.25-8.02; $P < .001$) but differed in frequencies of DQB1 *03 allelic variants compared with patients with AFS ($P = .0004$). For HSD, nonatopic subjects had the highest DQB1 *03 association (OR vs healthy subjects = 8.63; 95% CI, 4.50-16.54; $P < .001$). DQB1 *03 allelic variants did not correlate with allergy skin test results, atopic status, total serum IgE levels, culture results, asthma, or aspirin-nonsteroidal anti-inflammatory drug hypersensitivity. CONCLUSION: Patients with AFS and HSD have HLA-DQB1 *03 alleles as a risk factor for disease, with AFS having the highest association. However, they differ in DQB1 *03 allelic variant frequencies, suggesting several potential roles for MHC class II in their immunopathogenesis.

Schumpert J.C. et al. *Patterns of asthma symptoms and perceptions of harm from seasonal atmospheric events in rural Western Montana.* Int J Occup Environ Health. 2006; 12(1) : 52-8.p **Abstract:** To characterize the frequency of and relationship between self-reported asthma symptoms and physician-diagnosed asthma, identify seasons associated with heightened symptoms, and describe the influence of seasonal atmospheric events and ambient environmental factors on asthma symptoms and perceptions of harm, a seven-county region of Western Montana was surveyed, utilizing a two-stage sampling method. Respondents were queried concerning asthma-related history, symptoms, and environmental concerns. Of 2,790 respondents, 12% reported physician-diagnosed asthma. Eighteen percent reported one or more and 9% reported two or more asthma-related symptoms. Over 70% of asthmatics reported worsened asthma symptoms during wildland-fire smoke exposure. Of those reporting summer as the season they experienced the greatest breathing problems, 81% reported breathing problems from wildland-fire smoke ($p < 0.01$). Of those reporting worsened symptoms in fall or winter, 61% reported breathing problems during winter inversions ($p < 0.001$).

Scott F. *Rethinking asthma. New ways of looking at an old problem.* Adv Nurse Pract. 2001; 9(11) : 59-62.p

Scott M.B. et al. *Once-daily budesonide inhalation suspension in infants and children < 4 and > or = 4 years of age with persistent asthma.* Ann Allergy Asthma Immunol. 2001; 87(6) : 488-95.p **Abstract:** BACKGROUND: Budesonide inhalation suspension (Pulmicort Respules; AstraZeneca LP, Wilmington, DE), a nebulized corticosteroid, was developed for use in infants and young children with persistent asthma. OBJECTIVE: To compare the efficacy and safety of once-daily budesonide inhalation suspension in children < 4 years of age and in those > or = 4 years of age with persistent asthma. METHODS: A retrospective analysis stratified by age group was performed on data from two randomized, double-blind, placebo-controlled, parallel-group studies that evaluated the efficacy and safety of budesonide inhalation suspension 0.25 mg, 0.5 mg, or 1.0 mg once daily for 12 weeks in children 6 months to 8 years of age with persistent asthma. Clinical assessments included nighttime and daytime asthma symptoms, breakthrough medication use, adverse events, and hypothalamic-pituitary-adrenal-axis function. RESULTS: In both randomized studies, budesonide inhalation suspension demonstrated statistically significant improvement in nighttime and daytime asthma symptom scores compared with placebo. In the retrospective analysis of pooled data from these studies, the efficacy

of budesonide was maintained when children were stratified by age group. Clinical improvements from baseline in nighttime and daytime asthma symptom scores were observed in both age groups at all budesonide inhalation suspension dose levels. No significant differences were observed between age groups in breakthrough medication use in any of the treatment groups. No differences were observed in the incidence of adverse events between the two age groups, and significant ($P < 0.01$) effect on hypothalamic-pituitary-adrenal-axis function was apparent only in children < 4 years of age at the 0.25-mg dose level. CONCLUSIONS: Once-daily budesonide inhalation suspension is effective in the treatment of persistent asthma in children aged < 4 and > or = 4 years of age.

Sebastian A. *Pulmonary function tests in Indian girls.* Indian J Pediatr. 2005; 72(12) : 1060-1; author reply 1061.p

Segala C. et al. *[Odors and health: a descriptive epidemiological study around a wastewater treatment plant].* Rev Epidemiol Sante Publique. 2003; 51(2) : 201-14.p **Abstract:** BACKGROUND: Following community concern regarding potential health effects associated with odors of a wastewater treatment plant, a descriptive epidemiological study was conducted to assess the complaints and the health status of the community and to identify potentially more susceptible groups. METHODS: Questionnaires were administered by telephone to nearly 3,000 subjects, randomly selected in the 8 nearby towns, using a geographical Information System. Residents of three areas were compared, according to the distance from the site: 0-1.5 km (high exposed group), 1.5-3 km (moderate exposed group) and 3-4.5 km (low exposed group). Questions measured demographic characteristics, concerns, perceived environmental risk and health effects (symptoms in the past 1 month and in the past 1 year). Multivariate logistic models study the relationships of complaints and health effects, with area and susceptibility factors. RESULTS: Two thousand eight hundred and sixty seven eligible adults participated in an interview. Taking in account confounding factors, population of high and moderate exposed groups reported more odor complaints than the low exposed group, with adjusted odds ratio (OR) of 4.73 (CI95%: 3.63-6.14) and 2.06 (CI95%: 1.59-2.66) respectively. But these 2 groups did not report more frequent health effects compared to the low exposed group. Several health effects were significantly more frequent in persons with self-reported chemical intolerance and in persons considering malodor in terms of health threat. In this last sub-group of population, rhinitis were significantly more frequent in the high exposed group compared to low exposed group, whereas respiratory infections and asthma attacks showed the same non significant patterns. CONCLUSION: If 24,2% of the total sample complaints from odors of the site, this study did not show a higher frequency of health effects in people living near the site (high exposed group). But 2 susceptible groups (with a higher frequency of symptoms potentially related to odors) were identified: persons with self-reported chemical intolerance, among those, many allergic and asthmatic subjects, and persons considering malodor in terms of health threat.

Sekerel B.E. et al. *Middle lobe syndrome in children with asthma: review of 56 cases.* J Asthma. 2004; 41(4) : 411-7.p **Abstract:** OBJECTIVE: Middle lobe syndrome (MLS) is one of the complications of asthma. Its signs and symptoms are often nonspecific, causing delay in appropriate treatment. We aimed to review our pediatric asthmatic patients and provide differential characteristics between MLS and asthma worsening in order to target early diagnosis. METHOD: File records of all asthmatics ($n=3528$) seen in our clinic during the last 2 years were retrospectively reviewed to identify the patients with MLS, and a case-control study was undertaken. Files of 56 asthmatic children diagnosed as MLS, with a total of 63 episodes, and 63 matched controls with asthma worsening were analyzed and compared. RESULTS: The incidence of MLS was 1.62% and half were below or at the age of 6. All cases with MLS were documented radiologically, and only 5 of the 63

episodes had physical findings suspicious for MLS. The most affected segments were right middle lobe (50%) and left lingula (26.2%). Although in all cases symptoms cleared, in 23 (36.5%) cases, atelectasis persisted radiologically. Compared to controls, patients with MLS included less atopics (34.9% vs. 59.4%, $p < 0.05$) and fewer boys (52.4% vs. 71.4%, $p < 0.05$), and they reported less frequent dyspnea (57.1% vs. 85.9%), more frequent sputum production (49.2% vs. 7.8%), and longer duration of complaints (22.0 \pm 6.23 vs. 2.4 \pm 0.31 days) ($p < 0.001$, for each). Furthermore, the resolution of symptoms took significantly longer (45.2 \pm 9.3 vs. 3.3 \pm 0.4 days, $p < 0.001$). **CONCLUSION:** We conclude that complicating MLS in childhood asthma is more frequent in younger ages, girls, and nonatopics. In most cases, physical findings are not informative, and chest radiographs diagnose most but not all cases. The most suggestive symptoms are unresolving/persisting symptoms during admission and/or following treatment.

Sekerel B.E. et al. *Childhood asthma perception in Turkey under real-life environment (CAPTURE) study.* *Pediatr Allergy Immunol.* 2001; 12(5) : 266-73.p **Abstract:** Successful management of asthma requires good communication between patients and the healthcare team. The background and expectations of a patient inevitably influence the success of any partnership. A questionnaire-based survey was performed to obtain data on the perception of the impact of asthma in daily life among children (age-range 6-14 years) and adolescents (age-range 15-20 years). A total of 756 patients (384 children, 372 adolescents) were randomly selected from 11 Turkish cities and interviewed face-to-face. Of the total study population, 71.3% received regular follow-up and 75.9% currently took asthma medication. Almost 50% reported that asthma affected their lives significantly. Even though half of the patients had symptoms at least once a week, one-third were not receiving regular prophylactic treatment. Exercise produced asthma symptoms in 45.5% of children and 27.4% of adolescents. The finding that asthma continues to be a major health problem clearly indicates an urgent need for further management programs in Turkey.

Sekhsaria S. et al. *Efficacy and safety of inhaled corticosteroids in combination with a long-acting beta2-agonist in asthmatic children under age 5.* *J Asthma.* 2004; 41(5) : 575-82.p **Abstract:** The incidence of asthma in children under age 5 is higher than in any other segment of the population. Current NAEPP guidelines recommend treatment of some asthmatics in this age group with the combination of an inhaled corticosteroid and a long-acting beta2-agonist even though this practice has never been studied with children younger than 4. This retrospective study analyzes the efficacy and safety of a combination of fluticasone propionate (FP) and salmeterol (SA) in children under 5. Fifty patients who started using FP/SA before the age of 60 months were included in the analysis. To determine efficacy, we tracked the change in emergency room visits, hospitalizations, and the frequency of wheezing as a result of treatment. Emergency room visits were reduced from 78 to 5 ($p < 0.001$), hospitalizations were reduced from 43 to 2 ($p < 0.001$) and frequency of wheezing, daily, weekly, or monthly, was also reduced significantly ($p < 0.003$). In terms of safety, there was only a 3.4% reduction in height percentile ($p = 0.37$). Combination therapy is highly efficacious and safe for asthmatics under the age of 5. A well-designed prospective study is necessary to further evaluate the benefits and risks of this treatment method.

Sellers W.F. et al. *Rapidly repeated intravenous boluses of salbutamol for acute severe asthma.* *Anaesthesia.* 2003; 58(7) : 680-3.p **Abstract:** We describe the use of intravenous boluses of salbutamol given rapidly (over 1-2 min) in children (5 microg x kg-1) and young adults (250 microg) with acute severe asthma who were not improving with doses of nebulised salbutamol. Intravenous boluses were repeated within a short time until improvement was seen. Two of the seven patients required tracheal intubation and ventilation.

Selnes A. et al. *Diverging prevalence trends of atopic disorders in Norwegian children. Results from three cross-sectional studies.* *Allergy.* 2005; 60(7) : 894-9.p **Abstract:** **BACKGROUND:** During the last decades there has been extensive epidemiological research to explore the increasing prevalence of asthma and allergy in childhood. The worldwide variations in prevalence of these diseases necessitate regional reports. Furthermore, time-trend analyses with comparable methods are important in order to monitor the rapidly changing prevalence of these diseases. **METHODS:** Three cross-sectional questionnaire-based studies of asthma and allergy in schoolchildren were conducted in the counties of Troms and Finnmark, in northern Norway in 1985, 1995 and 2000. The two former studies included children from randomly selected primary schools ($n = 1794/1985$, $n = 1432/1995$). The latter study was a part of ISAAC-II Europe study ($n = 3853$). Identical items of asthma and allergy were employed. The analyses comprised only children 9-11 years of age. **RESULTS:** The prevalence of asthma was 9.3, 13.2 and 13.8% in 1985, 1995 and 2000, respectively. However, great gender differences were detected; the prevalence of asthma increased in males from 1995 to 2000, from 14.1 to 17.0%, $RR = 1.2$ (95% CI 1.0-1.5), but decreased in females 1995 to 2000, from 12.3 to 10.5%, $RR = 0.9$ (95% CI 0.7-1.1). Furthermore, in children with asthma, a changing trend was found in the external factors that perceived symptoms, from typical allergens towards other, unspecific agents. The prevalence of self-reported atopic eczema/dermatitis syndrome (AEDS) was 13.4, 21.1 and 20.8% in 1985, 1995 and 2000, respectively. The prevalence of self-reported allergic rhinoconjunctivitis was in 16.5, 24.7 and 29.6% 1985, 1995 and 2000, respectively, RR (2000/1995) = 1.2 (95% CI 1.1-1.3). **CONCLUSION:** The prevalence of asthma in girls has reached a plateau and even decreased from 1995 to 2000 which is in contrast to the asthma prevalence in boys that tends to continuously increase. The prevalence of AEDS which increased substantially between 1985 and 1995 did not change from 1995 to 2000. However, the prevalence of allergic rhinoconjunctivitis increased steadily from 1985, 1995 to 2000.

Selroos O. et al. *Once-daily inhaled budesonide for the treatment of asthma: clinical evidence and pharmacokinetic explanation.* *J Asthma.* 2004; 41(8) : 771-90.p **Abstract:** **BACKGROUND:** Budesonide, a widely used inhaled corticosteroid (ICS) with a favorable therapeutic ratio, is available via a dry powder inhaler (Pulmicort Turbuhaler) and as a suspension for nebulization (Pulmicort Respules). **METHODS:** MEDLINE and an AstraZeneca database were searched to identify relevant controlled clinical trials published between 1986 and 2002 using the key words budesonide OR inhaled corticosteroid, AND once daily. **RESULTS:** Thirty-four controlled clinical studies involving once-daily administration of budesonide to asthmatic patients were identified. Excluding long-term studies, this review presents data from 23 controlled studies for 4466 adults or adolescents and 1532 children with asthma and demonstrates efficacy of budesonide in both corticosteroid-naive patients and patients previously treated with ICS. Once-daily administration of budesonide achieves clinical efficacy comparable with that of twice-daily regimens in patients with mild-to-moderate asthma and is equally effective when given in the morning or evening. Once-daily administration simplifies treatment regimens and may improve patient compliance. The tolerability profiles of budesonide once-daily via Turbuhaler or as budesonide inhalation suspension are good and comparable with those for twice-daily dosing. **CONCLUSIONS:** Once-daily budesonide is effective and well tolerated as initial treatment for adults and children with mild asthma and as maintenance therapy in patients with more severe asthma once asthma control has been achieved.

Selroos O. et al. *Formoterol Turbuhaler 4.5 microg (delivered dose) has a rapid onset and 12-h duration of bronchodilation.* *Pulm Pharmacol*

Ther. 2002; 15(2) : 175-83.p **Abstract:** Clinical trials show that formoterol (Oxis) Turbuhaler 4.5 microg delivered dose (6 microg metered dose) has a rapid onset of bronchodilation similar to that of salbutamol and a 12-h duration of action. Maximum increase in FEV(1) and duration of bronchodilation are dose-dependent, the 4.5 microg dose being the lowest dose tested giving both effects. Clinical studies investigating onset of bronchodilation show a significant increase in specific airway conductance occurring within 1 min after inhalation of formoterol Turbuhaler 4.5 microg. When measured from 3-20 min after inhalation, formoterol Turbuhaler 4.5 microg showed similar increases in FEV(1) to salbutamol administered via pMDI. No difference in onset of bronchodilation was observed between the formoterol Turbuhaler 4.5 and 9 microg doses. Single-dose studies and studies of 1-12 weeks' duration show that formoterol Turbuhaler 4.5 microg produces a significant and clinically important mean bronchodilating effect for > or =12 h after inhalation. In the cited studies no significant differences in duration of bronchodilation were observed between the formoterol Turbuhaler 4.5 and 9 microg doses. **Conclusion:** clinical data show that formoterol Turbuhaler 4.5 microg is an effective dose in patients with asthma, with a rapid onset of bronchodilation and a duration of at least 12 h.

Sener O. et al. *Comparison of skin tests to aeroallergens in Ankara and Seoul.* J Investig Allergol Clin Immunol. 2003; 13(3) : 202-8.p **Abstract:** **BACKGROUND:** The environment contains many allergenic proteins, and skin test reactivity to aeroallergens may be different among people living in different regions. **OBJECTIVE:** To compare skin test results of Turkish and Korean patients with respiratory allergies. **METHODS:** The charts of 304 (160 male, 144 female) patients from Ankara, Turkey, and 208 (111 male, 97 female) patients' charts from Seoul, Korea, who had undergone skin prick tests were reviewed. Skin tests were classified as positive when the allergen-induced wheal size was the same size or larger than that caused by histamine. **RESULTS:** Grass pollens were found to be major allergens more often in Ankara than in Seoul (74.34% vs. 15.87%, $p < 0.001$). Skin test reactivities in Ankara were significantly lower ($p < 0.001$) than in Seoul to weed (6.91% vs. 37.50%) and tree pollens (4.61% vs. 39.42%). Allergic reactions to indoor allergens were significantly higher ($p < 0.001$) in Seoul than in Ankara: house dust mites (HDM) (83.17% vs. 32.90%), cockroaches (45.67% vs. 1.97%), and cats (17.79% vs. 1.65%). **CONCLUSION:** Due to the different aeroallergen environment, the positive skin test results were different in both cities: grass pollens were the most common allergens in Ankara, while patients from Seoul reacted more commonly to indoor allergens, especially to HDMs and cockroaches.

Senior M.L. et al. *Morbidity, deprivation and drug prescribing: factors affecting variations in prescribing between doctors' practices.* Health Place. 2003; 9(4) : 281-9.p **Abstract:** Analyses are reported of the prescribing quality and behaviour of 131 doctors' practices in a South Wales health authority during the first quarter of 1997. Prescribing of specific groups of drugs are examined, namely antidepressants; bronchodilators and inhaled corticosteroids for treating asthma; and oral antidiabetics and insulin for diabetes. It is hypothesised that the volumes and costs of prescriptions are determined by the characteristics of both doctors/practices (number and age of doctors; training and fundholding status of practices; single-handed practices and doctors per patient) and their patients (age; gender; ethnicity; deprivation). The health authority's population is characterised by substantial inequalities in wealth and health. Statistical analyses reveal the consistent influence of deprivation on prescribing costs and volumes, with the exception of items of insulin. Supply factors exert more selective influences. Thus, the number of doctors per practice and per patient has a positive influence on antidepressant prescribing; fundholding status is associated with lower costs for bronchodilator prescribing; and older doctors tend to prescribe more bronchodilators and oral antidiabetics. Residuals from the statistical analyses suggest further systematic influences, notably advice from

hospital consultants, as well as more localised and less consistent effects.

Sevar R. *Audit of outcome in 455 consecutive patients treated with homeopathic medicines.* Homeopathy. 2005; 94(4) : 215-21.p **Abstract:** This paper reports an audit of clinical outcome in 455 consecutive patients (1100 consultations) presenting for private homeopathic treatment of a chronic illness in which conventional treatment had either: failed, reached a plateau in effect, or was contra-indicated by side effects, age or condition of the patient. Three hundred and four patients (66.8%) derived benefit from homeopathic treatment. One hundred and forty-eight patients (32.5%) were able to stop or maintain a substantial reduction in their conventional drugs. The 10 most frequent clinical conditions treated were eczema, anxiety, depression, osteoarthritis, asthma, back pain, chronic cough, chronic fatigue, headaches and essential hypertension. These 195 patients constitute 43% of the total, 151 of them (77%) were improved. The success rate of treatment is similar between age ranges. There was a difference in outcome between the sexes in adults: 296 females treated, success rate 71.3%; 159 males treated, success rate 58.5%. Two patients (0.4%) had prolonged aggravation of their presenting complaints apparently attributable to homeopathic treatment.

Sevar R. *Sanicula aqua: three clinical cases and a heuristic.* Homeopathy. 2005; 94(2) : 125-31.p **Abstract:** The cases presented are of three children who responded well to *Sanicula aqua*. I have used the exact words of the patients or their mothers. All 3 are: firstborn girls, tall and very thin with blue-green eyes. Two with recurrent otitis media with perforated tympanic membrane and smell of rotting fish, the third atopic eczema and asthma. The case analyses, *materia medica* of *Sanicula aqua* and the creation of a remedy heuristic, are discussed.

Sexton K. *Comparison of recruitment, retention, and compliance results for three children's exposure monitoring studies.* J Expo Anal Environ Epidemiol. 2005; 15(4) : 350-6.p **Abstract:** The School Health Initiative: Environment, Learning, Disease (SHIELD) study, the Minnesota Children's Pesticide Exposure Study (MNCPEs), and the National Cooperative Inner-City Asthma Study (NCICAS) are three of the most intensive and invasive exposure-monitoring projects ever undertaken in children. An intrinsic facet of each study was the need to recruit children and their families, retain them for the duration of the project, and ensure that they completed monitoring protocols successfully. All of the studies used fiscal incentives to encourage participation, retention, and compliance. Recruitment rates varied from 40% in MNCPEs, to 57% in SHIELD, to 64% in NCICAS, while retention rates varied from 85% in SHIELD, to 94% in MNCPEs, to 95% in NCICAS. Rates of compliance with exposure sampling procedures were typically >80% for each study. For example, > or =85% of the enrolled children provided all requested urine samples (1 for NCICAS, 2 for SHIELD, 3 for MNCPEs), and 82% of the children in SHIELD provided two out of two blood samples (optional in MNCPEs and NCICAS). However, compliance rates were substantially lower (34% SHIELD, 40% NCICAS, not applicable to MNCPEs) for the more complex and time-consuming protocol used to collect peak flow data. Overall, results demonstrate that it is practical and affordable to conduct demanding exposure-monitoring studies in children, including children from poor minority communities.

Shachor J. et al. *Genetic polymorphisms of the beta-2 adrenergic receptor in Israelis with severe asthma compared to non-asthmatic Israelis.* Isr Med Assoc J. 2003; 5(11) : 821-4.p **Abstract:** **BACKGROUND:** It has been argued that arginine replacement in locus 16 (Arg16) of beta 2 adrenergic receptor with glycine (Gly16)

increases asthma severity, while glutamin replacement in locus 27 (Gln27) with glutamic acid (Glu27) decreases it. In addition, ethnic dependency of these polymorphisms has been described, but few studies investigated its relation to asthma severity in a non-anglosaxic population. OBJECTIVES: To investigate non-anglosaxic ethnic influences on beta 2AR polymorphisms and its correlations to asthma severity. METHODS: Sixty-six Israeli Jewish and Arab asthmatics who had near-fatal asthma and/or severe nocturnal asthma and/or steroid-dependency were investigated for genetic polymorphisms of beta 2AR and compared to matched controls. The Jewish patients included both Ashkenazi (of European origin) and non-Ashkenazi (originating from the Middle East or North Africa). The results were compared with those of ethnically matched 113 non-asthmatic Israelis and non-asthmatic Anglo-Saxons described in the literature. RESULTS: We found no significant genetic differences between the asthmatics and their controls or between the various ethnic groups of our population. However, the prevalence of Glu27 was significantly lower in non-asthmatic Israelis compared to non-asthmatic Anglo-Saxons. CONCLUSIONS: The genetic distribution of beta 2AR polymorphisms in severe Israeli asthmatics is not different from that of non-asthmatic Israelis and therefore its clinical impact on asthma is probably minimal.

Shafazand S. et al. *Flunisolide HFA for the treatment of asthma: an old friend reformulated.* Expert Opin Pharmacother. 2004; 5(5) : 1163-73.p **Abstract:** The environmental mandate to eliminate the production of ozone-depleting products including chlorofluorocarbon (CFC) propellants has encouraged much needed research into improving modes of delivery of inhaled corticosteroids and enhancing drug deposition. Consequently, flunisolide CFC, an inhaled corticosteroid with a proven track record in the treatment of asthma, has been reformulated using a hydrofluoroalkane (HFA) as a propellant and is now awaiting FDA approval. Flunisolide HFA is a solution aerosol, unlike flunisolide CFC which is a suspension aerosol. As a solution aerosol, flunisolide HFA has a smaller mean particle size than flunisolide CFC. In addition, the built-in spacer included in the flunisolide HFA inhaler acts to reduce ex-actuator particle size; the smaller particle size of flunisolide HFA results in an improved deposition profile. Flunisolide HFA has substantially more lung deposition and much less oropharyngeal deposition than flunisolide CFC. Limited information is currently available on the clinical performance of flunisolide HFA. A single dose-response study has been performed in adults and in children comparing multiple doses of flunisolide HFA and flunisolide CFC. These studies indicate that flunisolide HFA is effective in controlling asthma. No unusual safety concerns have been noted, although further studies are needed to determine the long-term systemic effects of flunisolide HFA.

Shah S.M. et al. *Addicted schoolchildren: prevalence and characteristics of areca nut chewers among primary school children in Karachi, Pakistan.* J Paediatr Child Health. 2002; 38(5) : 507-10.p **Abstract:** OBJECTIVES: To evaluate the habits of betel quid use and areca nut chewing among school-aged children in Karachi, Pakistan. Areca nut (betel nut) is chewed by itself, in various scented preparations, and in betel quid (containing betel leaf, areca nut, slaked lime, condiments, sweeteners and sometimes tobacco) in various parts of Pakistan and India. It is associated with carcinogenesis, foreign body aspiration in children and oral submucous fibrosis, and may aggravate asthma. METHODS: We selected a stratified random sample of 160 primary school children between 4 and 16 years of age in Baba Island, Karachi. RESULTS: Seventy-four per cent of the children (118/159) used areca nut and 35% (55/159) used betel quid daily. More boys chewed areca nut than girls (72% vs 30%). The proportion of areca nut users increased by grade (from 48% in first grade to 90% in fifth grade). Most areca users first tried it with a family member (42%) or a friend (26%), and most (68%) consumed three or more packets a day. Children with fathers with three or fewer years of education were more likely to use areca nut (OR 3.2; 95% CI 1.2-8.4), and

children whose mothers helped with homework less likely (OR 0.5; 95% CI 0.2-0.91; P = 0.027) to use it. Boys (OR 6.6; 95% CI 2.3-18.7) and areca nut users (OR 8.8; 95% CI 2.8-27.0) were more likely to use betel quid. CONCLUSION: To reduce the use of areca nut, the Pakistan Government should consider imposing taxes on it, limiting advertising and actively communicating its health risks to the public.

Shaheen S.O. et al. *Paracetamol use in pregnancy and wheezing in early childhood.* Thorax. 2002; 57(11) : 958-63.p **Abstract:** BACKGROUND: We recently reported links between frequent paracetamol (acetaminophen) use and wheezing and asthma in adults and children, but data are lacking on possible effects of prenatal exposure on wheezing in early childhood. METHODS: In the population based Avon Longitudinal Study of Parents and Children (ALSPAC) women were asked twice during pregnancy (at 18-20 weeks and 32 weeks) about their usage of paracetamol and aspirin. Six months after birth, and at yearly intervals thereafter, mothers were asked about wheezing and eczema symptoms in their child. The effects of paracetamol and aspirin use in pregnancy on the risk in the offspring of wheezing at 30-42 months (n=9,400) and eczema at 18-30 months (n=10,216) and on their risk of different wheezing patterns (defined by presence or absence of wheezing at <6 months and at 30-42 months) were examined. RESULTS: Paracetamol was taken frequently (most days/daily) by only 1% of women. After controlling for potential confounders, frequent paracetamol use in late pregnancy (20-32 weeks), but not in early pregnancy (<18-20 weeks), was associated with an increased risk of wheezing in the offspring at 30-42 months (adjusted odds ratio (OR) compared with no use 2.10 (95% CI 1.30 to 3.41); p=0.003), particularly if wheezing started before 6 months (OR 2.34 (95% CI 1.24 to 4.40); p=0.008). Assuming a causal relation, only about 1% of wheezing at 30-42 months was attributable to this exposure. Frequent paracetamol use in pregnancy was not associated with an increased risk of eczema. Frequent aspirin use in pregnancy was associated with an increased risk of wheezing only at <6 months. CONCLUSIONS: Frequent use of paracetamol in late pregnancy may increase the risk of wheezing in the offspring, although such an effect could explain only about 1% of the population prevalence of wheezing in early childhood.

Shahid S.K. et al. *Increased interleukin-4 and decreased interferon-gamma in exhaled breath condensate of children with asthma.* Am J Respir Crit Care Med. 2002; 165(9) : 1290-3.p **Abstract:** Exhaled breath condensate analysis for noninvasive quantification of airway inflammation in asthma is a potentially useful research tool in children. There is an imbalance between T-helper (Th)-2 cells, which secrete interleukin (IL)-4, and Th1 cells, which secrete interferon (IFN)-gamma, in asthma. We measured concentrations of IL-4 and IFN-gamma in breath condensates of 37 children (11 normal, 12 steroid-naive, and 14 steroid-treated children with asthma). Exhaled IFN-gamma was significantly lower in steroid-naive and steroid-treated children with asthma compared with normal control subjects (3.7 +/- 0.2 versus 5.1 +/- 0.4 pg/ml, p < 0.01 and 4.1 versus 5.1 pg/ml, p < 0.05). By contrast, mean exhaled IL-4 was elevated in asthma (53.7 +/- 4.2 pg/ml) compared with normal children (35.7 +/- 6.2 pg/ml, p < 0.05) and concentrations were lower with steroid treatment (37.5 +/- 5.6 pg/ml, p < 0.05). Exhaled IL-4 was significantly lower in children with asthma on more than 600 microg inhaled steroid/day. The IL-4/IFN-gamma ratio was significantly greater in children with asthma compared with control children and the children with asthma on inhaled steroid therapy. We have shown for the first time that IFN-gamma and IL-4 can be assayed in exhaled breath condensate and shows an increased ratio of IL-4/IFN-gamma, consistent with predominance of Th2 cells in airways of children with asthma. Exhaled breath condensate analysis may have a useful role in studying allergic inflammation in childhood asthma.

Shakya K.N. et al. *Efficacy and tolerability of Ketotifen in Nepalese asthmatic children: a clinical study.* Kathmandu Univ Med J

(KUMJ). 2003; 1(4) : 242-7.p **Abstract:** OBJECTIVE: To assess the efficacy of Ketotifen in asthmatic children and to record its adverse effects, if any. DESIGN: Prospective clinical trial. SETTING: Pediatric asthma follow up clinic of a teaching hospital. PARTICIPANTS: 23 asthmatic children between 3 and 15 years; 100% completed the trial on full protocol. INTERVENTIONS: Ketotifen 1mg (adjusted according to body weight, 50 mcg/kg/dose) orally twice daily for 9 months. MAIN OUTCOME MEASURES: Primary outcome: Decrease in frequency of asthmatic attacks and severity of exacerbations with improvements in peak expiratory flow rates (PEFR). Other measures included decrease in bronchodilator requirement, steroid doses and parental perception regarding patient quality of life. RESULTS: 34.78% children were symptom free by the end of 2nd 3 months and 65.21% had no further attack by the end of 3rd 3 months of Ketotifen prophylaxis. Those children with activity and sleep 'affected' (8.69%) and 'may be affected' (30.43%) together improved to 'may be affected' group (21.73%) by the end of 2nd 3 months and further reduced to 8.69% by the conclusion of 3rd 3 months. The duration of exacerbations was reduced in the remaining cases. Variability of PEFR decreased from 26.08% to 8.69% of children after the 3rd 3 months of Ketotifen prophylaxis. No significant adverse effect of therapy was observed during the study. CONCLUSION: Oral Ketotifen is effective and well tolerated for use in prophylactic treatment of bronchial asthma in children.

Shames R.S. et al. *Effectiveness of a multicomponent self-management program in at-risk, school-aged children with asthma.* Ann Allergy Asthma Immunol. 2004; 92(6) : 611-8.p **Abstract:** BACKGROUND: Improving asthma knowledge and self-management is a common focus of asthma educational programs, but most programs have had little influence on morbidity outcomes. We developed a novel multiple-component intervention that included the use of an asthma education video game intended to promote adoption of asthma self-management behaviors and appropriate asthma care. OBJECTIVE: To determine the effectiveness of an asthma education video game in reducing morbidity among high-risk, school-aged children with asthma. METHODS: We enrolled 119 children aged 5 to 12 years from low-income, urban areas in and around San Francisco, CA, and San Jose, CA. Children with moderate-to-severe asthma and parental reports of significant asthma health care utilization were randomized to participate in the disease management intervention or to receive their usual care (control group). Patients were evaluated for clinical and quality-of-life outcomes at weeks 8, 32, and 52 of the study. RESULTS: Compared with controls, the intervention group had significant improvements in the physical domain ($P = .04$ and $P = .01$ at 32 and 52 weeks, respectively) and social activity domain ($P = .02$ and $P = .05$ at 32 and 52 weeks, respectively) of asthma quality of life on the Child Health Survey for Asthma and child ($P = .02$ at 8 weeks) and parent ($P = .04$ and $.004$ at 32 and 52 weeks, respectively) asthma self-management knowledge. There were no significant differences between groups on clinical outcome variables. CONCLUSIONS: A multicomponent educational, behavioral, and medical intervention targeted at high-risk, inner-city children with asthma can improve asthma knowledge and quality of life.

Shann F. *Intravenous salbutamol.* Pediatr Crit Care Med. 2003; 4(1) : 128; author reply 128-9.p

Shao C. et al. *Linkage and association of childhood asthma with the chromosome 12 genes.* J Hum Genet. 2004; 49(3) : 115-22.p **Abstract:** Several studies have shown linkage of chromosome region 12q13-24 to bronchial asthma and related phenotypes in ethnically diverse populations. In the Japanese population, a genome-wide study failed to show strong evidence of linkage of this region. Chromosome 12 genes that showed association with the disease in at least one report include: the signal transducer and activator of transcription 6 gene (STAT6), the nitrogen oxide synthetase 1 gene (NOS1), the interferon gamma gene (IFNG), and the activation-

induced cytidine deaminase gene (AICDA). To evaluate the linkage between chromosome 12 and childhood asthma in the Japanese population, we performed sib-pair linkage analysis on childhood asthma families using 18 microsatellite markers on chromosome 12. To investigate association between chromosome 12 candidate genes and asthma, distributions of alleles and genotypes of repeat polymorphisms of STAT6, NOS1, and IFNG were compared between controls and patients. Single nucleotide polymorphism of AICDA was also investigated. Chromosome region 12q24.23-q24.33 showed suggestive linkage to asthma. The NOS1 intron 2 GT repeat and STAT6 exon 1 GT repeat were associated with asthma. Neither the IFNG intron 1 CA repeat nor 465C/T of AICDA showed any association with asthma. Our results suggest that NOS1 and STAT6 are asthma-susceptibility genes and that chromosome region 12q24.23-q24.33 contains other susceptibility gene(s).

Shapiro G.S. et al. *A randomized, double-blind, single-dose, crossover clinical trial of the onset and duration of protection from exercise-induced bronchoconstriction by formoterol and albuterol.* Clin Ther. 2002; 24(12) : 2077-87.p **Abstract:** BACKGROUND: Inhaled short-acting beta(2)-adrenoceptor agonists are the most commonly used treatment for the prevention of exercise-induced bronchoconstriction (EIB). Formoterol, a long-acting beta(2)-adrenoceptor agonist, has been demonstrated to provide protection from EIB, although the onset and duration of this protection have not been defined. OBJECTIVE: The purpose of this study was to determine the onset and duration of the protective effect of a single dose of inhaled formoterol powder against EIB, comparing them with the effect of a single dose of placebo and albuterol administered via metered-dose inhaler (MDI). METHODS: In this double-dummy, 4-way crossover study, patients received single doses of formoterol (12 and 24 microg) via a powder inhaler, albuterol by MDI (180 microg), and placebo. Exercise challenge tests (ECTs) were conducted at 15 minutes and at 4, 8, and 12 hours postdose. Pulmonary function studies (forced expiratory volume in 1 second [FEV(1)] and peak expiratory flow rate) were performed before and after each exercise challenge. RESULTS: Twenty adolescent and adult patients (mean age, 23.8 years; range, 13-41 years; 9 male, 11 female) with asthma were enrolled in the study, and 17 completed all 4 treatment sequences. Compared with placebo, both doses of formoterol produced significantly greater inhibition of FEV(1) decreases at all time points ($P < 0.01$). There were no significant differences in efficacy measures between the 2 formoterol doses throughout the study. The exercise-induced decrease in FEV(1) after albuterol treatment was significantly reduced compared with placebo only at 15 minutes after dosing ($P < 0.05$). Formoterol and albuterol exhibited a similar rapid onset of action (<15 minutes), but formoterol continued to protect patients against EIB for at least 12 hours ($P < 0.01$), whereas albuterol was no longer clinically effective by the 4-hour ECT. CONCLUSIONS: Formoterol and albuterol, given as single-dose inhalations, both provided protection from EIB within 15 minutes in this group of patients. The bronchoprotection afforded by formoterol lasted up to 12 hours, whereas that of albuterol was no longer significant by 4 hours.

Sharek P.J. et al. *Agreement among measures of asthma status: a prospective study of low-income children with moderate to severe asthma.* Pediatrics. 2002; 110(4) : 797-804.p **Abstract:** BACKGROUND: Because no validated "gold standard" for measuring asthma outcomes exists, asthma interventions are often evaluated using a large number of disease status measures. Some of these measures may be redundant, whereas others may be complementary. Use of multiple outcomes may lead to ambiguous results, increased type I error rates, and be an inefficient use of resources including caregiver and patient/participant time and effort. Understanding the relationship between these measures may facilitate more parsimonious and valid evaluation strategies without loss of information. OBJECTIVE: To assess the relationships between multiple measures of asthma disease status over time.

DESIGN/METHODS: We used data from a randomized, controlled trial of a comprehensive disease management program involving 119 disadvantaged inner-city children aged 5 to 12 years with moderate to severe asthma. Spearman correlations were calculated between the following asthma disease status measures: parent-reported disease symptoms, parent-reported health care utilization, functional health status using the American Academy of Pediatrics' validated Child Health Survey for Asthma (CHSA), diary data (symptom scores, night wakings, and bronchodilator use), and pulmonary function tests at baseline, 32 weeks, 52 weeks, and changes from baseline to 52 weeks. **RESULTS:** Ninety-four (79%) of randomized patients participated at baseline and 52 weeks. Completion rates for outcome measures ranged from 79% (CHSA, spirometry data) to 64% (diary data). At baseline, asthma symptoms, health care utilization, and individual domains from the CHSA were significantly correlated ($r = 0.21-0.53$). These correlations were stable over the 52-week follow-up. Forced expiratory volume in 1 second and diary data did not correlate to any other measures at baseline, and these measures correlated only inconsistently with other measures at 32 weeks and 52 weeks. Baseline to 52-week changes in asthma symptoms, utilization, and the CHSA domains were significantly correlated ($0.22-0.56$), as were baseline to 52-week changes in symptom days, night wakings, and the CHSA domains ($r = 0.24-0.64$). Baseline to 52-week changes in forced expiratory volume in 1 second and diary data did not correlate with other measures. **CONCLUSIONS:** These results suggest that asthma status and change in asthma status over time after introduction of a disease management intervention are best characterized by parent-reported symptoms, parent-reported utilization, and functional health status measures. Asthma diaries and pulmonary function tests did not seem to provide additional benefit, although they may play an important role in individual patient management. Our findings suggest a parsimonious evaluation strategy would include collection of key data elements regarding symptoms, utilization, and functional health status only, without loss of vital response information.

Sharma A. et al. Lipid peroxidation in bronchial asthma. Indian J Pediatr. 2003; 70(9) : 715-7.p **Abstract:** **OBJECTIVE:** To study the levels of free oxygen radicals in children with bronchial asthma during an attack and symptom free interval. **METHODS:** Serum Malondialdehyde (MDA) levels were studied in 25 children between the age of 6 years-14 years who presented with an acute attack of bronchial asthma. In each patient, serum MDA levels were measured at the time of admission, 24-48 hours after good response to treatment and after a symptom free interval of 3 weeks. Results were compared with control group. **RESULTS:** In study group serum MDA levels were highest at the time of admission, which decreased significantly at 24-48 hours with treatment. After a 3 weeks symptom free interval serum MDA levels had decreased further but were still higher than healthy control group. **CONCLUSION:** Lipid peroxidation is increased in bronchial asthma during an acute attack and symptom free period.

Sharma A. et al. Subcutaneous epinephrine vs nebulized salbutamol in asthma. Indian J Pediatr. 2001; 68(12) : 1127-30.p **Abstract:** **OBJECTIVE:** This study was conducted to compare the efficacy of the subcutaneous epinephrine with nebulized salbutamol. **METHODS:** Fifty asthmatic children in the age range of 6-14 years were divided into two equal groups. Group I children were given subcutaneous epinephrine and Group II were nebulized with salbutamol. Patients were observed at 15, 20, 30, 60, 120, 180 and 240 minute intervals. Both the groups had comparable mean increase in peak expiratory flow rate (PEFR %) (Group I 27.7 +/- 0.7; Group II 28.8 +/- 0.06, $p > 0.05$). **RESULT:** In Group I there was significant increase in systolic blood pressure, 30 minutes after the start of treatment, however it settled on its own by 60 minutes. **CONCLUSION:** Both the groups had satisfactory improvement in clinical parameters which continued upto 4 hours after start of

treatment. Subcutaneous epinephrine can be safely used if nebulizers are not available.

Sharma S. et al. Salbutamol and/or beclomethasone dipropionate in asthma. Indian J Pediatr. 2003; 70(2) : 129-32.p **Abstract:** **OBJECTIVE:** Acute severe exacerbation of asthma is potentially life threatening and requires critical assessment and appropriate therapy. Now a days, steroids are often combined with bronchodilators for the treatment of bronchial asthma. Therefore, the present study was undertaken to compare effectiveness of beclomethasone dipropionate-salbutamol combination versus salbutamol alone by MDI (with or without spacer) in acute asthma. **METHODS:** A total of 57 paediatric patients (5-12 years) with acute attack of bronchial asthma attending emergency department of Indira Gandhi Medical College and Hospital was randomised to receive salbutamol (100 microg/puff) alone or with BDP (50 microg/puff) by metered dose inhaler with or without spacer. All baseline investigations were repeated one hour after the therapy. **RESULTS:** Clinical parameters indicative of severity of asthma improved statistically in all treatment groups. The increase in PEFR was better with MDI-S+B with spacer as compared to other groups, though it failed to reach statistical significance. The fall in serum potassium level is significantly more with MDI-S+B group when spacer was not used. No serious adverse effects were observed in any of the treatment groups. **CONCLUSIONS:** Metered dose inhalation of BDP-salbutamol combination with spacer provides better recovery whereas fall in serum potassium with MDI-S+B suggests use of spacer and monitoring of serum potassium during treatment.

Sharma S. et al. Lack of association of histamine-N-methyltransferase (HNMT) polymorphisms with asthma in the Indian population. J Hum Genet. 2005; 50(12) : 611-7.p **Abstract:** Histamine plays a major role in allergic disorders, including asthma. A major pathway of histamine biotransformation in the lungs is mediated by histamine N-methyltransferase (HNMT). We investigated the association of a functional SNP C314T; a SNP A929G, a (CA)_n repeat in intron 5, and a novel (CA)_n repeat (BV677277), 7.5 kb downstream of the HNMT gene with asthma and its associated traits such as total serum IgE levels in a case-control as well as in a family-based study design. In contrast to a previous study, no association was observed for the polymorphisms investigated with asthma ($P > 0.05$). When haplotypes were constructed for these loci and compared, no significant difference was observed in the distribution between cases and controls. In the family-based design, no biased transmission was observed for any of the polymorphisms and haplotypes with asthma using the additive model of inheritance in family-based association test (FBAT). Thus, consistent with the case-control findings, the polymorphisms and haplotypes in the HNMT gene are not associated with asthma in the Indian population.

Shaukat A. et al. Is being breastfed as an infant associated with adult pulmonary function? J Am Coll Nutr. 2005; 24(5) : 327-33.p **Abstract:** **OBJECTIVE:** Breastfeeding reduces the risk of asthma and respiratory infections in infants. Since respiratory infections are associated with reduced pulmonary function in adolescents, pulmonary function impairment may be carried into adulthood. Our aim was to determine whether a history of having been breastfed as an infant is a determinant of adult pulmonary function. **METHODS:** We analyzed data from a general population sample of residents of Erie and Niagara Counties between September 1995 and December 1999. We calculated forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) prediction equations and used multiple linear regression models to study the association between having been breastfed as an infant and percentage predicted FEV₁ (FEV₁(%)) and percentage predicted FVC (FVC(%)) after adjustment for covariates. **RESULTS:** Of 2305 subjects, 62% reported having been breastfed. After controlling for age, gender, weight, smoking status, pack-years of smoking, eosinophil counts

and dietary factors, there was no association between having been breastfed (yes/no) and FEV₁(%) or FVC% (regression coefficients 0.0049, $p = 0.46$ and 0.0055, $p = 0.43$, respectively). CONCLUSIONS: We did not find a strong or consistent association between having been breastfed as an infant and pulmonary function in adulthood.

Sheffer A.L. et al. *Long-term safety of once-daily budesonide in patients with early-onset mild persistent asthma: results of the Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) study.* Ann Allergy Asthma Immunol. 2005; 94(1) : 48-54.p

Abstract: BACKGROUND: The Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) study is a worldwide, randomized, prospective study to investigate early intervention with inhaled corticosteroids in recent-onset mild persistent asthma. OBJECTIVE: To evaluate the safety and tolerability of long-term treatment with once-daily budesonide therapy in patients with mild persistent asthma. METHODS: Patients aged 5 to 66 years with mild persistent asthma for fewer than 2 years and no previous regular corticosteroid treatment received budesonide or placebo once daily for 3 years, in addition to their usual asthma therapy. The daily budesonide dose was 200 microg for children younger than 11 years and 400 microg for those 11 years or older. RESULTS: Overall, 7,221 patients were included in the safety analysis, and a total of 21,520 adverse events were reported (10,850 in the budesonide group and 10,670 in the placebo group). The most commonly reported events included respiratory infections, rhinitis, pharyngitis, bronchitis, viral infections, and sinusitis. The number of deaths and serious adverse events were similar for children and adults in both treatment groups. Fewer asthma-related serious adverse events were reported with budesonide (162) compared with placebo (276). Oral candidiasis was reported more frequently with budesonide (1.2%) than with placebo (0.5%); the frequencies of other adverse effects previously reported to be associated with inhaled corticosteroids (psychiatric disorders, skin disorders, and allergic reactions) were similar. CONCLUSIONS: Three-year treatment with budesonide once daily (200 or 400 microg) is safe and well tolerated in children and adults with newly detected mild persistent asthma.

Sheikh A. et al. *House dust mite barrier bedding for childhood asthma: randomised placebo controlled trial in primary care.* BMC Fam Pract. 2002; 3 : 12.p

Abstract: BACKGROUND: The house dust mite is the most important environmental allergen implicated in the aetiology of childhood asthma in the UK. Dust mite barrier bedding is relatively inexpensive, convenient to use, and of proven effectiveness in reducing mattress house dust mite load, but no studies have evaluated its clinical effectiveness in the control of childhood asthma when dispensed in primary care. We therefore aimed to evaluate the effectiveness of house dust mite barrier bedding in children with asthma treated in primary care. METHODS: Pragmatic, randomised, double-blind, placebo controlled trial conducted in eight family practices in England. Forty-seven children aged 5 to 14 years with confirmed house dust mite sensitive asthma were randomised to receive six months treatment with either house dust mite barrier or placebo bedding. Peak expiratory flow was the main outcome measure of interest; secondary outcome measures included asthma symptom scores and asthma medication usage. RESULTS: No difference was noted in mean monthly peak expiratory flow, asthma symptom score, medication usage or asthma consultations, between children who received active bedding and those who received placebo bedding. CONCLUSIONS: Treating house dust mite sensitive asthmatic children in primary care with house dust mite barrier bedding for six months failed to improve peak expiratory flow. Results strongly suggest that the intervention made no impact upon other clinical features of asthma.

Shek L.P. et al. *Genetic susceptibility to asthma and atopy among Chinese in Singapore--linkage to markers on chromosome 5q31-33.* Allergy.

2001; 56(8) : 749-53.p **Abstract:** BACKGROUND: Asthma and atopy are complex genetic traits, influenced by the interaction of multiple genes and environmental factors. Linkage of these traits to chromosome 5q31-33 has been shown in other populations, but has not been well studied in the Chinese. We studied linkage between asthma and atopy with markers on chromosome 5q31-33 in the Singapore Chinese. This region contains many candidate genes, including the cytokine gene cluster. METHODS: We recruited 88 Chinese families with at least two affected offspring, totaling 373 subjects, with 125 and 119 sib-pairs for atopy and asthma, respectively. All individuals were genotyped with 19 polymorphic microsatellite markers spanning a distance of 41 cM along chromosome 5q31-33. Affected sib-pair and multipoint linkage analysis was performed. RESULTS: There was evidence for linkage of the asthma and atopy phenotypes with three markers, D5S2110, D5S2011, and D5S412 (P values of 0.001 to 0.00001). Multipoint analysis further substantiated this (nonparametric linkage scores of 1.8-2.9). These findings suggest that susceptibility genes for asthma and atopy are found in this region in the Chinese. CONCLUSION: This study has shown linkage of atopy and asthma to chromosome 5q31-33 in a heterogeneous Chinese population. These findings further substantiate the notion that chromosome 5q31-33 contains "universally" important susceptibility genes for these traits.

Shellehy D.C. et al. *The effect of a pediatric asthma management program provided by respiratory therapists on patient outcomes and cost.* Heart Lung. 2005; 34(6) : 423-8.p

Abstract: OBJECTIVE: The objective was to determine whether a pediatric asthma disease management program (ADMP) provided by respiratory therapists can improve patient outcomes and reduce cost. DESIGN: This was a pre-and post-intervention observational study. METHODS: Hospitalizations, non-intensive care unit (ICU) hospital days, ICU days, emergency department visits, doctor's office visits, school days missed, and associated costs were collected on 18 children with moderate to severe asthma, ages 3 to 18 years, 12 months before and after implementation of the ADMP. The ADMP consisted of eight home visits for assessment, environmental review, and patient education. RESULTS: There were significant reductions ($P < .05$) in hospitalizations, hospitalization cost, ICU days, non-ICU days, length of stay, emergency department visits and cost, physician office visits and cost, and school days missed. CONCLUSIONS: A pediatric in-home ADMP provided by respiratory therapists can improve outcomes and reduce cost in patients with moderate to severe asthma.

Shen J.J. et al. *The effect of liu-wei-di-huang wan on cytokine gene expression from human peripheral blood lymphocytes.* Am J Chin Med. 2003; 31(2) : 247-57.p

Abstract: Liu-Wei-Di-Huang Wan (LWDHW) has been used by traditional Chinese doctors to treat asthma patients. This study was to examine the potential effect of this decoction on the regulation of T helper (Th)1- and Th2-type cytokine gene expression in vitro. Peripheral blood mononuclear cells (PBMC) were activated with mitogen for 24 hours in the presence or absence of LWDHW extracts. Concentrations of different cytokines in the culture supernatants were determined with ELISA. RNA isolated from cultured cells was subjected to RT-PCR analysis. The results showed that the expression of all cytokines (Th2-type: IL-4, IL-5, IL-10, or IL-13 and Th1-type: IL-2 and IFN-gamma) examined was inhibited at both RNA and protein levels by LWDHW. Since the cell viability was similar in all cultures, the reduction of cytokine production was not due to the toxicity of LWDHW. Moreover, the cells either retained or increased their capacity to respond to mitogen stimulation after incubation with the LWDHW decoction. Therefore, the data suggest that LWDHW functioned directly on cytokine gene expression from activated PBMC.

Shenfield G. et al. *Survey of the use of complementary medicines and therapies in children with asthma.* J Paediatr Child Health. 2002;

38(3) : 252-7.p **Abstract:** OBJECTIVE: To survey the frequency of use of complementary medicines (CM) and complementary therapies (CT) in asthmatic children. **METHODOLOGY:** A 3-month survey of asthmatic inpatients and outpatients of a teaching hospital respiratory paediatrician was undertaken. Parents answered a structured questionnaire about their past and present usage and opinions of CM and CT. Parents and the physician independently assessed overall asthma control. 'Users' and 'non-users' of CM and CT were compared for characteristics of asthma, usage of conventional medications and parental demographics. **RESULTS:** One hundred and seventy-four children with 331 parents were enrolled in the study. All of the children were on bronchodilators and 150 (86.2%) were on disodium cromoglycate or inhaled steroids. Control was assessed by a physician as good in 95 children (54.6%), fair in 65 (37.4%) and poor or very poor in 13 (7.5%). Ninety (51.7%) of the children had used at least one CM in their lifetime. Out of the 145 preparations used, 90 (62.1%) were in current use. Vitamins and minerals (53.2%) and herbal preparations (29%) were used most commonly. Only 47.8% of parents had told their doctors about the use of CM. Costs ranged from \$A2-\$A200 (median \$A10) per month. Forty-three (24.7%) of the children had been taken to an alternative practitioner at a cost of \$A25-\$A400 (median \$A40) per month. Users of CM and CT were significantly more likely than non-users to have persistent asthma ($P < 0.02$), be on high-dose inhaled or oral steroids ($P < 0.05$), to have poor or very poor control of symptoms ($P < 0.04$), and more frequent doctor visits ($P < 0.05$). They also had more adverse reactions to relieving bronchodilators ($P < 0.02$) and were significantly older than non-users ($P < 0.02$). The most common reasons for using CM and CT were dissatisfaction with conventional therapies and concerns about steroid side-effects. **CONCLUSIONS:** Health professionals should be aware of the high rates of usage of CM and CT in asthmatic children and of parental attitudes to conventional and alternative therapies.

Shepherd K. *Inhaler devices for children.* Nurs Times. 2003; 99(11) : 48-9.p **Abstract:** The use of inhaled medicines for the management of asthma is common and is the preferred method of treatment (NICE, 2000a). It is recommended that bronchodilating drugs, such as beta 2-agonists, which provide symptom relief, and anti-inflammatory drugs, such as corticosteroids, are administered by inhalation (NICE 2000a). However, the number of devices available can leave the practitioner and the patient confused about which is the most appropriate inhaler. Guidance from the National Institute for Clinical Excellence states that: 'It is important to ensure that an inhaler device delivers the drugs to the airways consistently and in the appropriate quantity' (NICE, 2000a).

Sherriff A. et al. *Factors associated with different hygiene practices in the homes of 15 month old infants.* Arch Dis Child. 2002; 87(1) : 30-5.p **Abstract:** BACKGROUND: Improved hygiene in Westernised regions of the world may be partly responsible for the increased prevalence of diseases of the immune system, such as asthma and atopy. There is a paucity of data on cleanliness norms in young children in the UK and there has been no attempt to identify factors that influence the adoption of particular hygiene practices in the home. **AIMS:** To examine levels of hygiene in a contemporary cohort of children and identify social and lifestyle factors influencing hygiene practices in the home. **METHODS:** The sample under study are participants in the Avon Longitudinal Study of Parents and Children (ALSPAC). Parental self completion questionnaires provided data on hygiene levels in children at 15 months of age, and a hygiene score was derived from these responses. Multivariable logistic regression models investigated associations between high hygiene scores (top quintile) and a number of perinatal, maternal, social, and environmental factors. **RESULTS:** Maternal smoking during pregnancy, low maternal educational achievement, and living in local authority housing were factors independently associated with high hygiene scores, as was increased use of chemical household products. High hygiene scores were inversely related to living in

damp housing and attendance at day care. There were no gender or ethnic differences in hygiene score. **CONCLUSION:** Important data on cleanliness norms for infants have been presented. The adoption of hygiene practices is influenced to some degree by social, lifestyle, and environmental factors-with higher hygiene scores occurring in more socially disadvantaged groups. Increased use of chemical household products in the more socially disadvantaged groups within ALSPAC has emerged as an important confounder in any study of hygiene and ill health.

Sherriff A. et al. *Hygiene levels in a contemporary population cohort are associated with wheezing and atopic eczema in preschool infants.* Arch Dis Child. 2002; 87(1) : 26-9.p **Abstract:** BACKGROUND: The hygiene hypothesis states that insufficient exposure to certain infectious agents during childhood increases the risk of developing asthma and atopic diseases. Improvements in hygiene levels may be partly responsible for this decline in exposure. **AIMS:** To assess whether hygiene levels in infancy are associated with wheeze and/or atopic eczema, independent of a number of possible confounding factors. **METHODS:** Data were gathered from the Avon Longitudinal Study of Parents and Children (ALSPAC). Parental self completion questionnaires provided symptom data on infant wheeze and atopic eczema at 0-6 months and 30-42 months, respectively. A simple hygiene score was derived using questionnaire responses at 15 months, which ranged from least hygienic to most hygienic. Multivariable logistic regression models analysed the effect of hygiene scores on health outcomes, while adjusting for a number of important confounding variables. **RESULTS:** Increasing hygiene scores were independently associated with wheezing (OR = 1.04; 95% CI: 1.00 to 1.08) and atopic eczema (OR = 1.04; 95% CI: 1.01 to 1.07) between 30 and 42 months, but not in the first six months. The odds ratio was higher for atopic eczema if the rash was reported to have become sore and oozy (OR = 1.09; 95% CI: 1.02 to 1.16). **CONCLUSIONS:** High levels of hygiene at 15 months of age were independently associated with wheeze and atopic eczema reported between 30 and 42 months, and there was an increased risk for children with more severe eczema during this period. The importance of hygiene in public health should not be dismissed; however, the creation of a sterile environment through excessive cleanliness may potentially be harmful to the immune system.

Sherriff J.L. *The role of fats in the lifecycle stages: toddlers to preschool.* Med J Aust. 2002; 176 Suppl : S113-4.p **Abstract:** Toddlers (1-2-year-olds) are in transition from the high-fat diet of infancy to the relatively low-fat diet of preschoolers, school-aged children and adolescents. Toddlers and preschoolers need to be continually encouraged to try a wide range of foods supplying all types of fats, and with the emphasis on nutrient-dense foods. Reduced-fat and skim milks are not appropriate for toddlers, because milk is a major fat source for 1-2-year-olds, but reduced-fat milks are encouraged for preschool-aged children. No solid evidence exists to support the manipulation of dietary fat for the treatment of attention deficit hyperactivity disorder or the prevention and treatment of asthma.

Sherrill D.L. et al. *The relation of rhinitis to recurrent cough and wheezing: a longitudinal study.* Respir Med. 2005; 99(11) : 1377-85.p **Abstract:** BACKGROUND: Recurrent cough can be a clinical manifestation of rhinitis. However, it remains unclear if the association between rhinitis and recurrent cough among children is independent of asthma. **OBJECTIVE:** The aim of the present study was to determine, in a large longitudinal cohort, whether rhinitis is significantly associated with recurrent cough alone, wheezing alone, or the combination of both symptoms during childhood. **METHODS:** We investigated determinants of recurrent cough, with or without wheezing, using longitudinal data from the Tucson Children's Respiratory Study. Among the 1246 subjects originally enrolled, 1024 children completed at least one questionnaire between the ages of 6 and 18 years and were included in the present study. In any

survey, wheezing was defined as at least one wheezing episode during the past year and recurrent cough as two or more coughing episodes lasting at least 1 week without a cold during the past year. Generalized estimating equations were used to determine significant risk factors. RESULTS: After adjusting for sex, skin test reactivity and parental asthma, both rhinitis (OR = 2.47 CI = 1.84, 3.30) and sinusitis (OR = 1.54 CI = 1.11, 2.14) were associated with an increased risk of recurrent cough plus wheezing. The OR associated with rhinitis were significantly reduced for subjects reporting only recurrent cough or only wheezing (OR = 1.43, CI = 1.03, 1.99; and OR = 1.30, CI = 1.07, 1.58, respectively). Recurrent cough and wheezing, when examined independently, showed different patterns of risk factors. CONCLUSION: We found rhinitis to be an independent risk factor for both recurrent cough and wheezing during childhood. Different pathways may be involved in the association of rhinitis with recurrent cough and wheezing.

Sheth K.K. et al. *Concurrent use of intranasal and orally inhaled fluticasone propionate does not affect hypothalamic-pituitary-adrenal-axis function.* Allergy Asthma Proc. 2004; 25(2) : 115-20.p Abstract: Two double-blind, randomized, placebo-controlled, parallel group safety and efficacy studies included evaluation of the hypothalamic-pituitary-adrenal (HPA)-axis effects of concurrent treatment with intranasal and orally inhaled fluticasone propionate (FP). In the first study, patients with asthma who were > or =12 years of age were assigned randomly to receive twice-daily doses (either 88 or 220 microg) of orally inhaled FP delivered from a metered-dose inhaler (MDI). In the second study, patients were assigned randomly to receive either orally inhaled FP 250 microg or orally inhaled FP 250 microg/salmeterol 50 microg delivered via the Diskus device. In both studies, patients with rhinitis were allowed to continue the use of intranasal FP at their usual dosing. Treatment periods were 26 weeks and 12 weeks for the MDI and Diskus studies, respectively. HPA-axis effects were assessed using response to short cosyntropin stimulation testing. The number and percentage of patients with an abnormal cortisol response, defined as a morning plasma cortisol of <5 microg/dL, a poststimulation peak of <18 microg/dL, or a poststimulation rise of <7 microg/dL, were summarized in two subgroups: patients who used intranasal FP and those who did not. The concurrent administration of intranasal FP and orally inhaled FP via an MDI or Diskus or via Diskus with salmeterol was not associated with HPA-axis effects compared with orally inhaled FP alone. The results of these two studies suggest that concurrent use of intranasal FP with orally inhaled FP administered via MDI or Diskus for treatment of comorbid rhinitis and asthma does not increase the risk of HPA-axis abnormalities.

Shields A.E. et al. *Comparing asthma care provided to Medicaid-enrolled children in a Primary Care Case Manager plan and a staff model HMO.* Ambul Pediatr. 2003; 3(5) : 253-62.p Abstract: OBJECTIVE: To examine differences in selected processes of asthma care provided to Medicaid-enrolled children in a state-administered Primary Care Case Manager (PCCM) plan and a staff model health maintenance organization (HMO). METHODS: Retrospective cohort study assessing performance on 6 claims-based processes of care measures that reflect aspects of pediatric asthma care recommended in national guidelines. Analyzed Medicaid and HMO claims and encounter data for 2365 children with asthma in the Massachusetts Medicaid program in 1994. RESULTS: There were no plan differences in asthma primary care visits, asthma pharmacotherapy or follow-up care after asthma hospitalization. Children in the HMO were only 54% as likely (confidence interval [CI]: 0.37-0.80; P<.01) as those in the PCCM plan to experience an asthma emergency department (ED) visit or hospitalization. HMO-enrolled children were only half as likely (CI: 0.38-0.64; P<.001) to meet the National Committee for Quality Assurance (NCQA) definition for persistent asthma and only 32% as likely (CI: 0.19-0.56; P<.001) to have prior asthma ED visits or hospitalizations relative to children in the PCCM plan. Controlling for case mix and

other covariates, children in the HMO were 2.9 times as likely (CI: 1.09-7.78; P<.05) as children in the PCCM plan to receive timely follow-up care (within 5 days) after an asthma ED visit and 1.8 times as likely (CI: 1.05-3.01; P<.05) as those in the PCCM plan to receive a specialist visit during the year. CONCLUSIONS: In this study, the HMO served a less sick pediatric asthma population. After controlling for case mix, the staff model HMO provided greater access to asthma specialists and more timely follow-up care after asthma ED visits relative to providers in the state-administered PCCM plan. Further understanding of the impact of these differences on clinical outcomes could guide asthma improvement efforts.

Shima M. et al. *Effects of air pollution on the prevalence and incidence of asthma in children.* Arch Environ Health. 2002; 57(6) : 529-35.p Abstract: The effects of air pollution on asthmatic symptoms were assessed in a prospective cohort study of 3,049 schoolchildren in 8 different communities in Japan. Respiratory symptoms in these children were evaluated by questionnaires every year from the 1st through the 6th grades. The prevalence of asthma among the 1st graders was strongly associated with a history of allergic or respiratory diseases, but it was not associated with concentrations of air pollution. During the follow-up period, incidence rates of asthma were associated significantly with atmospheric concentrations of nitrogen dioxide. Particulate matter less than 10 microm in diameter (PM10) was also associated with a higher incidence of asthma, although the association was not significant. These findings suggest that air pollution, including nitrogen dioxide, may be an important factor in the development of asthma among children in urban districts.

Shin H.D. et al. *Association of Eotaxin gene family with asthma and serum total IgE.* Hum Mol Genet. 2003; 12(11) : 1279-85.p Abstract: The Eotaxin gene family (Eotaxin1, Eotaxin2 and Eotaxin3) recruits and activates CCR3-bearing cells such as eosinophils, mast cells and Th2 lymphocytes that play a major role in allergic disorders. To date, the effect of polymorphisms of Eotaxin genes on asthma phenotypes has not been thoroughly examined. In our research, we sequenced whole regions of the Eotaxin gene family to identify polymorphisms, which may be involved in the development of asthma and total serum IgE. We have identified 37 SNPs in the Eotaxin gene family (Eotaxin1, 2 and 3), and 17 common polymorphic sites were selected for genotyping in our asthma cohort (n=721). Statistical analysis revealed that the EOT2+1265A>G G* allele showed significantly lower frequency in asthmatics than in normal healthy controls (0.14 versus 0.23, P=0.002), and that distribution of the EOT2+1265A>G G* allele-containing genotypes was also much lower in asthmatics (26.3 versus 40.8%, P=0.003). In addition, a non-synonymous SNP in Eotaxin1, EOT1+123Ala>Thr showed significant association with total serum IgE levels (P=0.002-0.02). The effect of EOT1+123Ala>Thr on total serum IgE appeared in a gene-dose-dependent manner. Our findings suggest that the development of asthma may be associated with EOT2+1265A>G polymorphisms, and the susceptibility to high IgE production may be attributed to the EOT1+123Ala>Thr polymorphism. Eotaxin variation/haplotype information identified in this study might provide valuable insights into strategies for the control of asthma.

Shin H.D. et al. *Association of tumor necrosis factor polymorphisms with asthma and serum total IgE.* Hum Mol Genet. 2004; 13(4) : 397-403.p Abstract: Tumor necrosis factors (TNF; TNFA and TNFB) are major pro-inflammatory cytokines that are thought to be important in the pathogenesis of asthma. However, the functions of genetic polymorphisms in these cytokines have not been thoroughly examined in the context of asthma pathology. In an effort to discover polymorphism(s) in genes whose variant(s) have been implicated in asthma phenotypes, we examined the genetic effects of TNF (TNFA and TNFB) polymorphisms on asthma and total serum IgE level. Seven common single-nucleotide polymorphisms (SNP) in TNF

genes were genotyped in a Korean asthma cohort (asthmatics n=550, normal controls n=171). Six common haplotypes could be constructed in the TNF gene cluster due to very strong LD between TNFA and TNFB, located 13 kb apart on chromosome 6p21. One SNP (TNFA-308G>A) showed a significant association with the risk of asthma (P=0.0004). The frequency of TNFA-308A allele-containing genotype in asthmatics (9.8%) was much lower than that in normal controls (22.9%). The protective effects of this polymorphism on asthma were also evident in separated subgroups by atopic status (P=0.05 in non-atopic subjects and P=0.003 in atopic subjects). The most common haplotype of the TNF gene (TNF-h1[GGTCCGG]) was associated with total serum IgE (immunoglobulin E) levels in asthma patients, especially in non-atopic patients (P=0.004). Genetic variants of TNF might be involved in development of asthma and total serum IgE level in bronchial asthma patients. The results of this study could be helpful to understand the function of important TNF genes in asthma and IgE production.

Shin J.W. et al. *Atopy and house dust mite sensitization as risk factors for asthma in children.* Yonsei Med J. 2005; 46(5) : 629-34.p **Abstract:** Asthma is commonly described as an atopic disease in childhood, but some cases of this disorder do not fit this description. The aim of this study was to evaluate the frequency of atopy, asthma, and sensitization to house dust mites in children with allergic symptoms. This study was performed at the Severance Hospital of Yonsei University with patients who visited the allergy clinic for evaluation of nonspecific upper respiratory symptoms, typical symptoms of asthma, or a general health workup. The patients were divided into three age groups: 0-3 years (group 1), 4-7 years (group 2), and 8-12 years (group 3). Of the 1,244 children examined, 844 (67.8%) were atopic and 400 (32.2%) were non-atopic. The frequency of atopy and asthma increased with age. Asthma was diagnosed in the same proportion (64%) of atopic and non-atopic children. As risk factors for asthma symptoms, the positive values of house dust mite (HDM) sensitivity were significantly increased in groups 1, 2, and 3 to 53.5%, 68.9%, and 80.2%, respectively. A significant difference between the percentage of asthmatics sensitized to HDM and that of asthmatics not sensitized to HDM was found only in group 3. In conclusion, asthma is related to atopy with increasing age, and house dust mite sensitization seems to be an important determinant of asthma in older children in Korea.

Shrewsbury S. et al. *Salmeterol 100 microg: an analysis of its tolerability in single- and chronic-dose studies.* Ann Allergy Asthma Immunol. 2001; 87(6) : 465-73.p **Abstract:** **BACKGROUND:** A combination product containing fluticasone propionate 100 or 250 microg and salmeterol 50 microg has recently been made available in the United States. Some patients, if previously instructed to double their inhaled corticosteroids, may double this product, inadvertently receiving higher doses of salmeterol, potentially causing systemic beta2-agonist-related effects. **OBJECTIVES:** To examine the systemic effects of single and chronic doses of salmeterol 100 microg. **METHODS:** Forty-four studies including a salmeterol 100 microg treatment arm were identified. Data on predictable systemic effects were available in 10 single-dose and 9 chronic-dose studies lasting more than 7 days, in patients with asthma (6 adult, 2 pediatric) or chronic obstructive pulmonary disease (1 study), which were included in a weighted, pooled analysis. **RESULTS:** Single 100-microg dose studies: mean change from baseline in heart rate was +2.3 beats per minute and systolic blood pressure +0.4 mm Hg. Tremor and palpitations were reported in 5.7% and 2.8%. Other systemic effects included a decrease in serum potassium for 3 subjects (2.1%); an increase in serum glucose, 1 subject (0.7%); and electrocardiographic (ECG) events, 24 cases (17.0%). Twenty-three of these were from one crossover study which reported 27 ECG events after placebo. Chronic dose studies (salmeterol 100 microg): mean change in heart rate and systolic blood pressure were +1.8 beats per minute and -0.2 mm Hg. Tremor and palpitations were

reported in 5.6% and 1.7% of 1,504 patients. Thirteen recorded a decrease in serum potassium (0.9%) and 5 an increase in serum glucose (0.3%). Nine patients had ECG events (0.6%). Eight of these were "arrhythmia" from one study, which also reported 12 events before treatment. **CONCLUSIONS:** The mean systemic effects of salmeterol 100 microg are small and of doubtful clinical relevance. Patients (and their caregivers) can be reassured that inadvertently taking double doses of the new combination product are unlikely to affect them adversely.

Shute N. *Rx squalor?* US News World Rep. 2002; 133(12) : 76.p

Sicherer S.H. et al. *The impact of childhood food allergy on quality of life.* Ann Allergy Asthma Immunol. 2001; 87(6) : 461-4.p **Abstract:** **BACKGROUND:** Food allergy affects >6% of children, but the impact of this disease on health-related quality of life has not been well studied. **METHODS:** Parental perceptions of physical and psychosocial functioning were measured with the Children's Health Questionnaire (CHQ-PF50). This tool and an additional allergy-related questionnaire were sent to 400 members of the Food Allergy and Anaphylaxis Network with children aged 5 to 18, an age group on which the tool has been validated. **RESULTS:** Surveys were completed by 253 parents (63%). The mean age of the food-allergic children was 10.8 years (range, 5 to 18 yrs); 59% were male. Sixty-eight percent were allergic to one or two foods, the remainder to more than two foods. Concomitant chronic atopic diseases included: asthma with atopic dermatitis (33%), atopic dermatitis alone (13%), asthma alone (33%), and 21% had neither asthma nor atopic dermatitis. In comparison to previously established norms, the families scored significantly lower (more than 10 scale score points lower and P < 0.0001) for general health perception (GH), emotional impact on the parent (PE), and limitation on family activities (FA). Associated atopic disease, influenced primarily by those with both asthma and atopic dermatitis, accounted for a significant reduction in the GH scale (analysis of variance, P = 0.0001), but not for measures of PE and FA. Within the study group, food-allergic individuals with several (more than two) food allergies had significantly lower (P < 0.05) scores for 7 of 12 scales compared with individuals with few (one or two) food allergies. However, those with one or two food allergies scored significantly lower (P < 0.0001) than established norms on scales for GH, PE, and FA. **CONCLUSIONS:** Childhood food allergy has a significant impact on GH, PE, and FA. Factors that influence reductions in these scales include associated atopic disease and the number of foods being avoided.

Sidorchuk A. et al. *Epstein-Barr virus infection is not associated with development of allergy in children.* Pediatr Infect Dis J. 2003; 22(7) : 642-7.p **Abstract:** **BACKGROUND:** Differences in concentrations of antibodies to Epstein-Barr virus (EBV) in atopic and nonatopic children have been observed, suggesting that EBV infection may play a role in allergic diseases. **AIM:** To assess the association between EBV infection and atopy in Swedish children at 4 years of age. **MATERIALS AND METHODS:** Were studied 2561 children born in 1994 through 1996 in Stockholm, Sweden. The children were enrolled in a prospective birth cohort study focusing on the relation of exposure to various environmental and life style factors during early childhood and development of atopy. Blood samples were obtained when the children were approximately 4 years old, and immunoglobulin G to EBV was determined by indirect immunofluorescence. The relationship between the seroprevalence to EBV and various allergic disorders was assessed, with the use of logistic regression analysis to account for other risk factors. **RESULTS:** Totally 1347 of 2561 (52%) children were EBV-seropositive. Associations between EBV seropositivity and the occurrence of asthma [adjusted odds ratio (OR(adj)), 1.10; 95% confidence interval (95% CI) 0.81 to 1.49] or suspected allergic rhinitis (OR(adj) 0.97; 95% CI 0.76 to 1.25) were not apparent. In children whose mothers were up to 25 years old, a higher EBV seroprevalence was observed than in children of older mothers

(OR(adj) 1.34; 95% CI 1.04 to 1.71). Also in children whose mothers smoked, the seroprevalence was higher than in children of nonsmokers (OR(adj) 1.29; 95% CI 1.02 to 1.63). **CONCLUSIONS:** The study does not support the hypothesis that EBV infection in early childhood plays an important role in the pathogenesis of allergic diseases in children.

Sienra-Monge J.J. et al. [The quality of life of the asthmatic child caregiver]. *Gac Med Mex.* 2004; 140(2) : 139-45.p **Abstract:** Despite better understanding of the pathophysiology of asthma, the application of better drugs (potent anti-inflammatory medications and beta2 adrenergics with long-lasting effects), some symptoms persist and the illness itself, at the same time with exacerbation, may compromise the integrity of the patient. This calls for an evaluation of the impact of the ailment in different aspects of daily life of patients and of his/her caregivers. To address these situations, quality-of-life questionnaires for patients and caregivers were designed. With this study, our objective was to make up a quality-of-life questionnaire to be filled out by caregivers of asthmatic children treated with one of two therapeutic schemes: with inhaled steroids (EI), or the EI plus prolonged action bronchodilator (BAP). **MATERIALS AND METHODS:** Controlled, experimental, and comparative clinical trial polling asthmatic child caregivers, applying a questionnaire designed by Elizabeth Juniper (PACQLQ). Patients and caregivers were randomized in two groups: group A was treated with IE (Beclomethasone) plus BAP (Salmeterol) during a 6-week period, followed by a 2-week wash-out period followed by a 6-week period with only IE. Group B were treated only with EI followed by a 2-week period of wash-out and a six-week period with IE plus BAP. Caregivers filled in the questionnaires at the beginning, and at second, fourth, and sixth weeks of treatment. **RESULTS:** We included 30 patients and their caregivers who were randomized in two groups. Values in every group showed significant improvement in quality of life, as compared to basal values. Values between groups showed greater improvement in groups who received EI plus BAP at the beginning. **CONCLUSIONS:** Our study shows that administering treatment for asthma improves significantly the caregiver's appreciation of quality of life with respect to the PACQLQ questionnaire. The group that received EI therapy plus BAP at the beginning showed greater improvement. These results coincide with those published to date. We recommend the use of questionnaires at the beginning of the treatment as part of the integral evaluation of every patient with asthma.

Sigurs N. Case 2: assessment. A 7.5-year-old boy with respiratory syncytial virus. *Paediatr Respir Rev.* 2002; 3(3) : 273-4.p

Silkoff P.E. Monitoring nitric oxide: here to stay for bench and bedside. *Eur Respir J.* 2005; 25(6) : 949-50.p

Silkoff P.E. et al. Single-breath exhaled nitric oxide in preschool children facilitated by a servo-controlled device maintaining constant flow. *Pediatr Pulmonol.* 2004; 37(6) : 554-8.p **Abstract:** Fractional concentration of exhaled nitric oxide (FENO), an index of airway inflammation, is optimally measured in adults and school-age children using a single-breath online (SBOL) exhalation at constant flow. However, preschool-aged (<6 years old) children have difficulty exhaling at constant flow, and alternative methods are needed. We employed a servo-controlled variable resistance device (servo device) that controls expiratory flow while allowing the child to vary expiratory pressure. To validate this device, 8 children (aged 6-12 years) performed SBOL exhalations with and without the servo device at expired flow rates between 20-50 ml/sec. We then studied 32 young children aged 24-71 months with the servo device alone at exhalation flows of 30, 40, and 50 ml/sec. Test difficulty (TD) with each method was rated by questioning the older children, or as observed by the physician obtaining the data in the younger children (0 = no difficulty, 1 = mild difficulty, 2 = moderate difficulty, and 3

= unable to perform test). In the older children, SBOL exhalations with and without the servo device demonstrated equivalent flow-dependence of FENO values. Test difficulty was low (0.125-0.625) at all flow rates, with excellent agreement between the two methods ($P < 0.001$). Twenty-eight young children (<6 years old) were able to complete measurements at all three flow rates evaluated. The 4 subjects who were not able to successfully complete all the measurements were between 2-3 years old (mean 2.75 +/- SD). Exhaled NO (mean +/- SD; ppb) was 8.8 (+/-6.2), 10.6 (+/-6.7), and 13.2 (+/-8.8) ppb at flows of 50 ml/sec, 40 ml/sec, and 30 ml/sec, respectively. Mean values of SD scores were 1.00, 1.14, and 1.43 at flows of 50, 40, and 30 ml/sec, respectively ($P = NS$). In conclusion, exhaled NO measurement by the SBOL method was facilitated in preschool children by the use of a servo-controlled variable resistance device. This device may allow these measurements to be applied to aid in the diagnosis and treatment of asthma in the preschool child, where spirometry is generally impossible.

Siltanen M. et al. Respiratory symptoms and lung function in relation to atopy in children born preterm. *Pediatr Pulmonol.* 2004; 37(1) : 43-9.p **Abstract:** Respiratory morbidity is a major health problem among children. The aim of this study was to compare the background of respiratory problems of children born preterm with that of children born full-term, with special reference to atopy. The study comprised two cohorts of 10-year-old children: a group of 72 children born preterm with birth weights of less than 1,501 g, and a group of 65 children born full-term with birth weights of over 2,500 g. Histories of respiratory and atopic symptoms, and of risk factors for atopy, were collected with a questionnaire. Predisposition to atopy was verified by skin-prick testing and by measuring serum total and antigen-specific IgEs. Lung function was evaluated by spirometry testing. Children born preterm had significantly more wheezing. In them, the lifetime prevalence of wheezing was 43%, vs. 17% in children born full-term ($P = 0.001$; odds ratio, 3.71; 95% confidence interval, 1.67-8.25). In the full-term group, wheezing was associated with atopy: 64% of wheezers were atopic; in the preterm group, 23% of wheezers were atopic (difference between groups, $P = 0.024$). Children born preterm expired significantly lower spirometry values of forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), FEV1/FVC ratio, forced expiratory flow after 50% of vital capacity has been exhaled (FEF50), and forced expiratory flow during middle half of FVC (FEF25-75). In the preterm group, wheezing, asthma, and low gestational age, but not atopy, were significantly associated with lower lung function values. Wheezers of the preterm group who still wheezed at age 10 were significantly more often atopic than those who no longer wheezed (62% vs. 9%, $P = 0.006$). In conclusion, we demonstrated a significant difference between groups in the association of atopy with respiratory problems. However, although atopy was not associated with a lifetime prevalence of respiratory symptoms in prematurely born children, an atopic predisposition in them was found to associate with persistence of wheezing.

Silva D.A. et al. A sensitive reverse ELISA for the measurement of specific IgE to Der p 2, a major Dermatophagoides pteronyssinus allergen. *Ann Allergy Asthma Immunol.* 2001; 86(5) : 545-50.p **Abstract:** **BACKGROUND:** Epidemiologic studies have shown that the presence of IgE antibodies to house dust mite and other indoor allergens is an important risk factor for asthma. **OBJECTIVE:** The aim of this study was to develop a reverse ELISA (rELISA) for measuring specific IgE to Der p 2, a major Dermatophagoides pteronyssinus (Dpt) allergen, as a potential tool for followup of allergen immunotherapy. **METHODS:** Recombinant Der p 2 allergen or a monoclonal antibody to Der p 2 was used to coat plates in conventional ELISA (cELISA) and rELISA, respectively. Sera from 48 asthmatic patients with positive skin prick test (SPT+) to D. pteronyssinus extract were analyzed for total IgE and specific IgE to Der p 2, and the results were compared with a group of 41 SPT- asthmatic and 30 SPT- control subjects. **RESULTS:** The sensitivity

of the two assays for Der p 2-specific IgE was 3.9 EU/mL and their specificities were confirmed by inhibition tests, in a dose-dependent manner. There was a significant positive correlation between cELISA and rELISA ($r = 0.74$; $P < 0.0001$). However, rELISA was more sensitive than was cELISA, regarding both the positive sera percentage (70.8% vs 52.1%) and the Der p 2-specific IgE levels (28.4 vs 4.5 EU/mL) in SPT+ asthmatic patients. **CONCLUSIONS:** rELISA has shown to be a sensitive and alternative method for measuring Der p 2-specific IgE without using radioactive techniques. Detection of specific IgE to major allergens and relevant peptides, and identification of B cell epitopes in allergens will provide valuable information for the design of allergen analogs and peptides for immunotherapy.

Silver E.J. et al. *The relationship of caretaker anxiety to children's asthma morbidity and acute care utilization.* *J Asthma.* 2005; 42(5) : 379-83.p **Abstract:** **OBJECTIVES:** This study examined self-reported psychological distress in caretakers of inner-city children with asthma and examined its association to disease severity, as measured by day and night symptoms, and to acute care utilization for asthma. **METHOD:** We enrolled 193 English and Spanish-speaking caretakers (86% were mothers) of 2- to 12-year-olds who had at least one asthma hospitalization at a large urban medical center. They completed an interview asking about children's asthma symptoms and acute care utilization (provider visits, emergency department visits, hospitalizations for asthma) and a 29-item psychiatric symptom inventory. National guidelines criteria were used to classify asthma severity into three categories based on caretaker report of day and night symptoms in the past 4 weeks. These were: moderate-severe persistent (37%), mild persistent (27%), and mild intermittent (35%) asthma. **RESULTS:** Caretakers of children who were reported as having moderate-severe persistent asthma symptoms exhibited higher anxiety than caretakers reporting milder symptoms in their children, but symptom severity was unrelated to depression, anger, cognitive disturbance, or overall distress in caretakers. Three measures of acute care utilization in the last 6 months increased with reported symptom severity, but they were not associated with caretaker distress. **CONCLUSIONS:** Providers treating children with asthma should consider the potential importance of caretaker reports of daily symptoms both for the child's physical functioning and for parental anxiety.

Silverman R.A. et al. *The relationship of fall school opening and emergency department asthma visits in a large metropolitan area.* *Arch Pediatr Adolesc Med.* 2005; 159(9) : 818-23.p **Abstract:** **BACKGROUND:** Asthma morbidity is seasonal, with the fewest exacerbations occurring in summer and the most exacerbations in early fall. **OBJECTIVE:** To determine if the fall increase in pediatric asthma emergency department (ED) visits is related to the school year start. **DESIGN:** Time-series study of daily asthma ED visits taken from an administrative claims database for the years 1991 to 2002. **SETTING:** Eleven municipal hospitals in New York City, NY. Patients Emergency department visits with asthma as the primary diagnosis among children aged 2 to 4, 5 to 11, and 12 to 17 years and adults with asthma aged 22 to 45 years as comparative group. **Main Outcome Measure** Rate of asthma ED visits after the September school opening compared with before the opening, during a 60-day window of each year. The delayed effect of school opening was examined by the lagged school-opening indicator for lag 0 through 9 days. The model adjusted for factors that may influence morbidity. There were 86 731 ED visits within the study period. **RESULTS:** Asthma ED visits for children aged 5 to 11 years were significantly associated with school opening day, with the highest lagged rate ratio being 1.46 (95% confidence interval [CI], 1.29-1.65). For children aged 2 to 4 years, the highest rate ratio was 1.19 (95% CI, 1.06-1.35), and for children aged 12 to 17 years, the highest lagged rate ratio was 1.13 (95% CI, 0.98-1.31). The rise in adult ED visits following school opening was less substantial, with the highest lagged rate ratio being 1.07 (95% CI, 1.00-1.14). **CONCLUSION:** The start of the

September school year was associated with increases in pediatric asthma ED visits, particularly among grade school children.

Silverman R.A. et al. *Zafirlukast treatment for acute asthma: evaluation in a randomized, double-blind, multicenter trial.* *Chest.* 2004; 126(5) : 1480-9.p **Abstract:** **CONTEXT:** Acute asthma causes nearly 2 million hospital emergency department (ED) visits in the United States annually, and hospitalization after an ED visit and relapse after ED discharge are common. **OBJECTIVE:** To evaluate the adding of therapy with zafirlukast to standardized care for patients with acute asthma in the ED and a 28-day follow-up period. **DESIGN AND PATIENTS:** A total of 641 patients presenting to the ED with acute asthma were randomized to receive either single-dose zafirlukast, 160 mg (Z160) [162 patients], zafirlukast, 20 mg (Z20) [158 patients]), or placebo (321 patients) as adjunct treatment to standard care in this double-blind, multicenter trial. Assessments, including spirometry and symptom scores, were obtained before each albuterol treatment and at 4 h. Patients who were discharged from the ED after 4 h continued outpatient therapy over a 28-day period and received either Z20 bid (276 patients) or placebo (270 patients) in addition to prednisone, albuterol, and their previous asthma medications. FEV(1) was measured at clinic visits on days 10 and 28. Patients recorded outpatient clinical data twice daily on a home diary card. **MAIN OUTCOME MEASURES:** the effect of zafirlukast on relapse after ED discharge. Other assessments were the rate of extended care (ie, ED stay for > 4 h or hospitalization), FEV(1), and symptoms. **RESULTS:** At the end of the outpatient period, 65 of 276 patients (23.6%) treated with zafirlukast and 78 of 270 patients (28.9%) treated with placebo relapsed ($p = 0.047$; absolute reduction, 5.3%; relative reduction, 18.3%). At the end of the ED period, 16 of 162 patients (9.9%) treated with Z160, 26 of 158 patients (16.5%) treated with Z20, and 48 of 321 patients (15.0%) treated with placebo required extended care ($p = 0.052$; absolute reduction with Z160 compared to placebo, 5.1%; relative reduction, 34%). These findings were supported by a significant improvement in FEV(1) and dyspnea in the ED with the use of Z160 therapy, and by greater improvement in FEV(1) and symptoms during the outpatient period for patients treated with Z20. **CONCLUSIONS:** When added to standardized care, therapy with Z20 bid reduced the risk of relapse compared with placebo over a 28-day treatment period. One dose of Z160 in the ED also reduced the rate of extended care.

Silverman R.A. et al. *Age-related seasonal patterns of emergency department visits for acute asthma in an urban environment.* *Ann Emerg Med.* 2003; 42(4) : 577-86.p **Abstract:** **STUDY OBJECTIVE:** Asthma morbidity is greater in younger patients. The reasons are not fully understood, although identifying demographic patterns of seasonality may help determine causes and potential prevention. The objective of this study is to determine the relationship between age and seasonal asthma periodicity in patients presenting to the emergency department (ED). **METHODS:** We conducted a retrospective study of ED visits from 1991 to 2000 in 11 municipal hospitals in New York City, with 911 receiving facilities. There were 673,141 patients who presented to the ED during the study period and had a primary diagnosis of acute asthma. **RESULTS:** Distinct seasonal patterns were observed, with the highest number of visits occurring in the fall and the fewest in the summer. Seasonal fluctuations of ED visits were highest in children aged 13 years or younger (coefficient of variation [CV] 37.8%; 95% confidence interval [CI] 37.5% to 38.1%), with a peak in CV occurring at approximately age 7 years (CV 43.3%; 95% CI 43.0% to 43.6%). Less variability was noted with increasing age, and the population aged 30 years and older appeared to be the least susceptible to seasonal influences (CV 11.7%; 95% CI 11.3% to 12.1%). Although the total number of asthma visits decreased by more than 30% from 1991 to 2000, the CVs for each year remained within a relatively narrow range of 24.2% to 30.5%. **CONCLUSION:** In an urban population, seasonal variability of asthma episodes requiring ED visits are closely linked to age, which may be important

in understanding the causes of asthma and developing disease-management strategies for the prevention of asthma episodes.

Silverstein M.D. et al. *School attendance and school performance: a population-based study of children with asthma.* J Pediatr. 2001; 139(2) : 278-83.p **Abstract:** OBJECTIVE: To analyze school attendance and school achievement as outcomes of the care of children with asthma. METHODS: A previously identified Rochester, Minnesota, cohort of children with asthma and age- and sex-matched children without asthma were studied. School attendance, standardized achievement test scores, grade point average, grade promotion, and class rank of graduating students for children with asthma and control subjects were obtained from the Rochester Public School system. RESULTS: Children with asthma (n = 92) and age- and sex-matched non-asthmatic control subjects with 640 school-years of observation were studied. Children with asthma had 2.21 (95% CI, 1.41 to 3.01) more days absent than children without asthma. There was no significant difference in standardized achievement test scores (reading percentile difference 1.22% [95% CI, -3.68 to 6.12], mathematics percentile difference 2.36% [95% CI, -2.89 to 7.60], language percentile difference 2.96% [95% CI, -4.03 to 7.15]). There was no significant difference in grade point average, grade promotion, or class rank of graduating students. CONCLUSION: In this community, although children with asthma had 2 excess days of absenteeism, the school performance of children with asthma was similar to that of children without asthma.

Silvestri M. et al. *How can we best read exhaled nitric oxide flow curves in asthmatic children?* Monaldi Arch Chest Dis. 2001; 56(5) : 384-9.p **Abstract:** Orally exhaled nitric oxide (NO) levels are increased in children with asthma and thought to reflect the local inflammatory events in the airways. NO production in the lower respiratory airway is reflected in the plateau values of the NO curve, recorded while the patient is performing a slow vital capacity manoeuvre. In young patients, however, plateau values may be difficult to obtain, because the slow vital capacity manoeuvre is often terminated prematurely. In the present study, 60 steroid-naïve atopic asthmatic children and 17 normal age-matched controls were asked to perform a slow vital capacity manoeuvre, during which fractional exhaled NO (F_{Eno}) levels were measured and evaluated as: a) F_{Eno} plateau levels of last part of exhalation (NO plateau); b) F_{Eno} peak values, c) area under the F_{Eno} curve (AUC). Thirteen out of the 60 steroid-naïve patients were reevaluated after a short course of inhaled corticosteroid treatment. Independently of the type of data analysis, F_{Eno} values of asthmatics were significantly higher than those observed in normal controls (P < 0.001, each comparison). In addition, possibly because of upper airway NO contamination, F_{Eno} peak values were significantly higher than F_{Eno} plateau levels in asthmatic patients and in control subjects (P < 0.001, each comparison). Both in asthmatics and controls, highly positive correlations were observed between: a) F_{Eno} plateau and peak values (r > 0.7, P < 0.01, each correlation), b) F_{Eno} plateau and AUC values (r > 0.7, P < 0.01, each correlation) and c) F_{Eno} peak and AUC values (r > 0.9, P < 0.001, each correlation). In asthmatic patients, the three types of data analysis were equally sensitive in detecting the decrease in F_{Eno} levels induced by inhaled steroid therapy (P < 0.05, each comparison), with a good correlation between the three data analyses (r > 0.5, P < 0.05, each correlation). Thus, although quantitatively different, comparable data reflecting airway inflammation can be obtained evaluating F_{Eno} plateau, F_{Eno} peak, and area under the curve, on account of possible upper airway contamination in F_{Eno} peak, F_{Eno} plateau should be preferred to measure lower airway NO production.

Sim D. et al. *Adrenal suppression from high-dose inhaled fluticasone propionate in children with asthma.* Eur Respir J. 2003; 21(4) : 633-6.p **Abstract:** This cross-sectional study was designed to examine the prevalence of adrenocortical suppression in children with asthma

treated with high-dose inhaled fluticasone propionate (FP). Children and adolescents (n=50) with asthma, treated with inhaled FP at a dose of > or = 1,000 mg a day for > or = 6 months, were enrolled. Early morning serum cortisol was performed. Subjects with a serum cortisol of < 400 nmol x L(-1) had a tetracosactrin stimulation test. Fifty subjects of mean age 13.1 yrs were treated with a mean dose of 924.7 microg x m(-2) x day(-1) FP for a mean duration of 2 yrs. Of the 50 subjects, 36 (72%) had serum cortisol levels of < 400 nmol x L(-1) and underwent tetracosactrin stimulation test. Of these, 6 (17%) demonstrated a less than two-fold increase in serum cortisol from baseline and peak cortisol level of < or = 550 nmol x L(-1) at 30 or 60 min poststimulation. There was a significant negative correlation between the dose of FP x m(-2) and stimulated peak cortisol level. Biochemical evidence of adrenocortical insufficiency was demonstrated in 12% of the subjects, indicating that high-dose fluticasone propionate use may be associated with dose-dependent adrenocortical suppression.

Simons F.E. *H1-antihistamines in children.* Clin Allergy Immunol. 2002; 17 : 437-64.p **Abstract:** In children, as in adults, H1-antagonists are useful in the treatment of allergic rhinoconjunctivitis. Level 1 evidence for their efficacy in this disorder has been obtained in many well-designed pediatric studies. The widespread use of H1-antagonists in upper respiratory tract infections or otitis media in children is not supported by a strong scientific rationale. H1-antagonists are not harmful in children with asthma and, indeed, may have some beneficial effects in children with mild asthma. Their role in delaying or preventing asthma from developing in high-risk infants and toddlers is currently an important area of clinical investigation. The evidence base for their use in children with urticaria or atopic dermatitis still contains large gaps. First-generation H1-antagonists are presumed to be safe for use in infants and children. While they have undoubtedly been administered without apparent harm to millions in this age group, they impair CNS function far more commonly than is generally realized. Their use should be restricted to two uncommon situations: children with urticaria or atopic dermatitis whose pruritus is so severe that the sedation produced by an old H1-antagonist, such as hydroxyzine, is a benefit rather than a risk; and children with anaphylaxis who require intravenous diphenhydramine as adjunctive treatment to epinephrine and other modalities. Apart from these exceptions, in patients of all ages, second-generation H1-antagonists free from CNS adverse effects are clearly the medications of choice. Pediatric formulations of the new H1-antagonists cetirizine, fexofenadine, and loratadine are now available for use.

Simpson A. et al. *The role of allergen avoidance in primary and secondary prevention.* Pediatr Pulmonol Suppl. 2004; 26 : 225-8.p

Simpson A. et al. *Skin test reactivity to natural and recombinant Blomia and Dermatophagoides spp. allergens among mite allergic patients in the UK.* Allergy. 2003; 58(1) : 53-6.p **Abstract:** BACKGROUND: Many asthmatics in tropical and subtropical areas have positive skin prick tests to both Dermatophagoides spp. and to the mite Blomia tropicalis. This may be due to recognition by IgE of cross-reactive allergens between the different mite species or because of sensitization to species-specific allergens. A 14-kDa Blomia tropicalis allergen, Blo t 5, has been cloned and shows 40% sequence homology with Der p 5. The aim of this study was to investigate reactivity to B. tropicalis in patients known to be sensitized to D. pteronyssinus and to assess allergenic activity and cross-reactivity of recombinant (r) Group 5 allergens amongst these patients, who live in the UK and who are not exposed to B. tropicalis in their homes. METHODS: Patients (n = 19) with asthma and/or rhinitis were selected based on clinical history and a positive skin prick test to D. pteronyssinus extract and were compared with non-allergic skin test negative controls (n = 10). IgE antibody responses to Blomia tropicalis, Dermatophagoides pteronyssinus, rDer p 5 and rBlo t 5 were compared by quantitative intradermal skin testing using serial

10-fold dilutions of each allergen. End point titre was the highest dilution giving an 8 x 8 mm wheal at 15 min. IgE antibodies to *Blomia tropicalis*, *Dermatophagoides pteronyssinus*, rDer p 5 and rBlo t 5 were measured using RAST, CAP and RIA, respectively. RESULTS: All 19 patients had positive skin tests to *D. pteronyssinus* at concentrations of 0.001 to 1 AU/ml and 10 were skin test positive to rDer p 5 at concentrations of 10-4 to 5 micro g/ml. Positive intradermal tests to *Blomia tropicalis* were seen in 12/19 patients at concentrations of 0.002 to 2 micro g/ml. However none of the patients had positive skin tests to rBlo t 5. Non-allergic controls were all skin test negative at the highest concentration of each allergen tested. All subjects had quantifiable specific IgE to *D. pteronyssinus*, but only two had IgE to *B. tropicalis*. IgE to Der p 5 was found in six patients, but no patients had IgE to Blo t 5. CONCLUSIONS: This study of patients naturally exposed to *D. pteronyssinus* but not to *Blomia tropicalis*, provides evidence for IgE mediated cross-reactivity between allergens produced by both mite species. The results suggest that the Group 5 allergens of *D. pteronyssinus* and *B. tropicalis* are species-specific.

Simpson T. et al. *Four-year-old with cough and wheeze.* *Pediatr Nurs.* 2005; 31(6) : 494-5.p

Sin D.D. et al. *Spirometric findings among school-aged First Nations children on a reserve: a pilot study.* *Can Respir J.* 2004; 11(1) : 45-8.p **Abstract:** BACKGROUND: Asthma and chronic obstructive pulmonary disease (COPD) are increasing concerns for First Nations peoples in Canada. Although hospital utilization for asthma and COPD among First Nations peoples has been increasing, the prevalence of asthma or wheezing is comparable to national averages. OBJECTIVES: A pilot study was conducted to determine the prevalence of impaired lung function in school-aged First Nations children. PATIENTS AND METHODS: A First Nations community in northern Alberta was selected to participate. Consent forms and a school health survey were completed by parents or guardians. Children with consent completed spirometry at school, and results were compared with predicted values. RESULTS: A total of 36 children participated (response rate 70.6%). Of these, 19.4% of parents reported that their child had received a physician diagnosis of asthma at some point in their life; only 28.6% had a parental report of still having asthma. Parents smoked in 73.1% of the children's homes. The mean (+/- SD) percentage of forced expiratory volume in 1 s (FEV1) over forced vital capacity (FVC) was 82.6% +/- 6.9% (94.4% +/- 0.08% of predicted). Evidence of airflow obstruction was found in 25% of the children. Parental report of the child ever having asthma was associated with impaired lung function (OR 3.20; P=0.033). Children in a home with reported mold exposure were less likely to have impaired lung function (OR 0.68; P=0.030). CONCLUSIONS: Many children in this study already have established airflow obstruction and may be at increased risk for asthma or COPD. Exposure to mold appeared to be protective. Further research is needed to evaluate the lung health concerns of this population.

Singel L.J. et al. *'Yes, you can!'*. *Am J Nurs.* 2001; 101(8) : 24A-C.p

Singh D. et al. *Chronic/recurrent cough in rural children in Ludhiana, Punjab.* *Indian Pediatr.* 2002; 39(1) : 23-9.p **Abstract:** OBJECTIVE: To determine the prevalence, age distribution and common causes of chronic/recurrent cough in rural children. DESIGN: Prospective study. SETTING: Pediatric population in five villages of Dehlon Block of Ludhiana, Punjab. METHODS: 2275 children in the age group of 1 to 15 years were screened by house to house survey for chronic/recurrent cough using defined criteria. A detailed work up of selected cases was carried out. Underlying etiology was determined using clinical and laboratory parameters. Five hundred children in the study population formed the control group. Variables associated with chronic/recurrent cough were

analyzed in cases and controls. RESULTS: Twenty four children were diagnosed with chronic/recurrent cough showing a prevalence rate of 1.06 percent. The most common cause was bronchial asthma (66.7 percent) followed by postnasal drip syndrome (25 percent). Family history of allergy/asthma was noted in 11 (45.8 percent) children as compared to 52 (10.4 percent) in the control group (p < 0.01). Family history of smoking was recorded in 16.7 percent of cases in contrast to 6.4 percent in controls (p = 0.05). There was no significant association with overcrowding, pets and kind of cooking fuel used. CONCLUSIONS: The most common cause of chronic/recurrent cough was bronchial asthma. There was a significant association with family history of allergy/asthma and smoking.

Singh M. et al. *Evaluation of quality of life in indian children with bronchial asthma using a disease-specific and locally appropriate questionnaire.* *Acta Paediatr.* 2004; 93(4) : 554-5.p **Abstract:** AIM: To evaluate quality of life (QOL) in Indian children with bronchial asthma. METHODS: A disease-specific, locally appropriate QOL questionnaire was administered in asthmatic children and compared with FEV1, FVC, PEFR and asthma symptom score, on three occasions. RESULTS: QOL score had strong negative correlation with symptom score and weaker positive correlation with pulmonary function tests. CONCLUSION: Disease-specific QOL score correlates inversely with symptom score in children with bronchial asthma.

Singhi S. et al. *Pediatric emergencies at a tertiary care hospital in India.* *J Trop Pediatr.* 2003; 49(4) : 207-11.p **Abstract:** The aim of the present study was to study the epidemiological and clinical profile of patients attending an exclusive pediatric Emergency Department (ED). Data was retrieved from records of the patients seen over a 6-year period from 1995 to 2000. Descriptive analysis was done to define demographic and clinical details, and monthly admission rates and diagnoses. A total of 43800 patients were seen during the study period. Of these 42.1 per cent were admitted after initial evaluation. The ratio of boys to girls was 3:1; 47 per cent were infants under 1 year of age. The common reasons for attending the emergency department were gastrointestinal and respiratory illnesses (23 per cent each), neurological emergencies (16 per cent), and neonatal problems (15.6 per cent). Poisonings were seen in 0.6 per cent of patients. Eight illnesses, i.e. acute diarrhea, upper respiratory infection, pneumonia, acute asthma, seizures, meningitis, and neonatal sepsis and jaundice, comprised nearly half of all the emergency visits. Acute diarrhoeal diseases, pneumonia, asthma, and encephalitis showed a distinct seasonal trend. Our data implies that planning of staff training and triage and efficient resource utilization in the pediatric ED in a developing country such as ours should take into consideration the preponderance of infants, seasonal trends, and the most common emergencies (acute diarrhea, pneumonia, acute asthma, seizures and neonatal infection) as priorities.

Siret D. et al. *[Evaluation of systematic pulmonary function testing for asthma in children aged three to five years].* *Arch Pediatr.* 2002; 9(5) : 478-88.p **Abstract:** Pulmonary function testing is not usually done in the preschool child, despite the recent data showing early deterioration in airway function in asthma. METHODS: We evaluated feasibility and clinical interest of flow-volume loop by forced expiratory maneuver and measure of airway resistance by interrupter technique (interrupter resistance), before and after inhalation of salbutamol, in 75 children aged three to five years seen in the ambulatory setting for asthma. RESULTS: Feasibility rate (92%) and reproducibility rate (91%) of those techniques were good, so that 84% of the cases could be exploited (63 children of 75). We found few significant associations between clinical parameters and flow-volume loop. We found a significant association between elevated interrupter resistance at basis and night-symptoms (P = 0.03), between diminished interrupter resistance after salbutamol and

exercise-symptoms ($P = 0.03$), symptoms in the ambulatory setting ($P = 0.02$) and absence of inhaled corticosteroid treatment ($P = 0.046$). Pulmonary function testing resulted in treatment modification in 14% of cases. **CONCLUSION:** Our study shows that flow-volume loop and measure of airway resistance by interrupter technique can be done with a good reproducibility in the preschool child. Interrupter resistance appears to be better correlated than flow-volume loop with usually evaluated clinical parameters.

Siroux V. et al. *Role of gender and hormone-related events on IgE, atopy, and eosinophils in the Epidemiological Study on the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy.* J Allergy Clin Immunol. 2004; 114(3) : 491-8.p **Abstract:** **BACKGROUND:** The pattern of asthma over the lifespan is different in male and female patients, but etiologic differences according to gender are only partially understood. In women, information regarding factors explaining perimenstrual asthma and the role of hormone-related aspects on asthma-related phenotypes is scanty. **OBJECTIVE:** To assess the relationships of eosinophils, IgE, and atopy with (1) asthma according to gender and age of onset and (2) hormone-related events. **METHODS:** Using data from the Epidemiological study on the Genetics and Environment of Asthma, Bronchial Hyperresponsiveness and Atopy, adults and children with asthma recruited in chest clinics ($n=313$) and first-degree relatives of patients with asthma ($n=214$) were compared with nonasthmatic controls ($n=334$) and first-degree relatives without asthma ($n=595$). **RESULTS:** Among asthmatic women, eosinophilia was significantly associated with perimenstrual asthma independently from age, smoking, and asthma severity (eosinophils/mm³ 330 vs 194; $P=.01$). In nonasthmatic women, IgE level was significantly decreased (by half) and atopy decreased with menopause, and IgE increased with oral contraceptive use, independently from age and smoking. Considering both genders, the increase of eosinophil counts with asthma was significantly greater in women with childhood-onset asthma than in women with adulthood-onset or in men in general. No interaction between gender and asthma was observed for eosinophils in children and for IgE level and atopy in children and adults. **CONCLUSION:** Results suggest a role of hormone-related events on asthma-related traits and support the hypothesis of the role of eosinophils in the persistence and severity of asthma.

Siroux V. et al. *Influence of asthma on the validity of reported lifelong environmental tobacco smoke in the EGEA study.* Eur J Epidemiol. 2004; 19(9) : 841-9.p **Abstract:** The aim of this study was to assess the short-term reproducibility and the validity of reported ETS (environmental tobacco smoke) exposure, with a special emphasis on the potential misclassification related to personal or family history of asthma. Analyses were based on the data on the Epidemiological study on the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy (EGEA), a case-control study of asthma that included first degree relatives of asthmatic cases. The study was comprised of 348 families of asthmatics recruited in six chest clinics throughout France and 416 population-based controls. For studying the validity of ETS reports, personal active smoking histories reported by family members were taken as reference. The reproducibility of ETS exposure report was good, and independent of asthma. The validity of the report of maternal and paternal smoking in childhood and spouse smoking during life was high (overall agreement $> \text{ or } = 84\%$). Mothers of asthmatic children significantly underreported their smoking habits when questioned on their children's passive tobacco exposure. Offspring of parents who had stopped smoking underestimated their ETS exposure in childhood. In conclusion, interviews with mothers on their personal active smoking habits may provide a more accurate estimate of their asthmatic child's passive exposure than asking mothers specifically about their children's passive exposure. There was no indication that asthma status (either of the parent/spouse or of the respondent) by itself influences the report of ETS exposure during childhood or adulthood.

Siwula C.M. *Managing pediatric emergencies: no small matter.* Nursing. 2003; 33(2) : 48-51.p

Skoner D.P. et al. *Evaluation of the safety and efficacy of levalbuterol in 2-5-year-old patients with asthma.* Pediatr Pulmonol. 2005; 40(6) : 477-86.p **Abstract:** The purpose of this study was to evaluate the safety and efficacy of single-isomer (R)-albuterol (levalbuterol, LEV) in children aged 2-5 years. Children aged 2-5 years ($n = 211$) participated in this multicenter, randomized, double-blind study of 21 days of t.i.d. LEV (0.31 mg or 0.63 mg without regard to weight), racemic albuterol (RAC, 1.25 mg for children <33 pounds (lb); 2.5 mg for children ≥ 33 lb), or placebo (PBO). Endpoints included adverse-event (AE) reporting, safety parameters, peak expiratory flow (PEF), the Pediatric Asthma Questionnaire(c) (PAQ), and the Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ). Baseline disease severity was generally mild in all groups, as defined by PAQ scores that ranged from 6.3-7.3 on a scale of 0-27 and 1.5 days/week of uncontrolled asthma. After treatment, the PAQ decreased in all groups ($P = \text{NS}$). In the subset of subjects able to perform PEF (51.7%), all active treatments improved in-clinic PEF after the first dose (mean \pm SD: PBO, 1.4 \pm 20.8; LEV 0.31 mg, 12.4 \pm 12; LEV 0.63 mg, 16.7 \pm 15.4; RAC, 18.0 \pm 16.5 l/min; $P < 0.01$). PACQLQ measurements improved more than the minimally important difference only in the LEV-treated groups, and were significant in children <33 lb ($P < 0.05$). Asthma exacerbations occurred primarily in children ≥ 33 lb, and one serious asthma exacerbation occurred in the 2.5-mg RAC group. RAC and LEV 0.63 mg, but not LEV 0.31 mg or placebo, led to significant increases in ventricular heart rate. In this study of levalbuterol in children aged 2-5 years with asthma, LEV was generally well-tolerated, and in children able to perform PEF, led to significant bronchodilation compared with placebo.

Skov M. et al. *Immunoglobulin allotypes and IgG subclass antibody response to Aspergillus fumigatus in cystic fibrosis patients.* J Cyst Fibros. 2004; 3(3) : 173-8.p **Abstract:** **BACKGROUND:** A majority of patients with cystic fibrosis (CF) become colonised with Aspergillus fumigatus (Af.), but only a minority develops allergic bronchopulmonary aspergillosis (ABPA). ABPA is associated with increased levels of specific immunoglobulin G (IgG) anti-Af. antibodies with a characteristic IgG subclass distribution. We examined whether this characteristic immune response was under the influence of GM and KM allotypes, which are genetic markers (antigenic determinants) on gamma- and kappa-light chains, respectively. **METHODS:** Sera from 233 CF patients were typed for seven GM determinants and two KM determinants. The types were correlated to IgG subclass anti-Af. antibody levels and to the presence or absence of Af. colonisation as well as ABPA. **RESULTS:** The IgG2 antibody level was significantly higher in heterozygous GM (1,2,17 23 5,21 and 1,3,17 23 5,21) compared to homozygous GM allotypes ($p = 0.02$). Patients with the same allotypes tended to have higher IgG1 ($p = 0.051$). In patients with ABPA, being heterozygous for G1M and G3M was linked to higher IgG4 and lower IgG3 as compared to the other genotypes. The KM markers did not influence the antibody levels. The allotype GM(3 23 5), associated with atopic bronchial asthma, tended to make a relatively larger group in ABPA patients compared to non-ABPA and patients not colonised with Af. ($p = 0.09$). **CONCLUSIONS:** An influence of the GM allotypes on the immune response to Af. and on the development of ABPA in patients with CF is suggested.

Slater A. et al. *The ANZPIC registry diagnostic codes: a system for coding reasons for admitting children to intensive care.* Intensive Care Med. 2003; 29(2) : 271-7.p **Abstract:** **OBJECTIVE:** To describe the uniform diagnostic coding system used in Australia and New Zealand to code reasons for admitting children to intensive care, and to highlight the benefits of a uniform approach. **DESIGN:** International, multicentre, observational study. **SETTING:** A registry of children admitted to intensive care in Australia and New Zealand.

PATIENTS: The records of 19249 children admitted to intensive care between 1997 and 2000 were analysed. **MEASUREMENTS AND RESULTS:** The system was designed empirically using expert consensus. The principal diagnosis or main reason for intensive care admission and up to five associated diagnoses are coded. The system has four levels of coding: non-operative or post-procedural admission, diagnostic group, specific condition, and for injury and infection the aetiological factor. The main reason for intensive care admission was coded in all patient records, however, for 11.1% of records the code was limited to diagnostic group with the specific condition coded as "other diagnosis". Two or more diagnoses were coded in 61% of records. The most frequent reason for admission was asthma. **CONCLUSIONS:** The major advantage of the system is that units in the region use the same method of coding. A uniform international approach to coding reasons for admitting children to intensive care is needed.

Sleath B.L. et al. *Literacy and perceived barriers to medication taking among homeless mothers and their children.* Am J Health Syst Pharm. 2006; 63(4) : 346-51.p **Abstract:** **PURPOSE:** The relation of medical literacy to women-reported barriers to taking medication themselves or giving medication to their children was studied. **METHODS:** Women in 18 homeless shelters in four counties in central North Carolina were recruited. Head-of-household homeless mothers with psychiatric or substance-abuse disorders and dependent children were eligible to participate. Trained interviewers administered a site-specific questionnaire on medication use. **RESULTS:** One hundred sixty-four homeless women participated. Forty-two percent of the women were currently taking a medication. Forty-six percent of the women stated that there was a barrier to taking their medications as prescribed. Medical literacy was not significantly related to whether women felt there were barriers to taking a medication. Seventy-five percent of the women reported having one or more children living with them. Thirty-seven percent reported having a child with asthma live with them, and 12% reported having a child with attention-deficit disorder. Forty percent reported a barrier to giving their child a needed medication. Taste was the most commonly reported barrier. Women with lower medical literacy and younger women were significantly more likely to report a barrier to giving their children a needed medication. Over 80% of women listed pharmacists as their first or second choice for receiving drug information orally. **CONCLUSION:** Race and perceived barriers to medication use affected the medication-taking behavior of homeless women, while their age and literacy level affected the reporting rates of the barriers to medication use for their children. Homeless women preferred receiving both written and oral drug information from a physician or a pharmacist.

Slieker M.G. et al. *The diagnostic and screening capacities of peak expiratory flow measurements in the assessment of airway obstruction and bronchodilator response in children with asthma.* Monaldi Arch Chest Dis. 2003; 59(2) : 155-9.p **Abstract:** Although the measurement of peak expiratory flow (PEF) is frequently used in general practice as a surrogate for forced expiratory volume in one second (FEV1) in the assessment of airway obstruction and bronchodilator response (BDR), its use has never been validated in children with asthma. Spirometry and PEF measurements (mini-Wright peak flow meter) were performed in 271 children with asthma who attended the hospital for a routine pulmonary evaluation. Airway obstruction was defined as FEV1 as a percentage of predicted (FEV1% pred) < 80%; a positive BDR was defined as an increase in FEV1% pred > or 9% after inhaling 800 micrograms salbutamol. The Spearman correlation coefficient between the percent-predicted values of PEF (PEF% pred) and FEV1% pred was 0.36. Commonly used cut off values for airway obstruction of PEF% pred < 75% and PEF% pred < 80% had a high specificity (95%, 91%) and NPV (95%, 95%), but a moderate sensitivity (54%, 57%) and PPV (54%, 41%). After administration of the bronchodilator, the Spearman correlation coefficient between the

different expressions of delta PEF and delta FEV1% pred ranged between 0.52 and 0.54. Commonly used cut off values for BDR of delta PEF% init (increase in PEF as percentage of initial value) > or = 20% and delta PEF% init > or = 25% had a high specificity (96%, 96%), a reasonable NPV (74%, 69%) and PPV (74%, 85%), but a moderate sensitivity (51%, 53%). In conclusion, PEF testing has the properties to be a good screening test to exclude airway obstruction and BDR (high specificity and NPV), but is of less clinical value as a diagnostic test (moderate sensitivity and PPV).

Slutsky P. et al. *Developing a comprehensive, community-based asthma education and training program.* Pediatr Nurs. 2001; 27(5) : 449-52, 455-7, 461.p **Abstract:** The Community Asthma Prevention Program (CAPP) is a comprehensive, community-based asthma education and training program focused on the prevention of asthma exacerbations in the pediatric/adolescent population. Details of starting a community-based education program are described. The asthma class series is taught for 5 hours, delivered in 1-hour sessions once each week. Programs are held in schools, daycare centers, churches, and community centers. Classes are conducted simultaneously in separate rooms with parents being taught by a health educator and children taught by a peer educator. To date, 774 parents and 570 children have completed the community classes. The retention rate of participants who complete the 5-week program is 80%. The train-the-trainer model is used for training community members such as parents, teens, school nurses, daycare providers, and foster care workers to provide the community with many members who are trained in asthma education. Strategies used to obtain support and promote program visibility and use in the targeted community are presented.

Smart J.M. et al. *Polyclonal and allergen-induced cytokine responses in adults with asthma: resolution of asthma is associated with normalization of IFN-gamma responses.* J Allergy Clin Immunol. 2002; 110(3) : 450-6.p **Abstract:** **BACKGROUND:** Atopic disease is associated with skewing of immune responses away from a T(H)1 toward a T(H)2 profile. Previous studies have implicated this cytokine imbalance in the development of disease. However, it is not known whether normalization of this imbalance is conversely associated with disease resolution. **OBJECTIVE:** To further delineate the role of reduced T(H)1 and increased T(H)2 cytokine production in the pathogenesis of atopic disease and to determine whether disease resolution is associated with alteration of cytokine profiles, we investigated cytokine responses in a cohort of adult patients with asthma followed from childhood. **METHODS:** A cohort of wheezy children and control subjects aged 7 to 10 years were recruited from 1964 to 1967. Subjects were reevaluated every 7 years to monitor the outcome of childhood asthma. At the 42-year follow-up, 89 subjects from this cohort were evaluated for mitogen and house dust mite (HDM)-induced T(H)1 (IFN-gamma) and T(H)2 (IL-4, IL-5, and IL-13) cytokine responses. Cytokine responses were compared in patients with ongoing asthma, patients with resolved asthma, and control subjects. **RESULTS:** Patients with severe ongoing asthma had significantly reduced HDM-induced IFN-gamma production compared with that of control subjects and patients with resolved asthma. In contrast, HDM-induced IFN-gamma production in patients with resolved asthma was equivalent to that seen in control subjects. Patients with ongoing and resolved asthma produced significantly higher levels of IL-5 in response to HDM compared with that seen in control subjects, with levels being equivalent in patients with active and resolved asthma. HDM-induced IL-13 production was significantly increased in the patients with resolved asthma when compared with that seen in the control subjects. PHA-induced cytokine responses did not parallel HDM-induced responses. **CONCLUSION:** Patients with persistent and severe atopic asthma have a reduced HDM-induced T(H)1 response, whereas those with resolved asthma do not. This suggests that reduced HDM-induced IFN-gamma production might be an important factor contributing to ongoing severe asthma and that normalization of allergen-induced

T(H)1 responses might be important for disease resolution. The finding that all subjects with a history of asthma displayed increased HDM-induced T(H)2 (IL-5 and IL-13) cytokine responses, irrespective of the presence or absence of asthma, suggests that increased T(H)2 responses reflect the presence of the atopic state per se rather than being specifically linked to asthma.

Smart J.M. et al. *Increased Th1 and Th2 allergen-induced cytokine responses in children with atopic disease.* Clin Exp Allergy. 2002; 32(5) : 796-802.p **Abstract:** BACKGROUND: Polyclonal cytokine responses following stimulation of T cells with mitogens or superantigens provides information on cytokine production from a wide range of T cells. Alternatively allergen-induced T cell responses can provide information on cytokine production by allergen-reactive T cells. While there is evidence of increased Th2 and reduced Th1 cytokine production following T cell stimulation with non-specific mitogens and superantigens, the evidence that Th1 cytokine production to allergens is decreased in line with a postulated imbalance in Th1/Th2 responses is unclear, with studies finding decreased, no difference or increased IFN-gamma responses to allergens in atopic subjects. OBJECTIVE: To examine childhood polyclonal and allergen-induced cytokine responses in parallel to evaluate cytokine imbalances in childhood atopic disease. METHODS: PBMC cytokine responses were examined in response to a polyclonal stimulus, staphylococcal superantigen (SEB), in parallel with two inhalant allergens, house dust mite (HDM) and rye grass pollen (RYE), and an ingested allergen, ovalbumin (OVA), in (a) 35 healthy children (non-atopic) and (b) 36 children with atopic disease (asthma, eczema and/or rhinitis) (atopic). RESULTS: Atopic children had significantly reduced IFN-gamma and increased IL-4 and IL-5 but not IL13 production to SEB superantigen stimulation when compared with non-atopic children. HDM and RYE allergens stimulated significantly increased IFN-gamma, IL-5 and IL-13, while OVA stimulated significantly increased IFN-gamma production in atopic children. CONCLUSION: We show that a polyclonal stimulus induces a reduced Th1 (IFN-gamma) and increased Th2 (IL-4 and IL-5) cytokine pattern. In contrast, the allergen-induced cytokine responses in atopic children were associated with both increased Th1 (INF-gamma) and Th2 (IL-5 and IL-13) cytokine production. The increased Th1 response to allergen is likely to reflect prior sensitization and indicates that increases in both Th1 and Th2 cytokine production to allergens exists concomitantly with a decreased Th1 response to a polyclonal stimulus in atopic children.

Smith A.D. et al. *Diagnosing asthma: comparisons between exhaled nitric oxide measurements and conventional tests.* Am J Respir Crit Care Med. 2004; 169(4) : 473-8.p **Abstract:** International guidelines recommend a range of clinical tests to confirm the diagnosis of asthma. These focus largely on identifying variable airflow obstruction and responses to bronchodilator or corticosteroid. More recently, exhaled nitric oxide (FE(NO)) measurements and induced sputum analysis to assess airway inflammation have been highlighted. However, to date, no systematic comparisons to confirm the diagnostic utility of each of these methods have been performed. To do so, we investigated 47 consecutive patients with symptoms suggestive of asthma, using a comprehensive fixed-sequence series of diagnostic tests. Sensitivities and specificities were obtained for peak flow measurements, spirometry, and changes in these parameters after a trial of steroid. Comparisons were made against FE(NO) and sputum cell counts. Sensitivities for each of the conventional tests (0-47%) were lower than for FE(NO) (88%) and sputum eosinophils (86%). Overall, the diagnostic accuracy when using FE(NO) and sputum eosinophils was significantly greater. Results for conventional tests were not improved, using a trial of steroid. We conclude that FE(NO) measurements and induced sputum analysis are superior to conventional approaches, with exhaled nitric oxide being most advantageous because the test is quick and easy to perform.

Smith A.F. et al. *The economic and quality of life impact of seasonal allergic conjunctivitis in a Spanish setting.* Ophthalmic Epidemiol. 2005; 12(4) : 233-42.p **Abstract:** INTRODUCTION: Seasonal allergic conjunctivitis (SAC) is a highly prevalent condition that exacts a range of costs from its sufferers. The aim of this study was to examine quality of life (QoL) and economic consequences of SAC amongst private health care patients in Spain. METHODS: 201 sufferers of SAC and 200 controls were recruited from four private eye clinics and one public hospital in five Spanish cities: Alicante, Madrid, Albacete, Las Palmas de Gran Canarias and Valladolid. Participants were between 10 and 80 years of age and Spanish speaking. All potential participants were asked selected questions and sorted into one of the two groups or excluded. Sufferers were administered a set of four questionnaires by researchers consisting of the EQ-5D Health Questionnaire, the National Eye Institute (US) Visual Functioning Questionnaire 25 (VFQ-25), the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and a Health Economic and Demographic Questionnaire (HEDQ). Control participants self-administered the full EQ-5D and VFQ-25 and abbreviated versions of the RQLQ and HEDQ. RESULTS: The groups were comparable in terms of age and sex, but sufferers had a significantly higher hourly income than controls (p = 0.02). Sufferers exhibited a significantly higher incidence of asthma, nasal symptoms, perennial allergic conjunctivitis, food allergies and other allergies (p < 0.01 for all comorbidities). Sufferers returned significantly lower quality of life scores than controls in all EQ-5D domains other than mobility (p = 0.14). SAC VFQ-25 scores were significantly less than in controls in the overall vision (p < 0.01), distance vision (p < 0.01), ocular pain (p < 0.01), mental health (p = 0.01), role limitations (p < 0.01), and dependency (p = 0.01) domains. Mean scores for the activity domain of the RQLQ were greater in the sufferer group than the control group (P < 0.01). The total mean per-sufferer cost of SAC amongst our sample of private patients was 348.50 Euros. DISCUSSION: Sufferers experienced QoL reductions in general health and specific aspects of vision as a result of their SAC. In relative terms, the per-capita economic cost of the condition was higher than in a previous public health care study. This was ascribed to sufferers' willingness-to-pay for symptom alleviation. The unexpectedly high expenditure of the proportion of SAC sufferers who receive private health care serves to highlight the importance of SAC as a costly condition. It also illustrates the need to account for both private and public health care modalities when attempting to ascribe a total cost to a medical condition.

Smith J. *An update on bronchopulmonary dysplasia: is there a relationship to the development of childhood asthma?* Med Hypotheses. 2003; 61(4) : 495-502.p **Abstract:** There appears to be some interesting commonalities between asthma and BPD. The prevalence of both conditions is on the rise, both conditions tend to cluster in families, and they share wheezing phenotypes, i.e., mild-moderate reversible airway obstruction and a similar degree of response to pharmacological provocation. Furthermore, significant overlap exists with regard to the presence of elevated concentrations of airway inflammatory mediators concurrent with reduced levels of anti-inflammatory activity, in serum and BAL fluid, as well as histological evidence for airway 'remodelling'. Both BPD and asthma are characterized by increased smooth muscle contraction, and in asthma, the smooth muscle may be involved in the primary development of the asthmatic phenotype. Since wheezing is a common finding among children with BPD, an interesting question is whether BPD is a phenotypic variant of asthma?

Smith J.M. *Atopy and asthma: an epidemic of unknown cause.* J Allergy Clin Immunol. 2005; 116(1) : 231-2; author reply 232.p

Smith L.A. et al. *Rethinking race/ethnicity, income, and childhood asthma: racial/ethnic disparities concentrated among the very poor.* Public Health Rep. 2005; 120(2) : 109-16.p **Abstract:** OBJECTIVE: Past studies of the prevalence of childhood asthma

have yielded conflicting findings as to whether racial/ethnic disparities remain after other factors, such as income, are taken into account. The objective of this study was to examine the association of race/ethnicity and family income with the prevalence of childhood asthma and to assess whether racial/ethnic disparities vary by income strata. **METHODS:** Cross-sectional data on 14,244 children aged <18 years old in the 1997 National Health Interview Survey were examined. The authors used logistic regression to analyze the independent and joint effects of race/ethnicity and income-to-federal poverty level (FPL) ratio, adjusting for demographic covariates. The main outcome measure was parental report of the child having ever been diagnosed with asthma. **RESULTS:** Bivariate analyses, based on weighted percentages, revealed that asthma was more prevalent among non-Hispanic black children (13.6%) than among non-Hispanic white children (11.2%; $p < 0.01$), but the prevalence of asthma did not differ significantly between Hispanic children (10.1%) and non-Hispanic white children (11.2%; $p = 0.13$). Overall, non-Hispanic black children were at higher risk for asthma than non-Hispanic white children (adjusted odds ratio [OR]=1.20; 95% confidence interval [CI] 1.03, 1.40), after adjustment for sociodemographic variables, including the ratio of annual family income to the FPL. Asthma prevalence did not differ between Hispanic children and non-Hispanic white children in adjusted analyses (adjusted OR=0.85; 95% CI 0.71, 1.02). Analyses stratified by income revealed that only among children from families with incomes less than half the FPL did non-Hispanic black children have a higher risk of asthma than non-Hispanic white children (adjusted OR=1.99; 95% CI 1.09, 3.64). No black vs. white differences existed at other income levels. Subsequent analyses of these very poor children that took into account additional potentially explanatory variables did not attenuate the higher asthma risk for very poor non-Hispanic black children relative to very poor non-Hispanic white children. **CONCLUSIONS:** Non-Hispanic black children were at substantially higher risk of asthma than non-Hispanic white children only among the very poor. The concentration of racial/ethnic differences only among the very poor suggests that patterns of social and environmental exposures must overshadow any hypothetical genetic risk.

Smith L.A. et al. *Knowledge of welfare reform program provisions among families of children with chronic conditions.* Am J Public Health. 2002; 92(2) : 228-30.p **Abstract:** **OBJECTIVES:** This study examined the knowledge of and application for health-related welfare program provisions among beneficiaries with children who have chronic conditions. **METHODS:** We administered a survey to 143 parents of children aged 3 to 16 years with asthma or sickle cell anemia in 2 clinical settings. **RESULTS:** Respondents indicated incomplete knowledge of work requirements (69.9%) and work exemptions (50.3%). Applications for work exemptions were rare, even among Supplemental Security Income recipients (30%). **CONCLUSIONS:** Welfare beneficiaries with children who have chronic conditions show limited knowledge and use of program provisions, placing them at risk for penalties or benefit termination.

Smith L.J. et al. *Dietary intake of soy genistein is associated with lung function in patients with asthma.* J Asthma. 2004; 41(8) : 833-43.p **Abstract:** To determine if micronutrient intake is associated with asthma severity, we administered the Block food frequency questionnaire to participants in a randomized clinical trial of the safety of influenza vaccine for asthmatics. The nutrition substudy included 1033 participants, aged 12-75. Intake of antioxidant vitamins, soy isoflavones, total fruits and vegetables, fats, and fiber was compared with asthma severity at baseline [forced expiratory volume in 1 second (FEV1), peak expiratory flow rate (PEF), asthma symptoms] and the rate of asthma exacerbations during the 2 weeks following influenza vaccination. The only nutrient that had a consistent association with asthma severity was genistein, a soy isoflavone. None of the nutrients evaluated were related to asthma exacerbation rate when adjusted for known confounders. The FEV1

in genistein consumers of at least 250 microg/1000 Kcal/day was 82.1% predicted, 79.9% predicted for those who consumed between 1 and 249 microg/1000 kcal, and 76.2% predicted in genistein nonconsumers ($p = 0.006$); the PEF was 82.7% predicted, 80.8% predicted, and 78.3% predicted, respectively ($p = 0.009$). There were no differences in the Asthma Symptom Utility Index (ASUI). We could not account for these results based on differences in demographics, body mass index, or consumption of other nutrients. Thus, increasing consumption of genistein is associated with better lung function in patients with asthma. Further studies are needed to determine whether dietary supplementation with genistein can reduce asthma severity.

Smith M.J. et al. *A descriptive analysis of asthma-related medical services and prescription utilization among recipients in a Medicaid program.* J Asthma. 2005; 42(6) : 447-53.p **Abstract:** One objective of the Healthy People 2010 initiative calls for the establishment of a surveillance system to track asthma illness and management in at least 25 states. Our objective was to report patterns of asthma-related medical services and pharmacotherapy use among recipients of Texas Medicaid. Texas Medicaid medical services and prescription administrative claims data dated between January 1 and December 31, 2000, for recipients between 6 and 64 years of age enrolled in a fee-for-service plan were extracted. Rates of recipients with asthma, rates of asthma-related medical services use, and patterns of pharmacotherapy use were reported. There were 31,509 recipients identified with asthma at a rate of 22.8 per 1000. Children under 15 years of age, males, and blacks had the highest rates of asthma, as well as asthma-related emergency department (ED) visits and hospitalizations compared with other demographic groups. Hispanics accounted for the largest proportion of ethnic groups but had the lowest rate of asthma compared with whites and blacks. The rate of ED visits and hospitalizations among children was more than twice the rate among adults. Blacks had more than twice the rate of ED visits and nearly double the rate of hospitalizations for asthma compared with other ethnic groups. Roughly 56% of the recipients had a claim for an inhaled anti-inflammatory medication. However, it appeared that recipients were using short-acting beta-agonists more frequently than inhaled corticosteroids. Use of medical services and prescription medications for asthma varied greatly on the basis of recipient demographic factors.

Smith S.R. et al. *Parental impressions of the benefits (pros) and barriers (cons) of follow-up care after an acute emergency department visit for children with asthma.* Pediatrics. 2002; 110(2 Pt 1) : 323-30.p **Abstract:** **OBJECTIVE:** Asthma morbidity, with increasing emergency department (ED) visits, is prevalent among low-income, urban children. Follow-up care after ED visits is infrequent. We developed and evaluated an instrument that describes the parental benefits (pros) and barriers (cons) of obtaining follow-up care for interventions to promote follow-up. **METHODS:** We enrolled a convenience sample of low-income, urban parents who brought their children to the ED for treatment of asthma. These parents rated 41 items about the pros and cons of making a follow-up visit. Principal component analysis was used to identify the underlying structure of the instrument. **RESULTS:** One hundred forty-seven participants were interviewed in the ED. Principal component analysis retained 24 total items, which were identified by this sample as highly associated with deciding to take their child to a follow-up visit. Two types of pros were identified, informational and attitudinal, including "ask the doctor questions," and "children with asthma are healthier if they see their doctor regularly." Two types of cons were identified, practical and attitudinal, including "I have to find transportation," and "I don't need to see the doctor unless my child is sick." The mean total pro and con scores were 4.05 +/- 0.63 and 1.73 +/- 0.67, respectively. **CONCLUSIONS:** The pros and cons are not unidimensional. Even among those with infrequent follow-up, pros were endorsed more highly than cons. Programs that target these pros

and cons may improve adherence to follow-up and regular care for low-income urban children.

Smith S.R. et al. *Improving follow-up for children with asthma after an acute Emergency Department visit.* J Pediatr. 2004; 145(6) : 772-7.p
Abstract: OBJECTIVE: To improve follow-up with primary care providers after acute Emergency Department (ED) asthma visits for children from low-income urban families. STUDY DESIGN: A prospective, randomized, controlled trial evaluated combined telephone asthma coaching and monetary incentive. The primary outcome was asthma-planning visits with primary care providers within 15 days of index ED visits. The subjects were urban parents whose children were treated for asthma in the ED and had Medicaid or no insurance. RESULTS: We enrolled 527 parents (264 control and 263 intervention). There was a significant difference ($P < .0001$) between the intervention (35.7%) and control (18.9%) groups in the proportion of children who had asthma-planning visits and decreased mean nights/days with asthma symptoms by 4.36 intervention and 3.31 control at 2 weeks. The proportions of children with asthma-planning visits and acute asthma care visits during the 16-day to 6-month period were similar for both groups. CONCLUSIONS: Telephone coaching and a monetary incentive significantly increased the proportion of low-income urban parents who brought their children for asthma-planning visits, and decreased asthma symptoms shortly after asthma ED visits. The intervention did not increase subsequent asthma-planning visits or decrease ED visits or hospitalizations.

Smith S.R. et al. *Recruitment into a long-term pediatric asthma study during emergency department visits.* J Asthma. 2004; 41(4) : 477-84.p
Abstract: OBJECTIVE: Asthma is the most common chronic illness in childhood. Recruiting children and their parents into a research study in a busy urban emergency department (ED) is challenging. The purpose of this manuscript is to describe the recruitment process and the results of our recruitment in soliciting children and their parents to participate in an ED-based asthma research study. METHODS: The data for this manuscript came from a National Heart, Lung, and Blood Institute-funded study: Study of Asthma Follow-up from the Emergency Department (SAFE). SAFE evaluated an ED-based intervention to link low-income urban children with asthma to their primary care providers. Two persons were assigned specifically to enrolling, which was done from 0700 to 2300 hours Monday through Friday. Data for the analysis come from the web-based database, the master log, and the hospital's patient database. A computerized randomization scheme chose 512 patients from all patients in the master log for more detailed demographic analyses. RESULTS: Five hundred twenty-seven subjects were enrolled between February 1999 and May 2001. There were 9188 children who presented for treatment of an acute asthma exacerbation during this interval. The number of eligible parents was similar to the predicted number. Chart reviews were conducted on a subset of patients presenting to the ED to ensure that the recruitment strategy did not bias the patients enrolled. Demographic characteristics of asthma patients were similar during enrollment and non-enrollment times. Comparison of patients who were enrolled with those who were not enrolled indicated no differences by gender, race, insurance status, age, or socioeconomic status of neighborhood residence. DISCUSSION: The high rate of enrollment was primarily due to the two dedicated enrollers. The enrollers quickly learned how to function within the ED and how to interact with both families and ED staff. Strategies identified by the enrollers as helpful in randomizing subjects included visits with the parents shortly after the physician had initiated treatment so that stability of the child had been achieved. Interacting with the child and showing concern for the comfort of both the child and parent during the ED stay were important as well. CONCLUSION: Recruiting subjects into long-term follow-up studies in the ED setting is a departure from traditional ED studies. The ED enrollment offers the distinct advantage of capturing subjects who are unlikely to present for care

in other locations. We were able to successfully recruit low-income urban parents of children with asthma for study of both short-term and long-term outcomes. Careful attention to planning and then integration of enrollers into the ED setting can result in successful recruitment of patients and their parents. The enrollment process successfully captured the subjects of interest without bias.

Smits W. et al. *Improved immunotherapy with a rapid allergen vaccination schedule: a study of 137 patients.* Ear Nose Throat J. 2003; 82(11) : 881-7.p
Abstract: Rapid allergen vaccination (RAV) is the updated term for what was previously called rush immunotherapy and rapid desensitization. RAV offers several advantages over traditional immunotherapy--that is, conventional allergen vaccination (CAV)--in terms of faster efficacy, better compliance, and cost-effectiveness. We used a 3-hour RAV protocol to treat 137 allergy patients. All patients were premedicated with either prednisone or prednisolone and an H1 antihistamine. Following the RAV procedure, all patients resumed a CAV schedule. Only six patients (4.4%) experienced a mild systemic reaction to RAV, and five (3.6%) experienced a mild systemic reaction to CAV 14 to 77 days later. All six patients who reacted to RAV quickly responded to treatment--in most cases, subcutaneous epinephrine and/or nebulized albuterol--and were sent home after a short period of observation. Compliance rates at 3, 6, and 12 months were 96.4, 94.2, and 75.9%, respectively, which is an improvement over rates previously reported for patients undergoing CAV therapy. We conclude that the 3-hour RAV protocol can be safely and successfully administered. Patients who undergo RAV are more compliant with their subsequent CAV regimen than are patients who do not undergo RAV because signs of clinical efficacy manifest almost immediately and because RAV is associated with substantially lower rates of systemic reactions. Moreover, RAV is associated with less morbidity and less expense. Our findings should encourage physicians who treat allergy patients to give further consideration to using RAV.

Snooks H. et al. *Hearing half the message? A re-audit of the care of patients with acute asthma by emergency ambulance crews in London.* Qual Saf Health Care. 2005; 14(6) : 455-8.p
Abstract: PROBLEM: An initial audit of the care provided to emergency asthma patients by the ambulance service was carried out in 1996. Some under-recognition and under-treatment of severe asthma was found as well as a lack of documentation of patient condition on scene. A re-audit was undertaken in 1999. DESIGN: A multidisciplinary advisory group was reconvened. The same method was adopted as for the first audit. Patients included were those administered nebulised salbutamol by crews in the catchment areas of four hospitals and those diagnosed with asthma at the Accident & Emergency (A&E) departments of those hospitals between January and March 1999. SETTING: London Ambulance Service. KEY MEASURES FOR IMPROVEMENT: (1) Accuracy of diagnosis and appropriateness of treatment, and (2) adherence to protocol. STRATEGIES FOR CHANGE: Following the first audit, treatment protocols were widened and brought into line with the British Thoracic Society guidelines for care of acute asthma patients. The results were widely disseminated within the service and training was initiated for all operational staff. EFFECTS OF CHANGE: The number of patients included in the re-audit more than doubled (audit 1: n = 252, audit 2: n = 532). The increase occurred exclusively in those administered nebulised salbutamol by ambulance crews but diagnosed with conditions other than asthma in A&E (audit 1: n = 15, audit 2: n = 161). The proportion of patients diagnosed with asthma in A&E who were administered nebulised salbutamol by their attending crew rose from 58% to 75%. However, 43 asthma patients were not treated; several of these were not recognised as suffering from asthma and others fell within the changed protocols for treatment. Adherence to protocol for administration of salbutamol remained high. Pre-hospital documentation of key observations did not improve. LESSONS LEARNED: Messages from the first audit

seem to have been acted upon selectively. Implementing change is complex, and re-audit is necessary to understand the effects of the changes made.

Sontag S.J. *Helicobacter pylori infection and reflux esophagitis in children with chronic asthma.* J Clin Gastroenterol. 2004; 38(1) : 3-4.p

Sorkness C.A. et al. *Recruitment strategies in the Asthma Clinical Research Network.* Control Clin Trials. 2001; 22(6 Suppl) : 222S-35S.p **Abstract:** In any clinical trial, recruitment of trial participants usually requires an intense effort to reach the target sample size. The Asthma Clinical Research Network (ACRN) was keenly aware of this issue at its inception and therefore initiated and emphasized recruitment strategies for each of its clinical trials. This article describes the recruitment strategies for the ACRN's first four major clinical trials. Particular attention is given to the strategies for the recruitment of women and minorities. Finally, the specific strategies of each of the six ACRN clinical centers are presented.

Soto-Quiros M.E. et al. *Epidemiological studies of the very high prevalence of asthma and related symptoms among school children in Costa Rica from 1989 to 1998.* Pediatr Allergy Immunol. 2002; 13(5) : 342-9.p **Abstract:** The aim of our study was to determine the prevalence of asthma and related respiratory symptoms in school children from Costa Rica during the last 10 years, from 1989 to 1998. Using nationally representative samples of school children from Costa Rica during the last 10 years we have performed three studies. Altogether 9,931 children were investigated. The age groups: study I, 5-17 years (n = 2,682), study II, 6-7 years (n = 2,944), 13-14 years (n = 3,200) and study III, 10 years (n = 1,105). The diagnostic criteria for asthma used in these studies was as follows: study I (1989), diagnosis by a doctor in combination with the presence of four kinds of respiratory symptoms; studies II (1995) and III (1998), history of wheeze in the past 12 months. The two latter were part of the International Study of Asthma and Allergies in Childhood (ISAAC). A very high prevalence of a history of wheezing was found in the three studies (46.8%, 42.9%, and 45.1%) as well as a diagnosis of asthma (23.4%, 27.7% and 27.1%). The physician's diagnosis of asthma reported in the first study (23%) increased from 23.1 in study II to 27.7% in study III (p = 0.004). This increment could be a real increase in asthma prevalence, or be due to a better awareness about asthma. In study II the group of 6-7-year-olds had respiratory symptoms significantly more often than 13-14-year-olds (p < 0.001). Boys more often had a history of wheezing (p = 0.001), wheeze during the previous 12 months (p = 0.01) and an asthma diagnosis at the age of 6-7 years (p = 0.002) than girls, but girls had more respiratory symptoms than boys at the age of 13-14 years (p < 0.005). Wheezing in the past 12 months was more common for those living in urban areas aged 6-7 years (p = 0.04), and there was an increase of wheeze after exercise (p = 0.01). For the 13-14-year-olds the risk of wheezing was higher during the previous 12 months if they lived in temperate areas (<20 degrees C) and at a high altitude (>1,000 m). Living in a rural area and in a warm region (>20 degrees C), increased the risk of dry cough during the previous 12 months in the group of 13-14-year-olds. In conclusion, Costa Rica is located in the tropics with a very high humidity, an enormous variety of flora and fauna and a very high prevalence of mite and cockroach allergens, which provide important risk factors that may explain the high prevalence of asthma and asthma-related symptoms. Further possible factors, such as the change towards a more Western life style, resulting in fewer infections and parasitic diseases in the first years of life and changes in bedding material, may also be unresolved. Increased environmental pollution may add to the very high prevalence of asthma and related respiratory symptoms. The very extensive exposure to mites and cockroaches in bed material and in homes with poor ventilation may be an important factor, but many asthmatic children behave as non atopic, with a viral respiratory infection as a major precipitating factor.

Souchet S. *[Asthma school nurse. Interview by Marie-France Guere].* Rev Infirm. 2005; (111) : 22-3.p

South M. *Computerised asthma action plans.* Med J Aust. 2003; 179(8) : 453.p

South M. *Second line treatment for severe acute childhood asthma.* Thorax. 2003; 58(4) : 284-5.p

Souza A.C. et al. *[Bronchial provocation tests using methacholine, cycle ergometer exercise and free running in children with intermittent asthma].* J Pediatr (Rio J). 2005; 81(1) : 65-72.p **Abstract:** **OBJECTIVE:** To compare airway responsiveness to methacholine, cycle ergometer exercise and free running in children with intermittent asthma. **METHODS:** A randomized study was conducted with 30 children of both genders with intermittent asthma. Each child was submitted to challenge testing on three separate days, in random order: a) Methacholine challenge using a dosimeter; b) Exercise challenge testing -- free running along a 50-meter-long corridor; c) Dry-air exercise challenge on a cycle ergometer. Target heart rate during exercise was 80 to 90% of the maximum predicted value. Spirometry was performed 3, 6,10,15,20 and 30 minutes after exercise. Exercise-induced bronchospasm was defined as a decrease in FEV1 of > or = 10% in comparison to pretest values. **RESULTS:** Mean age was 11+/-3 years. FEV1 and FEV1/FVC ratios were normal and similar before all provocation tests. The maximum heart rate was 178+/-7 bpm during cycling and 181+/-6 bpm during the free running test (p > 0.05). Significant bronchospasm was observed with methacholine in 23 cases, after free running in 19 and after cycling in 14 children (p < 0.05, methacholine vs exercise tests). Taking all FEV1 measurements after exercise into account, the free running test resulted in greater exercise-induced bronchospasm in comparison with exercise made on a cycle ergometer (p = 0.003, chi2 = 8.948). There was a significant, but poor, correlation between the maximum percentage decrease in FEV1 after free running and cycling (r = 0.46, p < 0.01). **CONCLUSIONS:** Methacholine challenge identifies a greater number of asthmatics in comparison to exercise tests. When bronchial provocation test with methacholine is not available, free running should be the test of choice due to its simplicity and greater ability to induce bronchospasm.

Spahn J.D. et al. *Effect of montelukast on peripheral airflow obstruction in children with asthma.* Ann Allergy Asthma Immunol. 2006; 96(4) : 541-9.p **Abstract:** **BACKGROUND:** Montelukast is a widely used controller agent in childhood asthma. It is modestly effective in reducing symptoms, decreasing the need for rescue albuterol, and improving forced expiratory volume in 1 second (FEV1). **OBJECTIVE:** To determine whether montelukast therapy improves peripheral airway obstruction as measured by lung volumes, air trapping, airway resistance (Raw), and specific conductance (Sgaw). **METHODS:** Twenty-one children aged 9 to 18 years with mild-to-moderate asthma were randomized into a double-blind, placebo-controlled study to receive montelukast (5 or 10 mg) or matching placebo daily for 8 weeks. Symptoms and albuterol use were recorded twice daily, and exhaled nitric oxide measurement, forced oscillometry, spirometry, and body box plethysmography (before and after beta-agonist use) were performed at randomization and at 2, 4, 6, and 8 weeks. Circulating eosinophil counts and serum eosinophil cationic protein (ECP) levels were obtained at randomization and at 8 weeks. **RESULTS:** Montelukast-treated patients had lower residual volume (P = .05), residual volume-total lung capacity ratio (P = .04), Raw (P = .02), Sgaw (P = .03), and serum ECP levels (P = .02) at 8 weeks compared with those treated with placebo. There was a trend toward reduced daytime and nighttime albuterol use, although the difference did not reach statistical significance. There were no significant differences in FEV1, FEV1-forced vital capacity ratio, exhaled nitric oxide levels,

or daytime and nighttime symptom scores between the 2 groups. CONCLUSIONS: Montelukast therapy was associated with less air trapping, hyperinflation, and Raw and better Sgaw compared with placebo. Lower serum ECP levels, a surrogate measure of airway inflammation, were associated with improvements in lung function.

Spahr J.E. et al. *The early origins of asthma: nature, nurture, or parturition?* Ann Allergy Asthma Immunol. 2005; 94(2) : 211-2.p

Spear S. *New research links poor air quality to increase in asthma cases.* J Environ Health. 2002; 65(2) : 47.p

Spengler J.D. et al. *Housing characteristics and children's respiratory health in the Russian Federation.* Am J Public Health. 2004; 94(4) : 657-62.p **Abstract:** OBJECTIVES: We studied housing characteristics, parental factors, and respiratory health conditions in Russian children. METHODS: We studied a population of 5951 children from 9 Russian cities, whose parents answered a questionnaire on their children's respiratory health, home environment, and housing characteristics. The health outcomes were asthma conditions, current wheeze, dry cough, bronchitis, and respiratory allergy. RESULTS: Respiratory allergy and dry cough increased in association with the home being adjacent to traffic. Consistent positive associations were observed between some health conditions and maternal smoking during pregnancy, many health conditions and lifetime exposure to environmental tobacco smoke (ETS), and nearly all health conditions and water damage and molds in the home. CONCLUSIONS: Vicinity to traffic, dampness, mold, and ETS are important determinants of children's respiratory health in Russia.

Srivastava P. et al. *Association of CCR5Delta32 with reduced risk of childhood but not adult asthma.* Thorax. 2003; 58(3) : 222-6.p **Abstract:** BACKGROUND: A number of potential candidate genes have been implicated in the pathogenesis of asthma. A 32 base pair deletion in the CCR5 gene renders this chemokine receptor non-functioning and has been shown to be associated with a reduced prevalence of asthma in childhood. The mechanism may be related to impairment of pathogen entry into cells and modified host inflammatory response. We sought to determine the influence of the CCR5Delta32 mutation on asthma and allergy in the transition from childhood to adulthood. METHODS: 627 individuals first studied as part of a whole population schoolchildren cohort in 1989 when aged 8-12 years were followed up 10 years later for respiratory and allergy symptoms and laboratory markers of atopy. CCR5Delta32 status was also characterised and the association with childhood and adulthood symptoms determined. RESULTS: The follow up sample was representative of the original cohort except for a slightly greater prevalence of symptomatic individuals. As children, none who were homozygous for the CCR5Delta32 mutation had a current physician's diagnosis of asthma. In multivariate analysis and controlling for known confounders, the protective effect of carrying the allele in childhood was highly significant (OR 0.31, 95% CI 0.14 to 0.72, p=0.006). There was no protective association with "current asthma" as classified in adulthood within the same population. Subjective or laboratory markers of atopy in childhood or adulthood were not associated with the CCR5Delta32 mutation. Methacholine bronchial hyperresponsiveness in adulthood was also unrelated to gene carrier status. CONCLUSIONS: In a population with a high allelic frequency for the CCR5Delta32 mutation, a significant protection against childhood asthma is evident which is independent of atopy. This protection is lost in the transition between childhood and early adulthood. The contribution of different genetic candidates to the expression of asthma may change with advancing maturity and confound the interpretation of association and linkage studies unless age is taken into account.

Srivastava R. et al. *Length of stay for common pediatric conditions: teaching versus nonteaching hospitals.* Pediatrics. 2003; 112(2) : 278-81.p **Abstract:** OBJECTIVE: Pediatric teaching hospitals provide particular expertise in caring for children with complex or severe illnesses, yet most patients within teaching hospitals have common pediatric conditions. No study has determined whether children with common conditions remain hospitalized at teaching institutions longer than at nonteaching institutions. The objective of this study was to compare length of stay (LOS) for common pediatric conditions between teaching and nonteaching hospitals. METHODS: This study uses Massachusetts's hospital data for all discharged children ages 0 to 17 years for 1995 and 1996. Discharges were included when the principal diagnosis indicated asthma, bacterial pneumonia, convulsions, dehydration, failure to thrive, gastroenteritis, or urinary tract infections. Hospitals were classified as either teaching or nonteaching using the 1995-1996 American Hospital Association Guide. Children were identified as having a chronic condition when any discharge diagnosis was 1 of those on a previously published catalog of chronic childhood illnesses. The analysis tested the association of hospital type with LOS, controlling for chronic conditions, insurance type, age, race, diagnosis, mortality, and disposition using multivariate linear regression. RESULTS: Of 17 890 discharges for a common pediatric condition during the study period, 52.3% were from teaching hospitals. Twelve percent of common condition discharges also had a chronic disease diagnosis; 75.1% of these were discharged from a teaching hospital. LOS from nonteaching hospitals was shorter than from teaching hospitals (2.42 days vs 3.20 days). Although LOS for stays with a chronic diagnosis were longer than those without (4.75 days vs 2.56 days), controlling for chronic illness and other covariates did not eliminate the difference between LOS for nonteaching hospitals versus teaching hospitals (1.65 days vs 2.23 days). CONCLUSION: Pediatric patients with common conditions have a shorter LOS in nonteaching hospitals than those admitted to teaching hospitals by a little more than half a day. These results are unchanged when accounting for chronic conditions despite the expected results of preferential admissions to teaching hospitals for this group of patients. Additional studies should better characterize differences in patient populations, describe differences in processes, and identify differences in patient experience and outcomes to understand better the potential benefits of treating children with specific conditions at particular types of hospitals.

Stadtler A.C. et al. *The Touchpoints Pediatric Asthma Program.* Pediatr Nurs. 2001; 27(5) : 459-61.p **Abstract:** The Brazelton Touchpoints Center at the Child Development Unit, Children's Hospital, Boston, MA, designed a program intended to change the way asthma is managed in medical offices across the United States. This program was recently implemented at five pediatric asthma practices in the Chicago area where asthma prevalence is alarmingly high.

Stafford R.S. et al. *National trends in asthma visits and asthma pharmacotherapy, 1978-2002.* J Allergy Clin Immunol. 2003; 111(4) : 729-35.p **Abstract:** BACKGROUND: Research is limited on physicians' compliance with recent clinical guidelines for asthma treatment. OBJECTIVE: Our purpose was to investigate the relationships among clinical guidelines, asthma pharmacotherapy, and office-based visits through use of nationally representative data. METHODS: Nationally representative data on prescribing patterns by office-based US physicians were extracted from the National Disease and Therapeutic Index. We tracked 1978-2002 trends in the frequency of asthma visits and patterns of asthma pharmacotherapy, focusing on the use of controller and reliever medications. RESULTS: The estimated annual number of asthma visits in the United States increased continuously from 1978 through 1990 (18 million visits); since 1990, it has remained relatively stable. Controller medication use increased 8-fold between 1978 and 2002, inhaled corticosteroids manifesting the biggest increases. The use of reliever medications, particularly short-acting oral beta(2)-agonists,

decreased modestly over this period. The aggregate use of controllers (83% of visits) superseded that of relievers (80%) for the first time in 2001. Improved appropriateness of asthma pharmacotherapy was also suggested by an increase in the controller-to-reliever ratio, which reached 92% in 2002. Xanthines, which once dominated asthma therapy (63% of visits in 1978), were used in only 2% of visits in 2002. More recent drug entrants have been adopted rapidly, single-entity long-acting inhaled beta(2)-agonists being used in 9% of visits and leukotriene modifiers in 24% of visits in 2002. CONCLUSION: Asthma pharmacotherapy has changed extensively in the past 25 years. Practices over the last decade are increasingly consistent with evidence-based guidelines. These changes in medication use might have contributed to the lack of a recent increase in asthma visits.

Stallberg B. et al. *Budesonide/formoterol adjustable maintenance dosing reduces asthma exacerbations versus fixed dosing.* Int J Clin Pract. 2003; 57(8) : 656-61.p **Abstract:** A guided, adjustable-dosing regimen with budesonide/formoterol was investigated in asthma patients. In a randomised, open, multicentre study, 1034 patients received budesonide/ formoterol (Symbicort, Turbuhaler.) 80/4.5 microg or 160/4.5 microg (depending on pre-study inhaled corticosteroid dose) two inhalations twice daily for four weeks, followed by adjustable or fixed maintenance dosing for six months. Patients receiving adjustable dosing stepped down to one inhalation twice daily if symptoms were controlled and could, if symptoms worsened, step up to four inhalations twice daily for one or two weeks according to a self-guided management plan. The primary efficacy variable was occurrence of exacerbations. Compared with fixed dosing, adjustable dosing was associated with fewer patients experiencing exacerbations (6.2% vs 9.5%, NNT 30, p<0.05), fewer daily inhalations of budesonide/formoterol (2.35 vs 3.95, p<0.001), lower costs (six-month saving Euros 98, p<0.001) and was similarly well tolerated. Adjustable maintenance dosing with budesonide/formoterol provides more effective asthma control than fixed dosing, and reduces costs.

Stark P.C. et al. *Fungal levels in the home and allergic rhinitis by 5 years of age.* Environ Health Perspect. 2005; 113(10) : 1405-9.p **Abstract:** Studies have repeatedly demonstrated that sensitization to fungi, such as *Alternaria*, is strongly associated with allergic rhinitis and asthma in children. However, the role of exposure to fungi in the development of childhood allergic rhinitis is poorly understood. In a prospective birth cohort of 405 children of asthmatic/allergic parents from metropolitan Boston, Massachusetts, we examined in-home high fungal concentrations (> 90th percentile) measured once within the first 3 months of life as predictors of doctor-diagnosed allergic rhinitis in the first 5 years of life. In multivariate Cox regression analyses, predictors of allergic rhinitis included high levels of dust-borne *Aspergillus* [hazard ratio (HR) = 3.27; 95% confidence interval (CI), 1.50-7.14], *Aureobasidium* (HR = 3.04; 95% CI, 1.33-6.93), and yeasts (HR = 2.67; 95% CI, 1.26-5.66). The factors controlled for in these analyses included water damage or mild or mildew in the building during the first year of the child's life, any lower respiratory tract infection in the first year, male sex, African-American race, fall date of birth, and maternal IgE to *Alternaria* > 0.35 U/mL. Dust-borne *Alternaria* and nonsporulating and total fungi were also predictors of allergic rhinitis in models excluding other fungi but adjusting for all of the potential confounders listed above. High measured fungal concentrations and reports of water damage, mold, or mildew in homes may predispose children with a family history of asthma or allergy to the development of allergic rhinitis.

Stelmach I. et al. *A randomized, double-blind trial of the effect of treatment with formoterol on clinical and inflammatory parameters of asthma in children.* Ann Allergy Asthma Immunol. 2002; 89(1) : 67-73.p **Abstract:** BACKGROUND: In addition to their bronchodilating effect, long-acting inhaled beta-agonists have

recently been shown to have some anti-inflammatory properties. OBJECTIVE: The purpose of this study was to evaluate the effect of formoterol on inflammatory mediators in children. METHODS: In this double-blind, randomized, placebo-controlled trial, 34 children, aged 6 to 18 years, with moderate atopic asthma, were randomly allocated to receive formoterol or matching placebo for 4 weeks. The primary endpoint of this study was to determine changes in serum levels of inflammatory markers after treatment with formoterol; secondary endpoints included clinical efficacy and bronchial hyperreactivity. The following parameters were measured: symptom score, forced expiratory volume in 1 second (FEV1), provocative concentration of histamine causing a 20% fall in FEV1 (PC20) for histamine and peripheral blood eosinophil count, serum levels of eosinophil cationic protein (ECP), soluble receptor of interleukin-2 (sIL-2R), level of interleukin-4 (IL-4), level of soluble intercellular adhesion molecule-1 (ICAM-1), and immunoglobulin E (IgE) level before and after treatment. RESULTS: Compared with placebo, treatment with formoterol significantly improved lung function. The mean value of FEV1 changed from 74% of predicted value before treatment to 80% of predicted value after treatment (P < 0.001). The mean concentration of eosinophil blood count before and after treatment was 379 and 310 cells/mm³ (P = 0.035); ECP was 93 and 83 mcg/L; and serum IL-4 was 0.13 and 0.11 pg/mL (P = 0.001). There was no significant difference between formoterol and placebo recipients in PC20H, and serum concentration of sIL-2R, sICAM-1, or IgE after treatment. The group that received formoterol showed improvement in pulmonary function as measured by FEV1 (P < 0.001), and PC20H (P = 0.04) after 4 weeks of treatment. These patients also showed improvement of clinical symptoms (P < 0.001). Serum marker measurements in the formoterol group showed decreased concentrations of eosinophil blood count, ECP, and IL-4, but there was no difference in before and after measurements of sIL-2R, sICAM-1, and IgE. CONCLUSIONS: These results indicate that formoterol has measurable anti-inflammatory properties and can diminish asthma symptoms and bronchial hyperreactivity.

Stelmach I. et al. *A randomized, double-blind trial of the effect of glucocorticoid, antileukotriene and beta-agonist treatment on IL-10 serum levels in children with asthma.* Clin Exp Allergy. 2002; 32(2) : 264-9.p **Abstract:** BACKGROUND: Levels of an immunoregulatory and anti-inflammatory cytokine IL-10 are reduced in asthmatic airways, potentially contributing to more intense inflammation. Triamcinolone has anti-inflammatory properties and the anti-inflammatory effects of montelukast and formoterol have been discussed. OBJECTIVE: The purpose of this study was to define the effect of treatment with triamcinolone, montelukast and formoterol on the serum level of IL-10, eosinophil blood counts, eosinophil cationic response (ECP) and clinical parameters (symptom score, FEV1 and PC20H) in children with moderate asthma. METHODS: An 8-week, placebo-controlled and randomized, double-blind trial was carried out. The subjects were 91 children with moderate atopic asthma who were allergic to dust mite. Patients were randomly allocated to receive 400 microg triamcinolone (n = 19), 5 or 10 mg (according to age) montelukast (n = 18), 24 microg formoterol (n = 18) or placebo (n = 36). RESULTS: Seventy-nine children completed the study. After treatment with triamcinolone and montelukast the level of IL-10 in blood serum significantly increased, eosinophil blood counts and ECP levels significantly decreased and all clinical parameters improved; treatment with formoterol had no effect on IL-10 level, eosinophil blood counts in serum and bronchial hyper-reactivity; ECP level significantly decreased after treatment and asthma symptoms and FEV1 improved significantly. Mean IL-10 levels in serum before and after treatment with triamcinolone were 7.23 pg/mL with 95% CI, 6.74 -7.72% and 14.24 pg/mL with 95% CI, 11.6-16.88%, respectively (P < 0.001); with montelukast they were 6.59 pg/mL with 95% CI, 6.26-7.23% and 10.94 pg/mL with 95% CI, 8.24-12.65%, respectively (P < 0.002); with formoterol they were 7.06 pg/mL with 95% CI, 6.61-7.52% and 7.04 pg/mL with 95% CI, 6.15-7.93%. We found statistically significant correlations between serum

level of IL-10 and serum level of ECP after treatment with triamcinolone and montelukast. CONCLUSION: This study demonstrates that one possible way by which triamcinolone and montelukast contribute to inhibition of inflammation is by increasing IL-10 levels.

Stelmach I. et al. *A randomized, double-blind trial of the effect of treatment with montelukast on bronchial hyperresponsiveness and serum eosinophilic cationic protein (ECP), soluble interleukin 2 receptor (sIL-2R), IL-4, and soluble intercellular adhesion molecule 1 (sICAM-1) in children with asthma.* J Allergy Clin Immunol. 2002; 109(2) : 257-63.p **Abstract:** BACKGROUND: Anti-inflammatory properties of leukotriene modifiers and their effect on bronchial hyperresponsiveness have not been studied in children with asthma. OBJECTIVE: The primary objective of this study was to determine the changes in serum levels of inflammatory mediators, clinical efficacy, and bronchial hyperresponsiveness after treatment with montelukast. METHODS: In this double-blind, randomized, placebo-controlled trial, 39 children with mild-to-moderate atopic asthma were randomly allocated to receive montelukast or placebo for 6 weeks. Main outcome measures were changes in serum concentrations of soluble interleukin 2 receptor (sIL-2R), IL-4, and soluble intercellular adhesion molecule 1 (sICAM-1); peripheral blood eosinophil count; and eosinophilic cationic protein (ECP). Asthma severity score, FEV₁, and bronchial hyperreactivity (BHR) for histamine were secondary end points. RESULTS: Compared to placebo, serum concentrations of IL-4, sICAM-1, and ECP and eosinophil blood counts significantly decreased after 6 weeks of treatment with montelukast. Montelukast significantly improved asthma control and FEV₁. Montelukast resulted in within-group significant decrease in levels of serum sIL-2R (611 vs. 483 pg/mL), IL-4 (0.123 vs 0.102 pg/mL), sICAM-1 (280 vs. 244 ng/mL), and ECP (74 vs. 59 microg/mL) and in eosinophil blood counts (349 vs. 310 cells/mm³). Mean FEV₁ value changed from 85% of predicted to 95% (P <.001) and for histamine (PC(20)H) from 2.8 mg/mL to 3.8 mg/mL (P <.001) after treatment with montelukast. There was no significant difference between montelukast and placebo recipients in the serum concentrations of sIL-2R and PC(20)H after treatment. CONCLUSION: Montelukast provides clinical benefit to patients with chronic asthma and decreases bronchial hyperresponsiveness. Montelukast caused a statistically significant decrease of serum concentrations in cytokine, ICAM-1, and ECP and peripheral blood eosinophil counts over the 6-week treatment period. This observation raises the possibility that leukotriene receptor antagonists, such as montelukast, may have effects on parameters of asthmatic inflammation.

Stelmach I. et al. *The effect of inhaled heparin on airway responsiveness to histamine and leukotriene D4.* Allergy Asthma Proc. 2003; 24(1) : 59-65.p **Abstract:** Inhaled heparin has been shown to reduce the early and late phase of asthmatic reactions and suppress an allergen-induced increase in bronchial hyperreactivity. The mechanism involved in the control of bronchial hyperreactivity in asthma by heparin is still not understood. The purpose of this study was to investigate the effect of inhaled heparin on the airway response to histamine and leukotriene D4. Children with a typical history of mild allergic asthma participated in this randomized, double-blind, placebo-controlled cross-over study. Subjects underwent provocation challenge tests with histamine or leukotriene D4 before and after inhalation of heparin and placebo. Twenty-three patients completed the study. We showed that placebo did not affect the bronchial hyperreactivity to histamine or leukotriene. A single dose of inhaled heparin significantly decreased bronchial hyperreactivity to histamine and leukotriene in children with mild asthma. Results of our study suggest that inhaled heparin, because of its antiallergic and/or anti-inflammatory properties, modifies airway hyperresponsiveness in children with allergic asthma.

Stelmach I. et al. *The prevalence of mouse allergen in inner-city homes.* Pediatr Allergy Immunol. 2002; 13(4) : 299-302.p **Abstract:** Mouse allergen has not been studied in detail in the general population. It is common for patients from inner-city environments to report significant mouse infestation in their homes and neighborhoods. The aim of this study was to determine the prevalence of mouse allergen in the homes of inner-city children with asthma in relation to the demographic features of these children and their specific housing characteristics. Seventy-eight dust samples from 39 inner-city homes of Lodz, Poland, were analyzed for mouse allergen. Skin-prick tests (SPTs) to mouse allergen were performed in all patients. In addition, data regarding the demographics and housing of the subjects were related to the mouse allergen levels. Mouse allergen was detected in 22 of 78 dust samples (28%), and in 18 of 39 homes (46%), including 13 kitchen (33%) and nine bedroom (23%) samples. Mouse allergen levels did not correlate between different rooms in the same home. The levels detected ranged from 0.09 to 2.34 micro g/g of dust. The highest levels were found in kitchens, with median levels of 0.2 micro g/g, 95% confidence interval (CI): 0.12-0.85 (range: 0.1-2.34 microg/g); in bedrooms the mean levels were 0.23 microg/g, 95% CI: 0.1-0.97 (range: 0.09-1.62 microg/g). Eleven of 18 children with detectable mouse allergen in house dust, and three of 21 without detectable mouse allergen in house dust, had a positive SPT to mouse allergen. On home inspection, 18% of the homes had evidence of mice in one or two rooms and had higher levels of mouse allergen (p < 0.01). None of the other subject or housing variables evaluated were associated with higher mouse allergen levels. In Polish children, mouse allergen is an important factor of sensitivity and should be recognized in the diagnosis of allergic diseases as well as in allergen-reduction programmes.

Stempel D.A. et al. *Patterns of asthma control: a 3-year analysis of patient claims.* J Allergy Clin Immunol. 2005; 115(5) : 935-9.p **Abstract:** BACKGROUND: The goal of asthma therapy is to maintain consistent control. OBJECTIVE: We sought to examine the patterns of asthma control recorded over 3 years using administrative claims and resource utilization definition. METHODS: We performed a retrospective observational study with a nationally representative patient-level database containing pharmacy and medical claims. Patients with asthma (International Classification of Diseases, Ninth Revision-Clinical Modification code 493.xx), patients undergoing treatment with at least 1 asthma medication, and patients with 36 months of continuous claims coverage during the calendar years 1996 through 2002 were identified. A total of 63,324 patients were included in the study. Patients were classified as having controlled asthma in year 1 if they had less than 4 claims for a short-acting beta 2 -agonist, no claims for an OCS, and no asthma-related emergency department visits or hospitalizations. Patients were then followed over the next 8 quarters (2 years) to observe whether control was maintained. Control during a quarter was defined with the same criteria, except the reliever threshold was adjusted to 2 or more claims per quarter. RESULTS: Thirty-nine thousand ninety-five (57%) patients were defined as having controlled asthma during year 1. During the 2-year follow-up period, a range of 10% to 14% of these patients with controlled asthma met the criteria of uncontrolled asthma during any given quarter. Overall, 46,227 (73%) patients identified met the criteria for uncontrolled asthma at least once during the 3-year period. CONCLUSIONS: This study demonstrates that almost 75% of asthmatic patients experience an uncontrolled asthma episode 1 or more times over a 3-year period. Furthermore, we found that significant fluctuations in asthma control exist, even in patients with prior controlled asthma.

Stempel D.A. et al. *Cost analysis of the use of inhaled corticosteroids in the treatment of asthma: a 1-year follow-up.* Respir Med. 2001; 95(12) : 992-8.p **Abstract:** A retrospective cohort using pharmacy and medical claims was analysed to determine whether the differences in efficacy of various inhaled corticosteroids

demonstrated in clinical trials lead to differences in costs of care observed in clinical practice. Subjects that had an ICD-9 (493.XX) code for asthma and a new pharmacy claim for inhaled fluticasone propionate 44 mcg (FP), beclomethasone dipropionate (BDP), triamcinolone acetonide (TAA), budesonide (BUD) or flunisolide (FLU) were identified and followed for 12 months. Annual asthma care charges (pharmacy and medical) over the 12-month observation period were significantly ($P < 0.03$) higher in patients treated with BDPTAA, BUD and FLU compared to FP, 24%, 27%, 34% and 45% respectively. In addition, patients treated with BDPTAA, and FLU were associated with significantly ($P < 0.005$) higher total healthcare (asthma + non-asthma) charges compared to patients on FP, 53%, 46% and 39% respectively. Asthma care and total healthcare charges remained lower for FP after including FP110 mcg and excluding patients who were extreme cost outliers (± 2 SD from the mean) in a univariate sensitivity analysis. This analysis supports recent randomized control trials that FP offers a superior efficacy profile at lower asthma care as well as total healthcare charges compared to other inhaled corticosteroids.

Stempel D.A. et al. *Treatment patterns for pediatric asthma prior to and after emergency department events.* *Pediatr Pulmonol.* 2005; 40(4) : 310-5.p Abstract: There are 2 million asthma-related emergency department (ED) events each year in the United States. Children share a disproportional burden of these events. This study was designed to describe the treatment patterns in children in the year prior to and 2 months after an ED event. This retrospective observational study utilized the PharMetrics Integrated Outcomes Database that contains administrative claims from over 20 managed-care plans across the United States. Children aged 1-17 years with at least one ED visit for asthma during 2001 were included. Patients were required to have data available 12 months prior to and 2 months following the ED visit. We identified 5,501 pediatric asthma-related ED admissions. In the year prior to the ED event, 19.4% of children received an inhaled corticosteroid (ICS), 31.4% an oral corticosteroid (OCS), and 58.3% a short-acting beta-agonist (SABA). Overall, there were 3.7 albuterol units for every ICS unit dispensed in the 12 months prior to the event. Ninety-four percent of the children had an office visit in the year prior to the ED visit. Prescriptions dispensed for ICS and OCS increased 2.9-fold and 8.2-fold, respectively, in the month after the ED event. However, the dispensing rates for both medications reverted to near baseline by the second month after the index event. In conclusion, this study demonstrates the dependence of children with asthma on the use of rescue medications. An ED event results in only an incremental and transient increase in ICS-containing controller treatment.

Stempel D.A. et al. *Inhaled corticosteroids plus salmeterol or montelukast: effects on resource utilization and costs.* *J Allergy Clin Immunol.* 2002; 109(3) : 433-9.p Abstract: BACKGROUND: Experimental clinical studies have demonstrated that the addition of salmeterol to inhaled corticosteroids (ICSs) is superior to the addition of montelukast to ICSs. Observational research from real-world clinical practice is needed to confirm these results. OBJECTIVE: The present study was designed to assess, in clinical practice, the comparative impact on health care utilization and cost of 2 dual-controller therapies, ICS + salmeterol and ICS + montelukast. METHODS: This study involved the use of a 24-month pre/post retrospective design in patients continuously enrolled in any of 14 United HealthCare plans. Outcomes assessed were post-index pharmacy costs, rates of emergency department visits and hospitalizations, numbers of filled prescriptions for short-acting beta-agonists (SABAs), total asthma costs, and total health care costs. RESULTS: Subjects in the ICS + salmeterol group had 35% fewer post-index SABA claims than subjects in the montelukast add-on group ($P < 0.05$). Subjects using ICS + montelukast were 2.5 times more likely to have an asthma-related hospitalization than subjects using ICS + salmeterol ($P < 0.065$). Total adjusted asthma costs were 63% higher for the patients receiving ICS + montelukast than

for the patients receiving ICS + salmeterol ($P < 0.0001$). In addition, total health care costs were 25% lower in the ICS + salmeterol group. ($P < 0.0004$). Additional reductions in hospitalization and emergency department visits were observed when the patients on FP + salmeterol were studied separately. CONCLUSION: In comparison with the use of montelukast and ICS, the use of salmeterol and ICS was associated with a significant reduction in SABA use, decreased hospital event rates, and significantly lower total asthma care costs.

Stempel D.A. et al. *The risk of hospitalization in patients with asthma switched from an inhaled corticosteroid to a leukotriene receptor antagonist.* *J Allergy Clin Immunol.* 2002; 110(1) : 39-41.p Abstract: Asthma-related hospitalization rates were compared over a 2-year period between a cohort of patients with asthma who switched from an inhaled corticosteroid in year 1 to a leukotriene modifier in year 2 ($n = 285$) and a matched cohort continuously treated with an inhaled corticosteroid ($n = 570$). During year 1, patients were well maintained, with a hospitalization rate of 1.1% to 1.4%. During year 2, 2.5% of the patients switched to a leukotriene modifier had one or more asthma-related hospitalizations compared with 0.6% of the patients continuously receiving an inhaled corticosteroid. Patients treated with a leukotriene modifier were at 7 times greater risk for an asthma-related hospitalization compared with patients who continued to receive an inhaled corticosteroid (risk-adjusted odds ratio, 7.1; 95% CI, 2.79-17.95). These data are consistent with the results of well-controlled clinical trials showing that leukotriene modifiers may be associated with deterioration of asthma control relative to inhaled corticosteroids. Considered in aggregate, the data support the conclusion that leukotriene modifiers should not be substituted for inhaled corticosteroids as a single-controller therapy for asthma.

Stempel D.A. et al. *Treatment patterns in the months prior to and after asthma-related emergency department visit.* *Chest.* 2004; 126(1) : 75-80.p Abstract: BACKGROUND: There are 2 million asthma-related emergency department (ED) events each year in the United States. The underrecognition and undertreatment of asthma is believed to be associated with this high level of morbidity. This study was designed to describe the treatment patterns in the year prior to the ED event and for 2 months after the event. METHODS: This retrospective observational study utilized an integrated managed care database that contained administrative claims from > 20 managed care plans across the United States. All patients with at least one ED visit for asthma during 2001 were included. Patients were required to have data available 12 months prior to and 2 months following the ED visit of interest, and were excluded if they had made an asthma-related ED visit within 12 months of the identified event. RESULTS: There were 12,636 patients identified with an asthma-related ED visit. In the year prior to the ED event, 25.1% of the patients received an inhaled corticosteroid (ICS), 29.9% received an oral corticosteroid (OCS), and 53.5% received a short-acting beta-agonist (SABA). Overall, there were three albuterol units dispensed for every ICS unit dispensed in the 12-month period prior to the ED event. Ninety-four percent of patients had made an office visit in the prior year, but only 13.3% underwent spirometry testing. Prescriptions dispensed for ICSs and OCSs increased 2.6-fold and 7.5-fold, respectively, in the month after the ED event, and dispensing rates reverted approximately to baseline rates by the second month after the index ED event. CONCLUSION: This study demonstrates the dependence of this population on the use of rescue medications, including SABA and OCS, to treat their asthma. Furthermore, the ED event resulted in only an incremental short-term improvement in ICS-containing controller treatment.

Stephen G.A. et al. *Assessment of respiratory symptoms and asthma prevalence in a U.S.-Mexico border region.* *Arch Environ Health.* 2003; 58(3) : 156-62.p Abstract: The authors studied children who were 10-12 yr of age and who resided in sister cities in a U.S.-

Mexico border region to determine the prevalence of asthma and respiratory symptoms. The relationship of symptoms to ambient levels of particulate matter less than 10 microm in diameter (PM10), and to several indoor environmental conditions, was assessed. The study was conducted in the border cities of Ambos Nogales (Nogales, Arizona [United States], and Nogales, Sonora [Mexico]). At the beginning of the 11-wk study, during the autumn of 1996, 631 students and their parents completed baseline questionnaires. While in school, the children completed daily symptom diaries and daily peak expiratory flow maneuvers. PM10 values and daily temperatures were also measured. The authors found that the prevalence of self-reported asthma among 5th-grade students was comparable on both sides of the border (i.e., 7.6% on the Arizona side and 6.9% on the Sonora side). Wheezing was a frequent complaint (29.5-35.6%), as was cough (16.8-29.6%). Smoking in the home was common on both sides of the border, and it was associated with a greater occurrence of self-reported asthma and respiratory complaints. Increased respiratory symptoms were also associated with increased ambient PM10 levels. The prevalence of respiratory symptoms such as wheezing and frequent cough among all children in this study, combined with the limitations inherent in self-reporting, suggest that asthma may actually be more prevalent than has been previously reported.

Sterling Y.M. et al. *Characteristics of African American women caregivers of children with asthma.* MCN Am J Matern Child Nurs. 2003; 28(1) : 32-8.p **Abstract:** PURPOSE: To describe the attributes and characteristics of African American women who were the primary caregivers of children with asthma. METHODS: Descriptive qualitative ethnography. Data collection consisted of formal interviews, participant observation, and fieldnotes. Each study participant was formally and informally interviewed (audiotaped) during a 1-year period. The researchers also observed and participated in family activities in various naturalistic settings. RESULTS: Six themes emerged that depict the characteristics of these women: (1) Knowledge about the child's asthma; (2) Gatekeepers to the child's care; (3) Being religious; (4) Support; (5) Roles as teacher, counselor, and advisor to the child; and (6) Self-sufficiency and industriousness. CLINICAL IMPLICATIONS: Nurses should use the information in this study to examine the ways in which they interact with caregivers of asthmatic children. The caregivers personal beliefs, need for information, and previous experiences with asthma and family illness should be assessed. These mothers and grandmothers should be respected as the gatekeeper to the family's healthcare. Nurses should be nonjudgmental and supportive of caregivers when they express their religious beliefs and practices. Nurses who understand how mothers cope can reinforce these coping skills and provide better nursing care.

Stevens E. et al. *Urban air pollution and children's asthma: what do parents and health professionals think?* *Pediatr Pulmonol.* 2004; 37(6) : 530-6.p **Abstract:** Our objective was to explore and compare, in the context of other exposures, lay and professional perceptions of the links between urban air pollution and children's asthma. We used a triangulated survey approach, using quantitative questionnaire surveys enriched by qualitative interviews. Derivation of indicators of actual local air quality used modelled air pollution and a geographical information system. Our setting involved families and community health professionals in the London borough of Ealing, and pediatric respiratory specialists across the United Kingdom. Participants included 863 parents of children aged 3-11 years, 151 reporting currently asthmatic children, of whom 20 were extensively interviewed; 98 local general practitioners and 50 practice nurses; and 75 paediatric respiratory consultants and 55 specialist nurses. Main outcome measures involved views about the links between urban air pollution and children's asthma, relative to other triggers. Comparison of assessments of local air quality, with actual pollution levels, was made by parents with and without asthmatic children. Many parents were unsure as to what factors

initiate asthma, but the most frequently cited was traffic pollution; it was also considered important in the exacerbation of asthma. Health professionals' assessments were inconsistent: specialists conformed to the dominant literature dismissing strong links between air pollution and asthma, while local clinicians reflected the views of parents in their community. Surrounding parents' views were difficulties defining exposures to urban air pollution, underlying concerns about risks to general health, perceived lack of control, unclear expert opinion, and widely accepted informal "messages" which assumed strong links. Parents with experience of asthma were found to have significantly less accurate (negatively biased) perceptions of local air quality. In conclusion, reactions to uncertainty surrounding associations between asthma and urban air pollution varied: parents' concerns were heightened (and propagated by other influences), specialist clinicians were dismissive, and community clinicians fell between these extremes.

Stevens M.W. et al. *Interrater agreement in the clinical evaluation of acute pediatric asthma.* *J Asthma.* 2003; 40(3) : 311-5.p **Abstract:** Prior studies of observer agreement of the clinical exam of children with asthma have focused on small numbers of specially trained observers, often in the setting of clinical trials. Our objective was to evaluate interobserver reliability in the physical exam of acute pediatric wheezing and asthma among a large group of diverse examiners, in a setting of routine clinical practice, and without prior special training. The setting was a large urban children's hospital. Observers were attending pediatric emergency physicians and fellows; hospital respiratory therapists; and emergency department (ED) nurses. Patients were children receiving nebulized medications for wheezing in the ED or inpatient asthma unit. Pairs of observers simultaneously but independently rated work of breathing, wheeze, decreased air entry, prolonged expiration, breathlessness, respiratory rate, mental status, and global (or overall) severity using a structured exam template. A total score for each exam was also evaluated. A total of 230 pairs of observations were performed; mean patient age was 5.3 years. For all pairs, the weighted kappa statistics for the exam components ranged from 0.61 to 0.74 (moderate or substantial agreement). The global severity category and total score had weighted kappas of 0.80 and 0.82, respectively (excellent agreement). Agreement was generally somewhat lower for unlike (different profession) observer pairs than for like observer pairs, but remained acceptable. Agreement in two age groups (< or = 3 years old and > or = 4) was at least moderate for all exam components analyzed. Spearman rank correlations between individual exam components and the global assessments of patient severity were all greater than 0.5, indicating at least moderate to good correlations. We found substantial interobserver agreement among a broad range of examiners in the components of the clinical examination of acute wheezing in both younger and older children. This is contrary to the commonly held observation that the poor interobserver reliability of physical exam findings in asthma may limit their usefulness as asthma outcome measures. Support for use of a structured respiratory exam format or template in asthma guidelines was also shown.

Stevenson J. *Relationship between behavior and asthma in children with atopic dermatitis.* *Psychosom Med.* 2003; 65(6) : 971-5.p **Abstract:** OBJECTIVE: The significance of psychological factors in asthma is a subject of considerable dispute. This study addressed the little investigated question of the potential role of psychological factors in the initial onset of asthma. MATERIALS AND METHODS: Data on the validated, standardized Behavior Screening Questionnaire were obtained prospectively from 35 to 53 months for 150 atopic children who had asthma by age 53 months and for 115 who did not. RESULTS: At each age, the children who had asthma by 53 months had more behavior problems. There was no evidence that the subsequent behavior of those children who had asthma became more problematic. However, for those children without asthma by 35 months, an elevated behavior problem score at that age was related to the subsequent onset of asthma by age 53 months. The

behavior problem score added significantly to the prediction of asthma onset (OR adjusted: 1.15; 95% CI: 1.02-1.29) when known risk factors of asthma and IgE levels for grass pollen and house dust mite at age 17 months were taken into account. **CONCLUSIONS:** Behavior problems may precede asthma onset in young atopic children. In this age group, behavior problems are not secondary psychological reactions to asthma onset. They may act as a marker for stress in the child's life. The presence of behavior problems should alert clinicians that the child may be at increased risk for transition from atopic dermatitis to asthma.

Stick S.M. *Non-invasive monitoring of airway inflammation.* Med J Aust. 2002; 177 Suppl : S59-60.p **Abstract:** What we know: Various techniques are available that purport to measure aspects of airway inflammation non-invasively, including analysis of volatile molecules in exhaled breath and components of breath condensates. Adapting and validating these methods for use in young children and infants poses significant methodological problems, but progress has been made, particularly with regard to measurements of exhaled nitric oxide. Future studies to validate such tests are likely to require access to airway tissue for examination as a "gold standard". What we need to know: How can we obtain airway tissue from infants and young children to better characterise the early airway changes in asthma? How do non-invasive tests of airway inflammation compare with a validated gold standard? How sensitive and specific are non-invasive tests of inflammation for predicting outcomes in asthma, including response to therapy?

Stick S.M. *Pulmonary physiology, airway responsiveness and asthma.* Med J Aust. 2002; 177 Suppl : S55-6.p **Abstract:** What we know: Tests that have allowed the measurement of lung function in infants have greatly enhanced our understanding of early pulmonary development and the pathophysiology of early respiratory disease. Airway responsiveness in infancy appears to be an independent determinant of symptoms and lung function later in childhood. New tests of airway responsiveness hold the promise of predicting, with increased specificity, infants at risk of developing asthma. What we need to know: What are the factors that determine airway responsiveness soon after birth? Why does airway responsiveness in the first weeks of life relate to lung function many years later? Do different challenge agents reflect different pathophysiological processes involved in the development of persistent asthma?

Stirbu I. et al. *Differences in avoidable mortality between migrants and the native Dutch in The Netherlands.* BMC Public Health. 2006; 6 : 78.p **Abstract:** **BACKGROUND:** The quality of the healthcare system and its role in influencing mortality of migrant groups can be explored by examining ethnic variations in 'avoidable' mortality. This study investigates the association between the level of mortality from 'avoidable' causes and ethnic origin in the Netherlands and identifies social factors that contribute to this association. **METHODS:** Data were obtained from cause of death and population registries in the period 1995-2000. We compared mortality rates for selected 'avoidable' conditions for Turkish, Moroccan, Surinamese and Antillean/Aruban groups to native Dutch. **RESULTS:** We found slightly elevated risk in total 'avoidable' mortality for migrant populations (RR = 1.13). Higher risks of death among migrants were observed from almost all infectious diseases (most RR > 3.00) and several chronic conditions including asthma, diabetes and cerebrovascular disorders (most RR > 1.70). Migrant women experienced a higher risk of death from maternity-related conditions (RR = 3.37). Surinamese and Antillean/Aruban population had a higher mortality risk (RR = 1.65 and 1.31 respectively), while Turkish and Moroccans experienced a lower risk of death (RR = 0.93 and 0.77 respectively) from all 'avoidable' conditions compared to native Dutch. Control for demographic and socioeconomic factors explained a substantial part of ethnic differences in 'avoidable' mortality. **CONCLUSION:** Compared to the native Dutch population, total 'avoidable' mortality

was slightly elevated for all migrants combined. Mortality risks varied greatly by cause of death and ethnic origin. The substantial differences in mortality for a few 'avoidable' conditions suggest opportunities for quality improvement within specific areas of the healthcare system targeted to disadvantaged groups.

Stokstad E. *Public health. Asthma linked to indoor dampness.* Science. 2004; 304(5675) : 1229.p

Stout J. *Is primary prevention of allergy-mediated asthma a viable idea?* Arch Pediatr Adolesc Med. 2002; 156(10) : 967-8.p

Strand M. et al. *Estimating effects of ambient PM(2.5) exposure on health using PM(2.5) component measurements and regression calibration.* J Expo Sci Environ Epidemiol. 2006; 16(1) : 30-8.p **Abstract:** Most air pollution and health studies conducted in recent years have examined how a health outcome is related to pollution concentrations from a fixed outdoor monitor. The pollutant effect estimate in the health model used indicates how ambient pollution concentrations are associated with the health outcome, but not how actual exposure to ambient pollution is related to health. In this article, we propose a method of estimating personal exposures to ambient PM(2.5) (particulate matter less than 2.5 microm in diameter) using sulfate, a component of PM(2.5) that is derived primarily from ambient sources. We demonstrate how to use regression calibration in conjunction with these derived values to estimate the effects of personal ambient PM(2.5) exposure on a continuous health outcome, forced expiratory volume in 1 s (FEV(1)), using repeated measures data. Through simulation, we show that a confidence interval (CI) for the calibrated estimator based on large sample theory methods has an appropriate coverage rate. In an application using data from our health study involving children with moderate to severe asthma, we found that a 10 microg/m³ increase in PM(2.5) was associated with a 2.2% decrease in FEV(1) at a 1-day lag of the pollutant (95% CI: 0.0-4.3% decrease). Regressing FEV(1) directly on ambient PM(2.5) concentrations from a fixed monitor yielded a much weaker estimate of 1.0% (95% CI: 0.0-2.0% decrease). Relatively small amounts of personal monitor data were needed to calibrate the estimate based on fixed outdoor concentrations.

Straub D.A. et al. *Correlation of nitrites in breath condensates and lung function in asthmatic children.* Pediatr Allergy Immunol. 2004; 15(1) : 20-5.p **Abstract:** We aimed to evaluate the value of exhaled breath condensates in monitoring airway inflammation in childhood asthma before and after high altitude climate therapy. Forty-eight asthmatic children on regular anti-asthma treatment with a normal FEV1 and positive skin prick test for house dust mites were recruited. All children had been referred to an alpine clinic for high altitude climate therapy, because of persistent asthmatic symptoms despite use of daily anti-inflammatory treatment. Subjects were assessed on their arrival and before departure from the alpine clinic. Spirometry, bronchial provocation tests and measurements of nitrites in breath condensates were performed. Median levels of nitrites were significantly higher before than after high altitude climate therapy (1.27 vs. 0.93 microm; p = 0.008). In addition, MEF50 improved significantly (p < 0.0005). There was a significant correlation between nitrites in breath condensates and MEF50 (r = -0.63, p < 0.0001), symptoms (r = 0.47, p = 0.0007) and airway hyper-reactivity (AHR) (r = -0.41, p = 0.004). In summary, we found a reduction in nitrites in breath condensates after a high altitude climate therapy. Significant correlations were found between nitrites and MEF50, AHR and symptoms. We conclude that the measurement of nitrites may be feasible to objectively assess airway inflammation in asthmatic children in order to detect ongoing inflammation in children with normal FEV1 but persistent symptoms.

Strunk R.C. et al. *Predictors of protocol adherence in a pediatric asthma clinical trial.* J Allergy Clin Immunol. 2002; 110(4) : 596-602.p
Abstract: BACKGROUND: Declining protocol adherence can threaten the validity of a clinical trial. OBJECTIVE: We sought to explore patient and family factors important for protocol adherence in the 133 patients followed at one of the 8 Childhood Asthma Management Program (CAMP) clinical centers. Difficulties with timely return of diary cards (diary card problem), with keeping or frequently rescheduling appointments (appointment problem), and with commitment to all aspects of the trial (commitment problem) were tracked prospectively during the treatment phase of CAMP, which ranged from 20 to 40 months at the time of the analysis. METHODS: We performed a cross-sectional analysis. RESULTS: During the course of this investigation, no St Louis CAMP patients dropped out of the study, although signs of eroding participation were observed in 44% of patients. For this cross-sectional analysis, the percentage of patients exhibiting protocol-adherence problems was greater the longer patients had been in the trial: 33.3% at 20 to 25 months, 39.5% at 26 to 30 months, 51.4% at 31 to 35 months, and 69.2% at 36 to 40 months ($P < .01$). The diary card problem was present in 22.2% of the patients enrolled in the trial for 20 to 25 months compared with 66.7% for patients enrolled for 36 to 40 months ($P < .005$). Appointment and commitment problems were present in smaller percentages of patients and did not change by time in the trial ($P = .41$ and $.22$, respectively). A logistic regression analysis of demographic characteristics indicated that age at randomization and time in the trial were significant factors: for every 2-year increase in age, a child was twice as likely to have a commitment problem (odds ratio [OR], 1.96; 95% CI, 1.50-2.57), and for each additional 5 months of participation in the study, a child was twice as likely to have a diary card problem (OR, 1.91; 95% CI, 1.76-2.07). There was no influence of family income, patient race, or patient sex on the occurrence of any of the 3 protocol-adherence problems. A similar analysis of psychologic characteristics of the child and family indicated (1) a 2-fold increase in the risk of a diary card problem with a 10% increase in the percentage of total commissions on the attention scale of the Gordon Diagnostic Study (OR, 2.18; 95% CI, 2.02-2.35), (2) a 2-fold decrease in the risk of an appointment problem with a 10-unit increase in the Child Manifest Anxiety Scale (OR, 0.46; 95% CI, 0.44-0.49), (3) a 2-fold decrease in risk of an appointment problem with a 10-unit increase in the cohesion subscale of the Family Environment Scale (OR, 0.58; 95% CI, 0.55-0.60), and (4) a 5-fold decrease in the risk of a commitment problem with a 10-unit increase in the Child Depression Index score (OR, 0.21; 95% CI, 0.18-0.24). CONCLUSIONS: Adherence and retention problems commonly occur in longer clinical trials. CAMP patients and families were selected in part on the basis of likelihood of being able to participate in the trial to enhance the conclusions of the trial. Despite this selection process, adherence problems were noted. Problems increased with duration of participation, increasing child age, and the presence of less family cohesion or attention problems in the child. In contrast, the presence of mild emotional distress (anxiety and depression) in the child was associated with fewer protocol-adherence problems. Incorporating procedures that help anticipate and identify adherence problems early might improve continued participation in all aspects of a trial and even retention in long-term clinical trials.

Sturdy P.M. et al. *Psychological, social and health behaviour risk factors for deaths certified as asthma: a national case-control study.* Thorax. 2002; 57(12) : 1034-9.p **Abstract:** BACKGROUND: Uncontrolled studies suggest that psychosocial factors and health behaviour may be important in asthma death. METHODS: A community based case-control study of 533 cases, comprising 78% of all asthma deaths under age 65 years and 533 hospital controls individually matched for age, district and asthma admission date corresponding to date of death was undertaken in seven regions of Britain (1994-98). Data were extracted blind from anonymised copies of primary care records for the previous 5 years and non-blind for the earlier period. RESULTS: 60% of cases and 63% of controls were female. The

median age in both groups was 53. Cases had an earlier age of asthma onset, more chronic obstructive lung disease, and were more obese. 48% of cases and 42% of controls had a health behaviour problem; repeated non-attendance/poor inhaler technique was related to increased risk of death. Overall, 85% and 86%, respectively, had a psychosocial problem. Four psychosocial factors were associated with increased risk of death (psychosis, alcohol/drug abuse, financial/employment problems, learning difficulties) and two with reduced risk (anxiety/prescription of antidepressant drugs and sexual problems). While alcohol/drug abuse lost significance after adjustment for psychosis, other associations appeared independent of each other and of indicators of severity and co-morbidity. None of the remaining 13 factors including family problems, domestic abuse, bereavement, and social isolation were significantly related to risk of asthma death. CONCLUSION: There was an apparently high burden of psychosocial problems in both cases and controls. The associations between health behaviour, psychosocial factors, and asthma death are varied and complex with a limited number of factors showing positive relationships.

Sturm J.J. et al. *Effects of tobacco smoke exposure on asthma prevalence and medical care use in North Carolina middle school children.* Am J Public Health. 2004; 94(2) : 308-13.p **Abstract:** OBJECTIVES: We sought to determine the effects of exposure to environmental tobacco smoke (ETS) and childhood cigarette smoking on asthma symptoms among middle school children in North Carolina. METHODS: During 1999-2000, information was collected from a survey completed by the children. Outcomes of asthma symptom reporting were regressed on tobacco smoke exposures. RESULTS: Children who currently smoked or reported any exposure to ETS were at increased risk of reporting active asthma symptoms. Exposure to ETS and childhood cigarette smoking was responsible for 15% of the asthma cases observed in the study population and \$1.34 million in excess medical expenditures. CONCLUSIONS: Even at low levels of exposure, childhood cigarette smoking and ETS are independently associated with asthmatic symptoms.

Subbarao P. et al. *Effect of ciclesonide dose and duration of therapy on exercise-induced bronchoconstriction in patients with asthma.* J Allergy Clin Immunol. 2006; 117(5) : 1008-13.p **Abstract:** BACKGROUND: Inhaled corticosteroid therapy improves exercise symptoms in asthmatic subjects. OBJECTIVE: We sought to evaluate exercise-induced bronchoconstriction (EIB) as a method of determining the dose and time responses of inhaled corticosteroid therapy. METHODS: In this double-blind, randomized, cross-over study with 2 parallel arms, 4 doses of inhaled ciclesonide (40 microg and 160 microg or 80 microg and 320 microg) were compared over 3 weeks of treatment. Twenty-six asthmatic subjects (age range, 14-27 years) with baseline FEV1 values of greater than 70% of predicted value were enrolled. The primary outcome was the maximum percentage decrease in FEV1 after standardized exercise challenge. RESULTS: After 1 week of therapy, the mean +/- SEM reduction in maximum decrease in FEV1 in the ciclesonide 40-microg/80-microg dose group was 9% +/- 2.6% (95% CI, 3.9% to 14%), with no additional reduction thereafter. In the ciclesonide 160-microg/320-microg dose group, there was an 8.7% +/- 2.5% (95% CI, 3.7% to 13.7%) reduction in maximum decrease in FEV1 after week 1, which continued in a linear fashion during subsequent weeks of treatment. No difference was found between the 2 treatment arms in the temporal response of EIB to ciclesonide treatment. The maximum percentage attenuation in EIB achieved was 51.1% +/- 7.9%, which was achieved by using the 320-microg dose after 3 weeks of treatment. CONCLUSIONS: A significant improvement in EIB was demonstrated for all doses of ciclesonide. Use of 160 microg/320 microg of ciclesonide resulted in a continuing improvement in FEV1 with time, and no plateau was seen in protective effect during 3 weeks of treatment. CLINICAL IMPLICATIONS: Attenuation in exercise-induced decrease can be seen as early as after 1 week of therapy with inhaled ciclesonide at doses greater than 40 microg.

However, maximal attenuation in exercise response continues to increase at doses greater than or equal to 200 microg, even after 3 weeks of therapy.

Sudhir P. et al. *Prevalence of exercise-induced bronchospasm in schoolchildren: an urban-rural comparison.* J Trop Pediatr. 2003; 49(2) : 104-8.p **Abstract:** To study the prevalence of exercise-induced bronchospasm (EIB), 400 schoolchildren, aged 7-15 years, 200 each from urban and rural areas were administered a standard respiratory questionnaire, spirometry and exercise challenge. The study documented a higher prevalence of EIB in urban areas compared with rural area, 13 vs. 10 per cent. The family members of urban children had significant histories of asthma and allergy.

Suissa S. et al. *Bias in observational study of the effectiveness of nasal corticosteroids in asthma.* J Allergy Clin Immunol. 2005; 115(4) : 714-9.p **Abstract:** **BACKGROUND:** A recent observational study suggests that intranasal corticosteroids used to treat allergic rhinitis are effective at preventing asthma outcomes, such as emergency visits. The approach to data analysis may have led to biased results because of misclassification of immortal time. **OBJECTIVE:** To illustrate the bias in the cohort approach and to present the proper time-dependent analysis by replicating the recent study using data from another source. **METHODS:** From an existing cohort of 30,569 patients with asthma age 5 to 44 years and identified from the Saskatchewan Health databases (1975-1997), we formed the cohort of all subjects who were in the source population between January 1, 1989, and December 31, 1991. Subjects were followed to the first asthma hospitalization. All prescriptions dispensed during follow-up were identified. We replicated the time-fixed approach to data analysis used in the recent study and compared it with time-dependent approaches. **RESULTS:** The cohort included 20,173 subjects, of whom 1849 were hospitalized for asthma between January 1, 1989, and December 31, 1991. The time-fixed approach misclassified more than 5000 person-years of follow-up, corresponding to 44% of the exposed person-time. As a result, the rate ratio of asthma hospitalization after any use of nasal corticosteroids (NCSs) was 0.57 by the biased time-fixed approach compared with 1.13 by the proper time-dependent approach. The time-fixed approach produced a paradoxical protective effect of NCS with 1 or less canisters dispensed per year (odds ratio, 0.47), which was further exaggerated when the cohort was extended to 5 years (odds ratio, 0.33). Adjusted time-dependent analyses found no protective effect, even when NCSs were dispensed regularly (rate ratio, 1.10; 95% CI, 0.54-2.21). **CONCLUSION:** The time-fixed approach to the analysis of the effectiveness of NCSs on asthma outcomes leads, by its inherent misclassification of immortal time, to a considerable exaggeration of the protective effect of these medications in preventing severe asthma exacerbations.

Sulit L.G. et al. *Associations of obesity, sleep-disordered breathing, and wheezing in children.* Am J Respir Crit Care Med. 2005; 171(6) : 659-64.p **Abstract:** Although it has been speculated that rising asthma rates may be partly due to increasing obesity, the causal mechanisms that relate these conditions are unclear. We assessed the extent to which sleep-disordered breathing (SDB) may explain associations between obesity and wheezing/asthma. A total of 788 participants (aged 8-11 years) in a community-based cohort study were classified according to two outcomes: wheezing and asthma. Sleep apnea was defined as an increased number of apneas and hypopneas on overnight monitoring. SDB was identified on the basis of either sleep apnea or habitual snoring. Multiple logistic regression models showed that children with wheeze were significantly more likely to be male (odds ratio [OR] 1.62; confidence interval [CI] 1.15, 2.29), black (OR 1.90; CI 1.35, 2.29), obese (OR 1.57; CI 1.10, 2.44), and have a maternal history of asthma (OR 1.93; CI 1.16, 3.22). Further adjustment for SDB attenuated the association between obesity and wheeze (OR 1.45; CI 0.93, 2.26), but did not

substantially alter the association between obesity and asthma. We conclude that SDB and obesity each are associated with asthma and wheeze. The relationship between obesity and wheeze may be partly mediated by factors associated with SDB.

Sullivan M.D. et al. *A treatment for vocal cord dysfunction in female athletes: an outcome study.* Laryngoscope. 2001; 111(10) : 1751-5.p **Abstract:** **OBJECTIVES:** This article reports the outcome of a speech pathology treatment program for vocal cord dysfunction (VCD) in 20 adolescent female athletes. **STUDY DESIGN:** A retrospective, nonrandomized group design was used to collect the outcome data. **METHODS:** Twenty consecutive referrals of female athletes diagnosed as having symptoms of VCD during exercise were assessed, treated, and followed for at least 6 months after treatment. **RESULTS:** Ninety-five percent of the participants reported the ability to control symptoms of VCD during exercise up to 6 months after treatment. Asthma medications were no longer used by 80% of the athletes. All of the females continued to participate in athletics. **CONCLUSION:** Speech pathology intervention focusing on respiratory control of VCD in adolescent female athletes is an effective treatment resulting in the athletes' ability to control the symptoms of VCD in exercise for at least 6 months after treatment.

Sullivan S.D. et al. *Cost-effectiveness analysis of early intervention with budesonide in mild persistent asthma.* J Allergy Clin Immunol. 2003; 112(6) : 1229-36.p **Abstract:** **BACKGROUND:** The Inhaled Steroid as Regular Therapy in Early Asthma (START) study reported that early intervention with budesonide in mild persistent asthma reduces severe asthmatic events and improves symptom outcomes and lung function in adults and children. **OBJECTIVE:** We sought to estimate the incremental cost-effectiveness of early intervention with budesonide, as observed within the START study. **METHODS:** START was a randomized, 3-year controlled trial of budesonide in early onset mild asthma among 7165 subjects ages 5 to 66 years. Three age groups (5-10, 11-17, and >or=18 years) were studied separately and overall. Differences in the probability of emergency treatments, symptom-free days (SFDs), and costs of health care were determined. Incremental cost-effectiveness ratios were estimated from the health care payer and societal perspectives. **RESULTS:** Compared with usual therapy, patients receiving budesonide experienced an average of 14.1 (SE, 1.3) more SFDs per year (P <.001), fewer hospital days (69%, P <.001), and fewer emergency department visits (67%, P <.05). From the health care payer perspective, the net cost of early use of budesonide was an additional US dollars 0.42 (SE, dollars 0.04) per day, and the resultant cost-effectiveness ratio was US dollars 11.30 (95% CI, US dollars 8.60-US dollars 14.90) per SFD gained. From the societal perspective, the cost offsets of lower absence from school or work reduced the net cost of early budesonide to US dollars 0.14 (SE, US dollars 0.07) per day and decreased the cost-effectiveness ratio to US dollars 3.70 (95% CI, US dollars 0.10-US dollars 8.00). Early intervention was more effective and cost saving in the youngest age group. **CONCLUSION:** Long-term treatment with budesonide appears to be cost-effective in patients with mild persistent asthma of recent onset.

Sullivan S.D. et al. *A multisite randomized trial of the effects of physician education and organizational change in chronic asthma care: cost-effectiveness analysis of the Pediatric Asthma Care Patient Outcomes Research Team II (PAC-PORT II).* Arch Pediatr Adolesc Med. 2005; 159(5) : 428-34.p **Abstract:** **BACKGROUND:** A decision to implement innovative disease management interventions in health plans often requires evidence of clinical benefit and financial impact. The Pediatric Asthma Care Patient Outcomes Research Team II trial evaluated 2 asthma care strategies: a peer leader-based physician behavior change intervention (PLE) and a practice-based redesign called the planned asthma care intervention (PACI). **OBJECTIVE:** To estimate the cost-effectiveness of the interventions. **METHODS:** This was a 3-arm, cluster randomized

trial conducted in 42 primary care practices. A total of 638 children (age range, 3-17 years) with mild to moderate persistent asthma were followed up for 2 years. Practices were randomized to PLE (n = 226), PACI (n = 213), or usual care (n = 199). The primary outcome was symptom-free days (SFDs). Costs included asthma-related health care utilization and intervention costs. RESULTS: Annual costs per patient were as follows: PACI, USD 1292; PLE, USD 504; and usual care, USD 385. The difference in annual SFDs was 6.5 days (95% confidence interval [CI], -3.6 to 16.9 days) for PLE vs usual care and 13.3 days (95% CI, 2.1-24.7 days) for PACI vs usual care. Compared with usual care, the incremental cost-effectiveness ratio was USD 18 per SFD gained for PLE (95% CI, USD 5.21-dominated) and USD 68 per SFD gained for PACI (95% CI, USD 37.36-361.16). CONCLUSIONS: Results of this study show that it is possible to increase SFDs in children and move organizations toward guideline recommendations on asthma control in settings where most children are receiving controller medications at baseline. However, the improvements were realized with an increase in the costs associated with asthma care.

Sullivan S.D. et al. *The cost-effectiveness of an inner-city asthma intervention for children.* J Allergy Clin Immunol. 2002; 110(4) : 576-81.p **Abstract:** BACKGROUND: Comprehensive management efforts to reduce asthma morbidity among children in urban areas with high levels of poverty and large minority populations have been inconclusive. The National Cooperative Inner-City Asthma Study (NCICAS) demonstrated improved symptom outcomes but did not evaluate cost-effectiveness in this population. OBJECTIVE: We sought to examine the incremental cost-effectiveness of a comprehensive social worker-based education program and environmental control in children with asthma stratified by baseline level of asthma control. METHODS: We performed a prospective cost-effectiveness analysis alongside a randomized trial. A total of 1033 children and their families residing in 8 inner-city urban areas in the United States were enrolled in the NCICAS. Outcomes included symptom-free days, cost per symptom-free day gained, and annual costs of asthma morbidity compared by baseline symptom control, previous hospitalization, and previous unscheduled physician visits. RESULTS: The NCICAS intervention significantly reduced asthma symptoms. First-year intervention costs were 245 US dollars higher for the intervention children compared with those receiving usual care. There were no additional intervention-related costs during the second year. When compared with usual care, the intervention improved outcomes at an average additional cost of 9.20 US dollars per symptom-free day gained (95% CI, -12.56 to 55.29 US dollars). The intervention was cost saving in 3 strata of children with increasing asthma severity. CONCLUSIONS: A multifaceted asthma intervention program reduced symptom days and was cost-effective for inner-city children with asthma. In children with more severe disease, the intervention was substantially more effective and reduced costs compared with that seen in control children. Organizations serving this population should consider this strategy as part of a comprehensive disease-management program for asthma.

Sun H.L. et al. *Differences in the prescription patterns of anti-asthmatic medications for children by pediatricians, family physicians and physicians of other specialties.* J Formos Med Assoc. 2006; 105(4) : 277-83.p **Abstract:** BACKGROUND: Prescription patterns of anti-asthma medications in children vary among doctors in different disciplines and settings, and may reflect differences in treatment outcome. The purpose of this study was to analyze the prescribing patterns of anti-asthma drugs by pediatricians, family physicians and other practitioners. METHODS: Data for a total of 225,537 anti-asthma prescriptions were collected from the National Health Insurance Research Database for the period from January 1, 2002 to March 31, 2002. These medications included inhaled and oral adrenergics, inhaled and oral corticosteroids, xanthine derivatives, and leukotriene receptor antagonists prescribed by general pediatricians, family physicians and physicians in other disciplines.

RESULTS: Oral beta2-agonist was the most commonly prescribed drug used as monotherapy, with prescription rates of 70.4%, 46.9% and 58.0% by pediatricians, family physicians and other physicians, respectively. A xanthine derivative was the next most commonly prescribed monotherapy. Oral corticosteroid combined with oral beta2-agonist, followed by oral beta2-agonist combined with a xanthine derivative were the two most commonly prescribed dual-agent combined therapies by all three physician categories. The prescription rate for inhaled corticosteroid monotherapy was 7.8% by pediatricians, 5.6% by family physicians, and 8.0% by other physicians. The prescription rate for inhaled adrenergic was the highest in family physicians (14.9%), followed by the other physicians (7.2%), and was lowest in pediatricians (3.1%). CONCLUSION: Pediatricians and family physicians appeared to share similar opinions on the medical management of children with asthma in that both most commonly prescribed oral beta2-agonists and xanthine derivatives, either alone or in combination. Family physicians were least likely to prescribe an inhaled corticosteroid and most likely to prescribe an inhaled adrenergic agent.

Sunderland R.S. et al. *Continuing decline in acute asthma episodes in the community.* Arch Dis Child. 2004; 89(3) : 282-5.p **Abstract:** BACKGROUND: Acute asthma episodes prompting consultation with general practitioners in the sentinel practices of the Weekly Returns Service (WRS) of the Royal College of General Practitioners increased through the 1980s and early 1990s, reaching a peak in 1993. AIMS AND METHODS: To report on trends in the incidence of asthma episodes in children reported to the WRS over the period 1980-2002. RESULTS: Data confirm the steady upward trend from 1980 to 1993. The downward trend since 1993 was consistent in both male and female preschool and school age children, in all regions of the country simultaneously, and during all seasons until 1999 since when it has stabilised. No causative factor has been identified and no temporal association found between factors previously postulated as causing the increase in acute asthma. The decline in acute asthma episodes in children is consistent with observed declines in all other respiratory infections in this community.

Sunyer J. et al. *Respiratory effects of sulphur dioxide: a hierarchical multicity analysis in the APHEA 2 study.* Occup Environ Med. 2003; 60(8) : e2.p **Abstract:** BACKGROUND: Sulphur dioxide (SO₂) was associated with hospital admissions for asthma in children in the original APHEA study, but not with other respiratory admissions. AIMS: To assess the association between daily levels of SO₂ and daily levels of respiratory admissions in a larger and more recent study. METHODS: Time series of daily counts of hospital emergency admissions were constructed for asthma at ages 0-14 years and 15-64 years, COPD and asthma, and all respiratory admissions at ages 65+ years in the cities of Birmingham, London, Milan, Paris, Rome, Stockholm, and in the Netherlands for periods of varying duration between the years 1988 and 1997. A two stage hierarchical modelling approach was used. In the first stage generalised additive Poisson regression models were fitted in each city controlling for weather and season. These results were then combined across cities in a second stage ecological regression that looked at potential effect modifiers. RESULTS: For an increase of 10 micro g/m³ of SO₂ the daily number of admissions for asthma in children increased 1.3% (95% CI 0.4% to 2.2%). Effect modification among cities by levels of other air pollutants or temperature was not found. The SO₂ effect disappeared after controlling for PM₁₀ or CO, but correlation among these pollutants was very high. Other respiratory admissions were not associated with SO₂. CONCLUSION: SO₂ is associated with asthma admissions in children, indicating that reduction in current air pollution levels could lead to a decrease in the number of asthma admissions in children in Europe.

Svanes C. et al. *Pet-keeping in childhood and adult asthma and hay fever: European community respiratory health survey.* J Allergy Clin Immunol. 2003; 112(2) : 289-300.p **Abstract:** **BACKGROUND:** Whether pet-keeping early in life protects against or promotes allergy remains unclear. **OBJECTIVE:** Our aim was to examine the effects of childhood pet-keeping on adult allergic disease in a large international population-based study, including information on sensitization, adult pet-keeping, and pet prevalence in the populations. **METHODS:** We used information from structured interviews (n = 18,530) and specific IgE to common aeroallergens in blood samples (n = 13,932) from participants in the European Community Respiratory Health Survey (ECRHS) to analyze the associations between keeping pets and adult asthma and hay fever. **RESULTS:** Keeping cats in childhood was associated with asthma only among atopic subjects, an association that varied between centers (P =.002) and was stronger where cats were less common (< 40% cats: odds ratio(wheeze) [OR(wheeze)] = 1.84, 95% CI = 1.31-2.57; 40%-60% cats: OR(wheeze) = 1.33, 95% CI = 1.10-1.61; > or =60% cats: OR(wheeze) = 0.98, 95% CI = 0.73-1.33). Dogs owned in childhood or adulthood were associated with asthma among nonatopic subjects (childhood: OR(wheeze) = 1.28, 95% CI = 1.13-1.46; adulthood: OR(wheeze) = 1.31, 95% CI = 1.14-1.51; both: OR(wheeze) = 1.69, 95% CI = 1.40-2.04). In atopic subjects, those who had owned dogs in childhood had less hay fever (OR = 0.85; 95% CI = 0.73-0.98) and no increased risk of asthma (OR(wheeze) = 1.01, 95% CI = 0.87-1.17). Respiratory symptoms were more common in subjects who had owned birds during childhood (OR(wheeze) = 1.12; 95% CI = 1.02-1.23) independent of sensitization. **CONCLUSIONS:** The effects of pet-keeping in childhood varied according to the type of pet, the allergic sensitization of the individual, and the wider environmental exposure to allergen. Cats owned in childhood were associated with more asthma in sensitized adults who grew up in areas with a low community prevalence of cats. Dogs owned in childhood seemed to protect against adult allergic disease but promote nonallergic asthma.

Svanes C. et al. *Early exposure to children in family and day care as related to adult asthma and hay fever: results from the European Community Respiratory Health Survey.* Thorax. 2002; 57(11) : 945-50.p **Abstract:** **BACKGROUND:** The literature indicates that early exposure to children in the family and to day care permanently influences the development of allergic disease. A study was undertaken to examine the associations of family size and day care with adult asthma and hay fever and to determine whether these associations are mediated through specific IgE production and whether they vary with allergic predisposition. **METHODS:** 18,530 subjects aged 20-44 years from 36 areas predominantly in the market economies participated in the European Community Respiratory Health Survey and provided information through interviewer-led questionnaires. 13,932 subjects gave blood samples for measurement of specific IgE. **RESULTS:** Hay fever was less common in subjects with many siblings (OR=0.92; 95% CI 0.90 to 0.95 per sib). There was a U-shaped relationship between asthma and number of siblings (quadratic effect of siblings, pwheeze=0.014, pFEV(1)=0.016). In subjects without siblings but exposed to children in day care, hay fever was less common (OR=0.76; 95% CI 0.60 to 0.98) and asthma symptoms were more common (ORwheeze=1.48; 95% CI 1.12 to 1.95). Adjustment for specific IgEs did not alter these associations. The inverse association of hay fever with siblings was found in sensitised subjects (OR=0.89; 95% CI 0.84 to 0.94) and in those with parental allergy (OR=0.91; 95% CI 0.85 to 0.97), but not in subjects without such a predisposition (OR=1.02; 95% CI 0.97 to 1.09). **CONCLUSION:** Subjects exposed to many children at home or in day care experienced less hay fever and more asthma in adulthood. Microbial challenge through children may contribute to a non-allergic immunological development giving less hay fever but more airways infections predisposing to asthma. These effects were not mediated through production of specific IgE. The protective effect of siblings on hay fever was particularly strong in those with an allergic predisposition.

Szalai C. et al. *Polymorphism in the gene regulatory region of MCP-1 is associated with asthma susceptibility and severity.* J Allergy Clin Immunol. 2001; 108(3) : 375-81.p **Abstract:** **BACKGROUND:** Chemokines play an important role in the pathophysiology of asthma and allergy. Recently, polymorphisms in the gene regulatory region of monocyte chemoattractant protein 1 (MCP-1) and in the promoter region of RANTES have been found; these polymorphisms increase the expression of the chemokines. **OBJECTIVE:** We investigated whether the presence of the polymorphisms was associated with atopy or asthma and whether these alleles influenced the severity of asthma in affected individuals. **METHODS:** Three groups of subjects-160 children with asthma (disease severity being classified according to the Global Initiative for Asthma guidelines, modified for children), 151 children with nonasthmatic but allergic phenotype, and 303 children without allergic or asthmatic disorders-were screened with a PCR-based assay for genotyping. **RESULTS:** The frequency of the -2518G polymorphism in the gene regulatory region of MCP-1 was significantly higher in asthmatic children than in controls (P <.001; odds ratio [OR] = 2.0 [1.4-2.6]) and nonasthmatic atopic children (P <.001; OR = 2.0 [1.4-2.9]). The MCP-1 G/G genotype correlated with asthma severity. In asthmatic children, the MCP-1 -2518G allele was also associated with an increased blood eosinophil level. The promoter polymorphisms in the RANTES gene did not have a detectable effect on the susceptibility to asthma or allergy or on the blood eosinophil count. **CONCLUSION:** In this cohort of children, there are associations between carrying G at -2518 of the MCP-1 gene regulatory region and the presence of asthma as well as between asthma severity and homozygosity for the G allele. In asthmatic children, the MCP-1 -2518G polymorphism correlated with increased eosinophil levels. This variant of MCP-1 might belong to the predictor gene set for asthma.

Szeffler S.J. *Airway remodeling: therapeutic target or not?* Am J Respir Crit Care Med. 2005; 171(7) : 672-3.p

Szeffler S.J. et al. *Safety profile of budesonide inhalation suspension in the pediatric population: worldwide experience.* Ann Allergy Asthma Immunol. 2004; 93(1) : 83-90.p **Abstract:** **OBJECTIVE:** To review the worldwide safety data for budesonide inhalation suspension (Pulmicort Respules) to provide a budesonide inhalation suspension pediatric tolerability profile. **DATA SOURCES:** Clinical study data were obtained from AstraZeneca safety databases used by the US Food and Drug Administration to support the approval of budesonide inhalation suspension and from postmarketing surveillance reports (January 1, 1990, through June 30, 2002). **STUDY SELECTION:** Completed parallel-group studies of patients with asthma 18 years and younger. **RESULTS:** Safety data for budesonide inhalation suspension were pooled from 3 US, 12-week, randomized, double-blind, placebo-controlled studies (n = 1,018); data from their open-label extensions (n = 670) were pooled with data from a fourth US open-label study (n = 335). Data for 333 patients 18 years and younger enrolled in 5 non-US studies also were analyzed. No posterior subcapsular cataracts were reported in any study, and the frequencies of oropharyngeal events and infection with budesonide inhalation suspension were comparable with those of reference treatments. No increased risk of varicella or upper respiratory tract infection was apparent, and budesonide inhalation suspension did not cause significant adrenal suppression in studies assessing this variable. There were small differences in short-term growth velocity between children who received budesonide inhalation suspension and those who received reference treatment in 2 of 5 trials that evaluated this variable. No increased risk of adverse events was apparent from postmarketing reports. **CONCLUSIONS:** Short- and long-term treatment with budesonide inhalation suspension, using a wide range of doses, is safe and well tolerated in children with asthma.

Szeffler S.J. et al. *Switching from conventional to extrafine aerosol beclomethasone dipropionate therapy in children: a 6-month, open-label, randomized trial.* J Allergy Clin Immunol. 2002; 110(1) : 45-50.p **Abstract:** BACKGROUND: In adults with asthma, hydrofluoralkane-134a beclomethasone dipropionate (HFA-BDP) extrafine aerosol provides equivalent asthma control at half the daily dose of conventional chlorofluorocarbon (CFC)-BDP. OBJECTIVE: We sought to compare the efficacy and tolerability of switching from CFC-BDP to HFA-BDP at half the daily dose in children with stable asthma. METHODS: This 6-month, open-label, randomized, multicenter study enrolled 520 children aged 5 to 11 years with well-controlled asthma receiving inhaled CFC-BDP or budesonide 200 to 800 microg/d x. (Four hundred fifty-two patients were using doses within the recommended range of 200-400 microg and were analyzed separately.) During a 4-week run-in period, patients used CFC-BDP plus a spacer (CFC-BDP+S) at approximately the same dose as they were using before study entry. Patients were then randomized in a 1:3 ratio to continue on CFC-BDP+S or switch to HFA-BDP Autohaler at half the daily dose. RESULTS: The change from baseline in morning peak expiratory flow was significantly greater in patients receiving 100-200 microg of HFA-BDP compared with those receiving 200-400 microg of CFC-BDP+S at weeks 7 to 8 (8.5 and 0.4 L/min, respectively; $P = .014$), with continuing improvement in both groups over 6 months (12.2 and 12.4 L/min, respectively, at month 6). There were no significant differences between treatments in mean change from baseline in FEV₁(1), percentage of days or nights without asthma symptoms, and daily beta-agonist use over the 6-month treatment period. The proportion of patients who had one or more asthma exacerbations, the incidence of adverse events, and the percentage change from baseline in 24-hour urinary free cortisol levels were similar in the 2 treatment groups. CONCLUSIONS: This study confirms that asthma control can be well maintained in children when switching from CFC-BDP+S to an HFA-BDP Autohaler at doses as low as 100 to 200 microg/d.

Szilagyi P.G. et al. *Improved asthma care after enrollment in the State Children's Health Insurance Program in New York.* Pediatrics. 2006; 117(2) : 486-96.p **Abstract:** BACKGROUND: Uninsured children with asthma are known to face barriers to asthma care, but little is known about the impact of health insurance on asthma care. OBJECTIVES: We sought to assess the impact of New York's State Children's Health Insurance Program (SCHIP) on health care for children with asthma. DESIGN: Parents of a stratified random sample of new enrollees in New York's SCHIP were interviewed by telephone shortly after enrollment (baseline, $n = 2644$ [74% of eligible children]) and 1 year later (follow-up, $n = 2310$ [87%]). Asthma was defined by parent report using questions based on National Heart, Lung, and Blood Institute criteria. A comparison group ($n = 401$) who enrolled in SCHIP 1 year later was interviewed as a test for secular trends. MAIN OUTCOME MEASURES: Access (having a usual source of care [USC], unmet health needs, problems receiving acute asthma care), asthma-related medical visits, quality (continuity of care at the USC, problems receiving chronic asthma care, use of antiinflammatory medications), and asthma outcomes (change in asthma care or severity) were the main outcome measures used. Bivariate and multivariate analyses compared measures at baseline (year before SCHIP) versus follow-up (year during SCHIP). RESULTS: Three-hundred eighty-three children (14%) had asthma at baseline, and 364 had asthma at follow-up (16%). No secular trends were detected between the baseline study group and the comparison group. After enrollment in SCHIP, improvements were noted in access: lacking a USC (decrease from 5% to 1%), unmet health needs (48% to 21%), and problems getting to the USC for asthma (13 to 4%). Children had fewer asthma-related attacks and medical visits after SCHIP (mean number of attacks: 9.5 to 3.8; mean number of asthma visits: 3.0 to 1.5; hospitalizations: 11% to 3%). Quality of asthma care improved for general measures (most/all visits to USC: 53% to 94%; mean rating of provider: 7.9 to 8.8 of 10) and asthma-specific measures (problems getting to the USC for asthma care when child was well: 13% to 1%). More than two thirds

of the parents at follow-up reported that both quality of asthma care and asthma severity were "better or much better" than at baseline, generally because of insurance coverage or lower costs of medications and medical care. CONCLUSIONS: Enrollment in New York's SCHIP was associated with improvements in access to asthma care, quality of asthma care, and asthma-specific outcomes. These findings suggest that health insurance improves the health of children with asthma.

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't Jong G.W. et al. *Unlicensed and off-label prescription of respiratory drugs to children.* Eur Respir J. 2004; 23(2) : 310-3.p **Abstract:** Many respiratory drugs are not available in formulations suitable for infants and toddlers. Efficacy and safety research is mostly restricted to older children. However, respiratory drugs are frequently used in children for common diseases like asthma, upper and lower respiratory tract infections, rhinitis and sinusitis. The unlicensed and off-label use of respiratory drugs in children were studied. A population-based cohort study was conducted by using the computerised medical records in the Integrated Primary Care Information project. The study population comprised a random sample from all children aged 0-16 yrs who were registered with a general practitioner in 1998. All prescriptions for respiratory drugs during the study period were classified according to their licensing and off-label status. The study population comprised 13,426 patients (51.7% male, median age 8.7 yrs), of whom 2,502 (19%) received 5,253 prescriptions for respiratory drugs in 1998. A total of 3,306 (62.9%) prescriptions concerned licensed drugs. Of the remaining 1,947 prescriptions (37.1%), 882 (16.8%) were unlicensed for use in children, and 1,065 (20.3%) were prescribed off-label. The 1-yr cumulative risk of receiving an unlicensed or off-label prescription was 45% among children with at least one prescription for a respiratory drug. This population-based study showed that a large proportion of respiratory drugs prescribed by the general practitioner are unlicensed for use in children, or licensed but prescribed in an off-label manner. Results have to be interpreted with caution because they may unjustly suggest inaccurate prescribing, whereas it may be difficult to treat children with respiratory symptoms and diseases, because for many respiratory drugs paediatric data on safety and efficacy are insufficient. These findings underline the importance of research on suitable formulations, dosages and efficacy of respiratory drugs in children.

Tabar A.I. et al. *Olerance of a cluster schedule with a house dust mite extract quantified in mass units: multicentre study.* J Investig Allergol Clin Immunol. 2004; 14(3) : 193-7.p **Abstract:** The standardisation of allergenic extracts in micrograms of the major allergen has encouraged the search for new treatment schedules, with the purpose of shortening the number of visits and doses required to reach the maintenance dose without eliciting a greater risk of adverse reactions for the patients. With this objective, a prospective multicentre pharmacovigilance study was designed that included 200 patient with allergic rhinoconjunctivitis and/or allergic asthma sensitised to mites (*Dermatophagoides pteronyssinu* and/or *farinae*). The dose increment period was carried out using a cluster schedule, where the optimal dose was reached after 4 visits, administering two doses in each visit. The duration of the study was 5 months and a total of 1902 doses were administered. At the end of the trial, 31 adverse reactions in 23 patients were recorded. Six of these were systemic (0.3% of administered doses) recorded in 6 patients (3% of the sample). One was an immediate reaction (grade 1) and delayed (4 mild and 1 moderate). Two were asthmatic exacerbations, 2 cutaneous reactions, 1 rhinitis and 1 an unspecific symptom (not IgE-mediated). Two appeared upon administration of the first vial and the remaining 4 after administration of the third cluster. Therefore, the

schedule tested presents an adequate tolerance profile, suggesting savings (compared to the conventional schedule of 13 doses per patient) of 1800 visits and 1000 treatment doses in the whole study.

Tahzib M.N. et al. *A 12-year-old girl with asthma, pneumonia, and pneumatoceles.* *Ann Allergy Asthma Immunol.* 2003; 90(5) : 480-4.p

Takaro T.K. et al. *Effect of environmental interventions to reduce exposure to asthma triggers in homes of low-income children in Seattle.* *J Expo Anal Environ Epidemiol.* 2004; 14 Suppl 1 : S133-43.p **Abstract:** The effectiveness of community health workers (CHWs) assisting families in reducing exposure to indoor asthma triggers has not been studied. In all, 274 low-income asthmatic children were randomly assigned to high- or low-intensity groups. CHWs visited all homes to assess exposures, develop action plans and provide bedding encasements. The higher-intensity group also received cleaning equipment and five to nine visits over a year focusing on asthma trigger reduction. The asthma trigger composite score decreased from 1.56 to 1.19 (Delta=-0.37, 95% CI 0.13, 0.61) in the higher-intensity group and from 1.63 to 1.43 in the low-intensity group (Delta=-0.20, 95% CI 0.004, 0.4). The difference in this measure due to the intervention was significant at the P=0.096 level. The higher-intensity group also showed improvement during the intervention year in measurements of condensation, roaches, moisture, cleaning behavior, dust weight, dust mite antigen, and total antigens above a cut point, effects not demonstrated in the low-intensity group. CHWs are effective in reducing asthma trigger exposure in low-income children. Further research is needed to determine the effectiveness of specific interventions and structural improvements on asthma trigger exposure and health.

Takemura Y. et al. *The relationship between fish intake and the prevalence of asthma: the Tokorozawa childhood asthma and pollinosis study.* *Prev Med.* 2002; 34(2) : 221-5.p **Abstract:** OBJECTIVE: The Japanese have a higher intake of fish and a lower incidence of asthma than occupants of western countries. The present epidemiological study investigated the relationship between dietary fish intake and the prevalence of asthma among a childhood population. METHODS: Subjects represented all public elementary and junior high schools in Tokorozawa City in Japan (age range: 6-15 years old). The study population included 1,673 currently asthmatic students and 22,109 controls. Participants' parents completed the Japanese version of American Thoracic Society and Division of Lung Diseases, National Heart, Lung, and Blood Institute questionnaire for children, adopted by the Japan Environment Agency. We added supplementary questions (e.g., parental history of asthma and questions about frequency of foods eaten, including frequency of fish intake). Odds ratios for cases of current asthma according to frequency of fish intake were calculated, and a logistic regression analysis was used to adjust for possible confounding variables. RESULTS: After adjustments for age, gender, parental history of asthma, and vegetables and fruits intake, a significantly higher prevalence of asthma was noted among subjects who ate fish one to two times a week than among those who ate fish one to two times a month (adjusted odds ratio: 1.117; 95% confidence interval: 1.005-1.241; P = 0.041). The risk increased gradually with increasing frequency of fish intake, and the positive trend was statistically significant. CONCLUSIONS: The results indicated that frequency of fish intake was positively related to the prevalence of asthma. This result might have important implications for health.

Taketomi E.A. et al. *Differential IgE reactivity to Der p 1 and Der p 2 allergens of Dermatophagoides pteronyssinus in mite-sensitized patients.* *J Investig Allergol Clin Immunol.* 2006; 16(2) : 104-9.p **Abstract:** Several studies have shown that the presence of IgE antibodies to house dust mites (HDM), particularly

Dermatophagoides pteronyssinus (Dpt), is an important risk factor for asthma. Allergen immunotherapy is indicated for patients with IgE antibodies to clinically relevant allergens. The aims of this study were to analyze the levels of specific serum IgE to Der p 1 and Der p 2 allergens in mite-sensitized atopic patients and to compare them with both in vivo (skin prick test) and in vitro (IgE-ELISA) sensitizations to Dpt crude extract. Forty-seven atopic patients with allergic rhinitis with or without intermittent or persistent mild asthma and positive skin prick test (SPT) to Dpt total extract were studied. Thirty age-matched healthy subjects with negative SPT to HDM were included as controls. Levels of total IgE and Dpt-, Der p 1- and Der p 2-specific IgE were measured by ELISAs in SPT-positive atopic patients and SPT-negative control subjects. Among 47 symptomatic atopic patients, 27 (57.4%) were double positive IgE to Der p 1 and Der p 2 allergens, 3 (6.4%) were single positive IgE to Der p 1, 4 (8.5%) were single positive IgE to Der p 2, and 13 (27.6%) were double negative IgE to both allergens. There was a significant correlation between Der p 1- and Der p 2-specific IgE levels, but not between Der p 1- or Der p 2-IgE levels and SPT results. The double negative IgE patients had the smallest skin test reactions although they showed high mean levels of total serum IgE. Therefore, the knowledge of specific IgE levels to Der p 1 and Der p 2 major allergens might support physicians for indication or follow-up in mite-sensitized patients under allergen-specific immunotherapy. These approaches might be important for obtaining improved safety and efficacy of the current clinical practice of allergen immunotherapy.

Tan H. et al. *Tourette's syndrome manifests as chronic persistent cough.* *Yonsei Med J.* 2004; 45(1) : 145-9.p **Abstract:** Tourette's syndrome (TS) is a neuropsychiatric disorder characterized by the presence of involuntary motor and phonic tics. Phonic tics can mimic respiratory system disorders such as asthma, and upper and lower respiratory system infections. We report on twins with chronic persistent cough (CPC): one of whom was followed as an asthmatic for a year and the other was diagnosed with recurrent respiratory tract infection. A careful history and neurologic assessment suggested that TS might be responsible for the first twin's symptoms but that the second one was probably in early TS. All the symptoms of the first patient diagnosed as TS showed a complete improvement with pharmacological treatment in two weeks. Since the history of CPC may in reality be TS, we recommend that TS should be considered in the differential diagnosis of pediatric CPC.

Tan T.N. et al. *Prevalence of allergy-related symptoms in Singaporean children in the second year of life.* *Pediatr Allergy Immunol.* 2005; 16(2) : 151-6.p **Abstract:** This study describes the cross-sectional prevalence of symptoms associated with eczema (chronic itchy rash), asthma (wheeze), and allergic rhinitis (rhinoconjunctivitis) in 1026 subjects between 18.5 and 23 months old (median age is 21 months) in Singapore. The first 2 yr cumulative prevalence of chronic itchy rash, wheeze, and rhinoconjunctivitis were 22.1% (n=227), 22.9% (n=235), and 8.4% (n=86) respectively. In total, 42.2% (414 of 979) reported ever having any of these symptoms. Eczema, although prevalent, was diagnosed only in 34.4% (n=78) of children with chronic itchy rash. Children with this eczematous rash were also more prone to wheeze (cOR=2.0, 95% CI: 1.2-3.0) and rhinoconjunctivitis (cOR=2.0, 95% CI: 1.4-2.8). Similarly, subjects who reported rhinoconjunctivitis and chronic itchy rash were 2.4 times (95% CI: 1.6-3.6) and 1.4 times (95% CI: 1.0-2.0) more at risk of wheezing respectively. Family history of allergy was a significant risk factor for chronic itchy rash (aOR=1.8, 95% CI: 1.3-2.4) and wheeze (aOR=1.7, 95% CI: 1.3-2.4). Thus, symptoms related to allergy were already prevalent during the second year of life. Significant proportions of these symptoms are likely to be due to true atopy as strong relationship with familial history and comorbidity with other potential allergic symptoms were observed.

- Tancredi G. et al.** *3-min step test and treadmill exercise for evaluating exercise-induced asthma.* Eur Respir J. 2004; 23(4) : 569-74.p
Abstract: A simple exercise test would be useful for detecting exercise-induced asthma, a common problem in asthmatic children. The current study compared the 3-min step test with treadmill exercise for evaluating exercise-induced asthma in asthmatic children and assessed whether responses to both tests are influenced by baseline lung function and habitual physical activity. A series of 154 asthmatic children (84 male children; mean age 12.9 +/- 0.9 yrs) underwent a 3-min step-test and treadmill testing on different days within a week at least 24 h apart. Before both tests each subject did spirometry to obtain the baseline forced expiratory volume in one second (FEV1). After both exercise challenges all subjects did serial spirometry and the lowest FEV1 recorded over time was used to calculate the fall in FEV1 expressed as a percentage of the measured pre-exercise (baseline) value (% fall in FEV1) and the area above the FEV1 curve (AAC0-30 min) expressed as a percentage of the pre-exercise value. Changes in both exercise variables were also analysed in percentile subgroups defined by questionnaire answers on habitual physical activity in hours. The mean % fall in FEV1 was significantly higher for treadmill exercise than for the step test (15.0 +/- 7.5 versus 11.7 +/- 5.9); and the AAC0-30 min was larger for treadmill than for the step test (-261.6 +/- 139.9% versus -197.3 +/- 105.0% min). In all subgroups defined by habitual physical activity the mean % fall in FEV1 decreased more after treadmill exercise than after the step test. After step test and treadmill exercise no significant correlation was found between % fall in FEV1 and baseline lung function, or between % fall in FEV1 among groups defined by habitual physical activity. Although the 3-min step test yields a lower % fall in forced expiratory volume in one second (FEV1) and a lower value of the area above the FEV1 curve than treadmill testing, it is a quick, economical, reproducible and portable alternative procedure for identifying exercise-induced asthma in outpatients and epidemiological studies. Baseline lung function and habitual physical activity have no influence on the amount or duration of exercise-induced asthma.
- Tang R.B. et al.** *Circulating adhesion molecules in sera of asthmatic children.* Pediatr Pulmonol. 2002; 33(4) : 249-54.p
Abstract: Infiltration of cells into the lung in asthma is regulated by several expressions of cell adhesion molecules (CAMs) on cells present in the airways, and may play a role in the pathogenesis of bronchial asthma. We sought to evaluate the role of serum concentrations of the soluble forms of intercellular adhesion molecule-1 (sICAM-1), vascular cell adhesion molecule-1 (sVCAM-1), and E-selectin (sE-selectin) in the control of disease activity in acute asthma. Circulating levels of sICAM-1, sVCAM-1, and sE-selectin in sera from 15 normal control subjects and from 20 allergic asthmatic children with acute exacerbations who had returned to stable condition were determined by using commercially available enzyme-linked immunosorbent assay kits. The mean concentration of serum sICAM-1 levels was significantly higher during an acute exacerbation of asthmatic children than in those with stable asthma (19.41 +/- 10.65 ng/mL vs. 13.46 +/- 5.44 ng/mL; P < 0.001) or in control subjects (9.83 +/- 2.02 ng/mL; P < 0.001). For sVCAM-1 and sE-selectin, the mean serum concentration of sVCAM-1 was slightly higher in children during an acute exacerbation asthma than when stable. However, the differences did not reach statistical significance. The mean serum concentrations of sVCAM-1 and sE-selectin in acute asthma or stable asthma were significantly higher than in control subjects. This study provides further evidence that serum concentrations of sICAM-1, sVCAM-1, and sE-selectin are increased in acute asthma. These findings further confirm that leukocyte endothelial adhesion plays a role in inflammatory airway disease.
- Tang R.B. et al.** *Detection of IgE reactivity to fungus antigens by immunoblotting in allergic diseases in children.* J Chin Med Assoc. 2003; 66(8) : 453-9.p
Abstract: BACKGROUND: Fungi are well-known as sources for allergens that cause allergic rhinitis and allergic asthma. The aim of this study was to evaluate the prevalence of sensitization to airborne fungi in allergic diseases in children. METHODS: The presence of IgE antibodies to common allergens in serum samples from 77 atopic and 5 non-atopic children was determined by multiple allergosorbent (MAST) chemiluminescent assay. The allergic extracts, *Penicillium notatum*, *Penicillium oxalicum*, and *Aspergillus fumigatus*, were prepared. IgE-binding fungal components were identified by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)-immunoblotting, using sera from the above-mentioned patients. RESULTS: The MAST data demonstrated that 62 (81%) of the 77 sera tested showed IgE antibodies to both *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. Only 2 and 1 of the 77 atopic sera were positive to *Penicillium* and *Aspergillus*, respectively. However, 13 (17%) sera showed positive IgE-immunoblotting. Eight and 6 of them demonstrated IgE antibodies to more than 10 different components of *P. notatum* and *P. oxalicum* respectively. Ten of the 13 sera showed IgE-immunoblotting reactivity to *A. fumigatus*, and only 1 of the 10 positive samples showed a positive MAST of class I to *Aspergillus*. All the other sera showed negative results in the MAST test to *Aspergillus*. The discrepancy observed between the results of IgE-immunoblotting using self-prepared extracts and the commercial MAST test of the serum samples tested may be due to the variations in the fungal strains and the allergenic extracts used, and the different assay systems employed. CONCLUSIONS: The results confirmed the importance of airborne fungi in association with allergic disorders in children.
- Tanihara S. et al.** *Trends in asthma morbidity and mortality in Japan between 1984 and 1996.* J Epidemiol. 2002; 12(3) : 217-22.p
Abstract: PURPOSE: To determine whether the increased prevalence of asthma in Japan has influenced its mortality. MATERIALS AND METHODS: A descriptive study was conducted by the data obtained from Patient Survey and Vital Statistics of Japan between 1984 and 1996. Asthma fatalities were expressed as the number of deaths from asthma per 100,000 asthmatic patients receiving medical treatment on the day when the survey was conducted. RESULTS: Mortality, prevalence and asthma fatalities showed different changing patterns among several age groups. Asthma mortality for the 10-24 and 25-44 year-old groups increased during the study period, while for other age groups, it decreased. The prevalence increased for all groups classified by age and sex. Asthma fatalities peaked in 1987 among the 10-24, 25-44 and 45-64 year-old groups, and decreased for others throughout the study period. CONCLUSIONS: There is a possibility that an age-specific phenomenon is at work here because asthma mortality increased only in the 10-24 and 25-44 year-old groups, although the prevalence of asthma increased in all groups, whether classified by age or sex. The asthma fatality of the 10-24, 25-44 and 45-64 year-old groups peaked in 1987: it is conceivable that this was influenced by the particular drug therapy used. The increase in asthma mortality in the 10-24 and 25-44 year-olds might be influenced by the increased prevalence.
- Taras H. et al.** *Impact of school nurse case management on students with asthma.* J Sch Health. 2004; 74(6) : 213-9.p
Abstract: This project determined asthma prevalence in a large school district, absentee rates, and potential effects of school nurse case management for student asthma over three years. Data were derived from an asthma tracking tool used by nurses in one school district for every student reported as having asthma by their parent. School nurses began collecting data in their schools in 1999-2000 when an asthma-management protocol was first developed. Nurses documented perceived asthma severity for each student, presence of medication and peak flow meters in school, and case management activities provided. This data base was cross matched with percentage of days students were absent for any illness. Prevalence of asthma, based on school nurse records of parent report, was between 5.1% to 6.2% during the three years. Between 13.5% and 15% were moderate or severe. Students with asthma were absent between one-half to one

and one-quarter days more often than those without asthma. In year three, 39% of students with asthma had medication at school, and 12% had a peak flow meter. Contacting a parent was the nurse case management activity provided for the largest number of students (27% of students with asthma), followed by asthma education (16.5%), contact with physician (6%), and home visits (1%). Students who received at least one school nurse case management intervention were more likely the next year to have an asthma medication at school, to use a peak flow meter at school, and to have a change in asthma severity. School nurse case management activity had no association with student absences. Availability of medication and peak flow meters at school was low, suggesting standards of care for asthma were not followed. School nurse case management, when performed outside a project or intervention, offers a promising strategy to improve asthma management.

Tauber E. et al. *Negative expiratory pressure: a new tool for evaluating lung function in children?* *Pediatr Pulmonol.* 2003; 35(3) : 162-8.p
Abstract: The negative expiratory pressure technique (NEP) has been applied in adults with chronic obstructive pulmonary disease (COPD), demonstrating flow limitation in many of these patients. Because this technique does not require patient cooperation, it is of potential interest for application in the pediatric population. This study was performed to test the feasibility of NEP in children, and to further investigate it in children with asthma and cystic fibrosis (CF). We performed NEP (0.3-0.7 kPa) measurements in 14 healthy children (13.3 years, +/- 2.4), in 12 children with asthma (11.7 years, +/- 3.0), and in 17 children with CF (13.3 years, +/- 2.7). NEP-derived flow-volume loops were visually analyzed for flow limitation at tidal breathing. In addition, expiratory flow at 50% of tidal volume (TEF(50)) was measured. In healthy children, the intraclass coefficient of correlation was 77%, and intraindividual short- and long-term variability was 5.8% and 10.8%, respectively. In asthmatics, TEF(50) was lower compared with controls, and increased after inhalation of salbutamol. However, appropriate size-correction has still to be established. Measurement of TEF(50) using NEP is feasible in children. Despite good reproducibility in individual patients, the high intersubject variability may limit its usefulness as a clinical tool. In addition, the lack of flow limitation using NEP even in severely obstructed patients with CF warrants further investigation.

Tay Y.K. et al. *The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children.* *Br J Dermatol.* 2002; 146(1) : 101-6.p
Abstract: **BACKGROUND:** Atopic dermatitis is a common disease that appears to be increasing in frequency during recent decades. Most of the studies are based on the Western population, and there are few data in the Asian population. **OBJECTIVES:** To determine the prevalence and descriptive epidemiology of atopic dermatitis among school children in the general community in Singapore. **METHODS:** This is a questionnaire study of 12 323 students done over a 1-year period, comprising 7 year olds (4605), 12 year olds (3940) and 16 year olds (3778) from 19 primary and 17 secondary schools randomly selected in Singapore. All children had a complete cutaneous examination. The diagnosis of atopic dermatitis was based on the U.K. Working Party diagnostic criteria. The questionnaire was translated into Chinese and both the English and Chinese versions were issued simultaneously to the students. **RESULTS:** The 1-year period prevalence of atopic dermatitis was 20.8%. Atopic dermatitis was present in 22.7% of 7 year olds, 17.9% of 12 year olds and 21.5% of 16 year olds. The overall sex ratio was equal. There were slightly more boys with atopic dermatitis among the younger children (6 and 12 year olds, 1.18 : 1 and 1.19 : 1, respectively) but more girls were affected (1.57 : 1) among the 16 year olds. Atopic dermatitis was more common among the Chinese (21.6%) and Malays (19.8%) compared with the Indians (16%) and other races (14%). The onset of the disease occurred before the age of 10 years in 49.5% of the 16 year olds. "Pure" atopic dermatitis without concomitant respiratory

allergies was noted in 788 respondents (30.7%); 1775 (69.3%) suffered from a "mixed" type, with 34.3% having allergic rhinitis, 9.5% having asthma and 25.5% having both asthma and allergic rhinitis. More boys had atopic dermatitis and concomitant respiratory allergies whereas more girls were affected with "pure" atopic dermatitis alone (1.4 : 1). At least one first-degree family member with atopy was noted in 1435 children (56%): atopic dermatitis (70%), asthma (62%) and allergic rhinitis (68%). Among siblings with one parent with atopic dermatitis, 37% had either a father or a mother with atopic dermatitis. Common aggravating factors reported included exercise, heat and sweating, grass intolerance, thick clothing and stress. Pityriasis alba was noted in 25% of the study population, keratosis pilaris in 13% and ichthyosis vulgaris in 8%. Most respondents had mild to moderate atopic dermatitis that could be controlled with a fairly simple regimen of moisturizers, topical steroids, antihistamines and antibiotics. **CONCLUSIONS:** The high prevalence of atopic dermatitis in Singapore is similar to that observed in developed countries, suggesting that environmental factors may be important in determining the expression of the disease.

Taylor B.W. et al. *The emergency department as an asthma surveillance tool at the community level: a decline in the burden of pediatric asthma in Halifax, Canada.* *J Asthma.* 2005; 42(8) : 679-82.p
Abstract: We report pediatric emergency department (PED) asthma visit and inpatient asthma (AS) admission data in our area over a 5-year period. AS visits decreased by 33.9%, AS admissions by 24.6%, both significant compared with the decline in elementary school enrollment. The decrease in asthma visits was due to a decrease in the number of asthmatic patients, not a decline in repeat visits, or use of alternate venues of care. Explanations include a decrease in the burden of disease or an improvement in ambulatory care, but not alternate treatment venues or improvement in acute (PED) care. Readily available, emergency department data are useful in the community surveillance of asthma.

Teach S.J. et al. *Spatial accessibility of primary care pediatric services in an urban environment: association with asthma management and outcome.* *Pediatrics.* 2006; 117(4 Pt 2) : S78-85.p
Abstract: **BACKGROUND:** Disadvantaged urban children with asthma depend heavily on emergency departments (EDs) for episodic care. We hypothesized that among an urban population of children with asthma, higher spatial accessibility to primary care pediatric services would be associated with (1) more scheduled primary care visits for asthma, (2) better longitudinal asthma management, and (3) fewer unscheduled visits for asthma care. **METHODS:** We enrolled children aged 12 months to 17 years, inclusive, who sought acute asthma care in an urban pediatric ED. Eligibility criteria included a history of unscheduled visits for asthma in the previous year. We collected comprehensive data on each participant's asthma medical management and prior health care utilization. In addition, we calculated each participant's spatial accessibility to primary care pediatric services, reported as a provider-to-population ratio at their place of residence. Patients then were stratified by their spatial accessibility to care and compared with respect to measures of medical management and health care utilization. **RESULTS:** Among the 411 eligible participants, the spatial accessibility of primary care ranged from 7.4 to 350.2 full-time pediatric providers per 100,000 children <18 years of age, with a mean of 57.7 +/- 40.0. Patients in the middle and highest tertiles of spatial accessibility made significantly more scheduled visits for asthma care than patients in the lowest tertile. There were no differences among tertiles of accessibility with respect to asthma management or with respect to unscheduled visits for asthma care. **CONCLUSIONS:** Within this highly urban, largely disadvantaged and minority population of children with chronic asthma, patients with higher spatial accessibility to primary care services made significantly more scheduled visits for asthma care.

- Teig N. et al.** *Chlamydomydia pneumoniae and Mycoplasma pneumoniae in respiratory specimens of children with chronic lung diseases.* Thorax. 2005; 60(11) : 962-6.p Abstract: BACKGROUND: Persistent infection with Mycoplasma pneumoniae and Chlamydomydia pneumoniae has been implicated in the progression or induction of asthma and chronic obstructive pulmonary disease. Evidence for this hypothesis has been obtained in adults either by serological methods or by direct pathogen detection using invasive procedures. METHODS: We investigated nasal brush specimens and induced sputum from 38 children with stable chronic lung disease (asthma, n = 26; chronic bronchitis n = 12) and from 42 healthy controls for the presence of M pneumoniae or C. pneumoniae DNA by polymerase chain reaction (PCR) using nested primers. RESULTS: None of the controls but 23.6% and 10.5% of the children with lung disease had positive PCR for C pneumoniae (p = 0.001) and M pneumoniae (p = 0.044) respectively. Significantly more children with non-atopic asthma than with atopic asthma were positive for C pneumoniae or M pneumoniae (4/8 v 1/18; p = 0.018). There were no unwanted side effects from sputum induction. No correlation was found between detection of Chlamydomydia and severity of lung disease. Colonisation with both organisms had occurred before adulthood in a significant proportion of children with stable chronic lung diseases. CONCLUSION: Combining nasal brush specimens with induced sputum may be a useful non-invasive method for studying the role of C pneumoniae and M pneumoniae infection in children with different chronic lung diseases.
- Telljohann S.K. et al.** *Effect of full-time versus part-time school nurses on attendance of elementary students with asthma.* J Sch Nurs. 2004; 20(6) : 331-4.p Abstract: Asthma, the most common chronic disease in children today, is the leading cause of absenteeism among students. It accounts for nearly 20 million lost school days annually. This study examined whether full-time (5 days per week) or part-time (2 days per week) school nurses would have a differential effect on the frequency of absences among elementary school students with asthma. This study found that students with asthma who were poor or who were African American and in schools with full-time nurses missed significantly fewer days (3 days, or 23% fewer missed days) than did their counterparts with asthma in schools with part-time nurses.
- Teper A.M. et al.** *Fluticasone improves pulmonary function in children under 2 years old with risk factors for asthma.* Am J Respir Crit Care Med. 2005; 171(6) : 587-90.p Abstract: This study assessed the effects of treatment with fluticasone in children younger than 2 years old with recurrent wheezing and risk factors of developing asthma. This double-blind placebo-controlled study randomized children to receive fluticasone (125 mug; n = 14) or placebo (n = 12) twice daily for 6 months. Pulmonary function was assessed at the beginning and end, and parents filled out a daily diary recording respiratory symptoms, need for rescue medication, and emergency care. The SD score of maximum flow at functional residual capacity was -0.74 +/- 0.6 at the beginning and 0.44 +/- 1 at the end for the fluticasone group (p = 0.001), and -0.79 +/- 0.3 at the beginning and -0.78 +/- 1.4 at the end for the placebo group (p = 0.97). A statistically significant difference (p = 0.02) was observed between treatments. The percentage of symptom-free days was 91.3 +/- 7% for fluticasone and 83.9 +/- 10% for placebo (p = 0.05). The number of respiratory exacerbations was 2.1 +/- 1.7 and 4.1 +/- 3 (p = 0.04), and the percentage of days on albuterol was 8.6 +/- 6% and 16.3 +/- 9% (p = 0.028). Treatment with fluticasone twice daily for 6 months improves pulmonary function and clinical outcomes in children with asthma younger than 2 years.
- Teran Santos J.** *[Increased upper airway resistance syndrome: a specific diagnosis?].* Arch Bronconeumol. 2002; 38(8) : 348-50.p
- Terreehorst I. et al.** *Prevalence and severity of allergic rhinitis in house dust mite-allergic patients with bronchial asthma or atopic dermatitis.* Clin Exp Allergy. 2002; 32(8) : 1160-5.p Abstract: BACKGROUND: Allergic rhinitis, asthma and atopic dermatitis are closely associated. Although population-based studies report a high prevalence of rhinitis among asthma patients, less is known of the association between rhinitis and atopic dermatitis and the severity of concomitant rhinitis. OBJECTIVES: We aimed to determine the prevalence and severity of allergic rhinitis among asthmatics and patients with atopic dermatitis and assessed whether age and comorbidity influence the severity of rhinitis signs and symptoms. METHODS: Three hundred and twenty-five patients recruited for a multicentre trial to study the effect of encasings of mattresses, pillows and duvets on signs and symptoms of allergic rhinitis and/or asthma and/or atopic dermatitis recorded visual analogue scores (VAS) and daily symptom scores and underwent nasal challenge tests with house dust mite (HDM). RESULTS: Based on history and clinical symptoms 92% of the 164 asthmatic patients and 85% of the 86 patients with atopic dermatitis could be diagnosed as having rhinitis. Inclusion of a positive provocation to HDM did not result in a substantial lower prevalence of rhinitis. Subjects reported moderate symptoms, with mean rhinitis VAS scores ranging from 40.0 to 55.0. Presence of atopic dermatitis was associated with lower rhinitis VAS and symptoms scores, whereas in multivariate analysis the presence of asthma was positively associated with nasal responsiveness to HDM. CONCLUSION: The prevalence of nasal symptoms in patients with bronchial asthma or atopic dermatitis and sensitized to house dust mites is high. Although the majority of patients experience mild to moderate symptoms, the presence of nasal disease needs to be examined in all patients with atopic disorders.
- Terzano C. et al.** *Corticosteroids administered by nebulization to children with bronchial asthma.* Adv Ther. 2001; 18(6) : 253-60.p Abstract: Inhaled corticosteroids are recommended for long-term control of asthma in children, and nebulization simplifies administration to patients who lack hand-to-lung coordination. Information on the efficacy and safety of nebulized corticosteroids in children with mild to moderate asthma is limited, however, and comparison between corticosteroids is lacking. One hundred thirty-three patients 6 to 14 years of age with bronchial asthma were randomly assigned to receive flunisolide 500 microg or budesonide 500 microg, both administered twice daily by nebulizer for 4 weeks. Morning peak expiratory flow rate (primary efficacy endpoint) increased significantly from baseline (P<.001) with both medications (P = NS between treatments). Use of salbutamol as rescue medication decreased by 82.6% with flunisolide and by 82.7% with budesonide; respective decreases in asthma score were 78.8% and 82.3% (P<.001 vs baseline, P = NS between treatments). Only flunisolide reduced the number of nocturnal awakenings (P<.001). Ten patients in the flunisolide group and 12 in the budesonide group reported adverse events, none of which required discontinuation of treatment. In children with asthma, nebulized corticosteroids are effective and have good safety and tolerability profiles. Flunisolide and budesonide seem to produce equivalent clinical responses.
- Thi Thuong N.P. et al.** *[Inhaled treatment for asthma in practice.].* Arch Pediatr. 2004; 11(11) : 1377-83.p Abstract: The modalities of an inhaled treatment depends on the characteristics of the aerosol, on the age of the child, and mainly on the inhalatory system. Before the age of 8 years, the pressurised metered dose inhaler must be used together with a spacer device. Above this age, the use of a breath-actuated inhaler or of a dry powder inhaler can be proposed. Demonstration and educational instructions will increase the probability of compliance and efficiency of the treatment.
- Thomas P.S. et al.** *The relationship of exhaled nitric oxide to airway inflammation and responsiveness in children.* J Asthma. 2005; 42(4) : 291-5.p Abstract: Exhaled nitric oxide (eNO) is a potential tool in

epidemiological studies of asthma. It was hypothesized that in a cross-sectional survey of asthma in adolescent children, eNO may contribute to the detection of this disease. A cohort of Australian school children in two educational years (n = 107, aged 14.7 +/- 2.3 years, 42.9% female) were surveyed in terms of exhaled nitric oxide (eNO), which was compared with other indicators of asthma: asthma symptoms, atopy [skin prick tests (SPT)], hypertonic saline bronchial reactivity, sputum inflammatory cells and eosinophilic cationic protein. Significant positive correlations were found with eNO and number of positive skin prick tests (p = 0.001; n = 98), symptoms (p = 0.05; n = 107), sputum eosinophils (p = 0.025; n = 83), and sputum eosinophilic cationic protein (p = 0.009; n = 83). There was no significant relationship with airway hyperresponsiveness (p = 0.3; n = 15). eNO had a negative predictive value for asthma of 83%, and a positive predictive value of 54%, which is comparable with most current tests for diagnosing asthma. eNO appears to be a useful indicator of atopy and airway inflammation, but in this population it was not closely related to airway hyperresponsiveness.

Thomsen S.F. et al. *The incidence of asthma in young adults.* Chest. 2005; 127(6) : 1928-34.p **Abstract:** STUDY OBJECTIVES: Longitudinal data on adult asthma are sparse. The objectives of this study were to determine the incidence of asthma and to establish the risk factors for the development of asthma in subjects who were 12 to 41 years old over an 8-year period. DESIGN: From birth cohorts over the period 1953 to 1982 in The Danish Twin Registry, 19,349 subjects with no history of asthma, as determined by a questionnaire-based survey in 1994, answered a follow-up questionnaire in 2002. The subjects were regarded as incident asthma cases when answering "yes" to the question "Do you have, or have you ever had asthma?" in 2002, and "no" to the same question in 1994. RESULTS: A total of 838 cases (4.3%) of new asthma were identified in 2002. The incidence rates of asthma were 4.5 and 6.4 per 1,000 person-years, respectively, among male and female subjects. For all ages, the probability of adult-onset asthma was greater for female subjects (odds ratio [OR], 1.49; p < 0.001), and for both sexes there was a slow decline in probability with increasing age. There was a positive association between increasing body mass index (BMI) and risk of adult-onset asthma applying to both sexes (OR, 1.05 per unit; p < 0.001). Furthermore, positive associations were found between incident asthma and a history of hay fever (OR: male subjects, 4.2; female subjects, 3.7; p < 0.001), eczema (OR: male subjects, 3.5; female subjects, 2.0; p < 0.001), and both (OR: male subjects, 6.9; female subjects, 8.0; p < 0.001). CONCLUSIONS: There is a continuing high incidence of asthma past childhood that is most pronounced among female subjects. Increasing levels of BMI are associated with a greater likelihood of developing asthma for both sexes. A substantial portion of cases of adult asthma is preceded by upper airway allergic symptoms and/or eczema, thus indicating a shared pathogenesis.

Thomson F. et al. *Persistent cough in children and the overuse of medications.* J Paediatr Child Health. 2002; 38(6) : 578-81.p **Abstract:** OBJECTIVE: Children referred for persistent cough were evaluated for the referring and final diagnosis, and the extent of the use of medications prior to referral and the side effects encountered. METHODS: Data on children seen by respiratory paediatricians for persistent cough (> or =4 weeks) in a tertiary respiratory setting were collected prospectively over 12 months. RESULTS: Of the 49 children, 61.2% were diagnosed with asthma at referral, with similar referral rates from general practitioners and paediatricians. Children with isolated cough were just as likely to have been diagnosed with asthma as children with cough and wheeze. Medication use (asthma, gastro-oesophageal reflux and antibiotics) prior to referral was high, asthma medications were most common, and of these 12.9% had significant steroid side effects. The most common abnormality found (46.9%) was a bronchoscopically defined airway lesion, and in 56.5% of these children, another diagnosis (aspiration, achalasia, gastro-oesophageal reflux) existed. No children had a sole final

diagnosis of asthma and pre-referral medications were weaned in all children. CONCLUSION: Over diagnosis of asthma and the overuse of asthma treatments with significant side effects is common in children with persistent cough referred to a tertiary respiratory clinic. Children with persistent cough deserve careful evaluation to minimize the use of unnecessary medications and, if medications are used, assessment of response to treatment is important.

Thumerelle C. et al. *Role of viruses and atypical bacteria in exacerbations of asthma in hospitalized children: a prospective study in the Nord-Pas de Calais region (France).* *Pediatr Pulmonol.* 2003; 35(2) : 75-82.p **Abstract:** We studied the role of viruses and atypical bacteria in children hospitalized with exacerbated asthma by a prospective study of children with acute asthma admitted to the Department of Pediatrics in Lille, and to 15 hospitals in the Nord-Pas de Calais region, from October 1, 1998-June 30, 1999. We included children aged 2-16 years with active asthma, defined as three or more recurrent episodes of reversible wheezing. The severity of asthma and of asthmatic exacerbations was recorded. Immunofluorescence assays (IFA) on nasopharyngeal secretions (NPS), serological tests, or both, were used for detection of influenza virus, respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, and coronavirus. Polymerase chain reaction (PCR) assays on NPS were used for rhinovirus and enterovirus. Serological tests for Chlamydia pneumoniae and Mycoplasma pneumoniae were performed. A control group of asymptomatic asthmatic outpatients was examined for respiratory viruses (using IFA and PCR). Eighty-two symptomatic children (mean age, 7.9 years) were examined. Viruses were detected in 38% (enterovirus, 15.8%; rhinovirus, 12%; RSV, 7.3%). Serological tests for atypical bacteria were positive in 10% of patients (C. pneumoniae, 5%; M. pneumoniae, 5%). Among the 27 control subjects (mean age, 7.9 years), one PCR was positive for enterovirus. There was no correlation between severity of chronic asthma or asthmatic exacerbations and the diagnosis of infection. Atypical bacterial pathogen infections were linked with prolonged asthmatic symptoms. In conclusion, we confirmed the high incidence of viral infection in acute exacerbations of asthma, especially enteroviruses or rhinoviruses. Persistent clinical features were more frequently associated with atypical bacterial infections, suggesting that these infections should be investigated and treated in cases of persistent asthmatic symptoms.

Thunqvist P. et al. *Asthma in children exposed to nitrogen dioxide in ice arenas.* *Eur Respir J.* 2002; 20(3) : 646-50.p **Abstract:** Very high concentrations of nitrogen dioxide (NO₂) have been measured in arenas using combustion engine-powered resurfacing machines. This study was performed to compare the occurrence of asthma in children playing ice hockey in arenas using propane-powered machines and in children attending arenas using electric machines. Children regularly playing hockey in the arenas (nine propane, six electric) were sent a questionnaire, including questions on allergic disease and risk factors. Measurements of NO₂ were performed with passive diffusion samplers during 3 consecutive days. The mean NO₂ concentration in the propane arenas was 276 microg x m(-3) (range 28-1015 microg x m(-3)) and 11 microg x m(-3) (2-30) in the electric arenas. Questionnaires were answered by 1,536 children (78%), with an overall prevalence of asthma of 16%. The odds ratio (OR) for asthma was 0.9 (95% confidence interval (CI) 0.7-1.2) comparing propane arenas to electric. However, children in propane arenas with higher than median concentration of NO₂ reported more wheezing (OR 1.4, 95% CI 1.0-1.9) and nasal symptoms (OR 1.7, 95% CI 1.3-2.3) than children in propane arenas with lower concentrations. In conclusion, children playing ice hockey in indoor arenas have a high prevalence of asthma, but it appears unlikely that increased exposure to combustion products, including nitrogen dioxide, is a major contributor to this excess risk.

- Thuvander A. et al.** *Chapter 11: environment-related health - focus on children.* Scand J Public Health Suppl. 2006; 67 : 247-55.p
- Tibbetts J.** *Buildings awareness of the built environment.* Environ Health Perspect. 2002; 110(11) : A670-3.p
- Timonen K.L. et al.** *Effects of air pollution on changes in lung function induced by exercise in children with chronic respiratory symptoms.* Occup Environ Med. 2002; 59(2) : 129-34.p **Abstract:** **OBJECTIVE:** To investigate how daily variations in ambient air pollution, especially in particles, during the cold of winter affect repeated measurements of baseline lung function and exercise induced bronchial responsiveness among primary school children with chronic respiratory symptoms. **METHODS:** During alternate school weeks (maximum five) from February to April 1994, 33 children took part in exercise challenge tests (n=141 tests). The exercise challenges were conducted outdoors in a school yard in the centre of Kuopio, Finland. Spirometric lung functions were measured indoors before the exercise, and 3 and 10 minutes after. Daily mean concentrations of PM(10), black smoke (BS), NO(2), CO, SO(2), and particle size and numbers were monitored at a nearby fixed monitoring site. **RESULTS:** Daily variations in ambient air pollution were not associated with enhanced bronchial responsiveness. However, increased concentrations of BS, PM(10), particle numbers, NO(2), and CO were consistently associated with an impairment of baseline lung functions. The reductions in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV(1)) were 0.5% and 0.6%, respectively, for each 10 microg/m(3) increase in BS (lag 2). **CONCLUSION:** Particles derived from combustion affect baseline lung function rather than bronchial responsiveness among children with chronic respiratory symptoms.
- Timsit S. et al.** *[Benefits of ipratropium bromide in the management of asthmatic crises in the emergency department].* Arch Pediatr. 2002; 9(2) : 117-25.p **Abstract:** **BACKGROUND:** To determine if the addition of ipratropium bromide in the emergency department (ED) for the treatment of childhood asthma reduces rates of hospitalization and relapses for moderate and severe exacerbations. **METHODS:** Patients were given an oral corticosteroid treatment (2 mg/kg) and received every 20 minutes either three nebulizations with albuterol (0.15 mg/kg) and ipratropium bromide (250 micrograms) or six nebulizations with albuterol alone (control group). The primary end point was the need for hospitalization, additional nebulizations or a relapse during the following week. Secondary end point included the effect of age. **RESULTS:** One hundred and forty three children, two to 15 years old, were randomized to ipratropium or control groups and 121 were evaluated on day seven. As a whole, the control group was less often hospitalized or in relapse than those treated with three nebulizations of albuterol and ipratropium (17.5% vs 37.9%, $p < 0.02$). The ipratropium group reached the same result after three additional albuterol nebulizations. The benefit of anticholinergic therapy was observed for children less than six years of age who had a similar rate of success (73.5 vs 75.7%). **CONCLUSION:** The association of ipratropium bromide to the first three doses of the albuterol protocol for acute asthma did not act as well as six nebulizations of albuterol alone. The effect was age dependent and two to six years old children needed more attention. Nevertheless the hospitalization rate did not support the use of ipratropium compared with repeated albuterol nebulizations.
- Tinkelman D. et al.** *School-based asthma disease management.* J Asthma. 2004; 41(4) : 455-62.p **Abstract:** **BACKGROUND:** Asthma is the most common chronic childhood illness and the leading cause of missed school days. School is a potential location for establishing an asthma education program for children and their parents/caregivers designed to improve disease management. **OBJECTIVE:** To determine whether a comprehensive, school-based asthma management program, in addition to a conventional disease management program, can reduce measures of asthma control, student absenteeism, and caregiver lost workdays. **METHODS:** School nurses recruited parents/caregivers of students with asthma from three urban elementary and middle schools. Children were identified as having asthma by a previous diagnosis from their personal physician. Parents were invited to attend educational sessions about the program. Students received peak flow meters and training in their use and had access to an interactive asthma diary to record symptoms, peak flow, and medicine usage. They received monthly asthma education at school and had access to an online asthma education program and additional handouts. Parents received several educational calls regarding asthma and had a 24-hour, 7-days-a-week emergency number to call if problems arose. **RESULTS:** At 6 months, missed school days and unscheduled doctor visits were reduced by two thirds ($n = 41$; $p < 0.01$ for each). Caregivers' perception of children's activity level increased by 11% ($n = 26$; $p = 0.037$). Daytime and nighttime frequency of symptoms dropped by 62% and 34%, respectively ($n = 32$; $p < 0.007$ and $p < 0.03$ for each). These trends continued at 12 months, although only reduction in frequency of symptoms attained statistical significance. **CONCLUSIONS:** A comprehensive, school-based asthma management program can successfully improve asthma control and reduce absenteeism in elementary and middle school students and caregiver lost workdays.
- Tobias A. et al.** *Short term effects of airborne pollen concentrations on asthma epidemic.* Thorax. 2003; 58(8) : 708-10.p **Abstract:** **BACKGROUND:** Few studies have used time series to investigate the relationship between asthma attacks and aeroallergen levels on a daily basis. **METHODS:** This study, based on time series analysis adjusting for meteorological factors and air pollution variables, assessed the short term effects of different types of allergenic pollen on asthma hospital emergencies in the metropolitan area of Madrid (Spain) for the period 1995-8. **RESULTS:** Statistically significant associations were found for Poaceae pollen (lag of 3 days) and Plantago pollen (lag of 2 days), representing an increase in the range between the 99th and 95th percentiles of 17.1% (95% confidence interval (CI) 3.2 to 32.8) and 15.9% (95% CI 6.5 to 26.2) for Poaceae and Plantago, respectively. A positive association was also observed for Urticaceae (lag of 1 day) with an 8.4% increase (95% CI 2.8 to 14.4). **CONCLUSIONS:** There is an association between pollen levels and asthma related emergencies, independent of the effect of air pollutants. The marked relationship observed for Poaceae and Plantago pollens suggests their implication in the epidemic distribution of asthma during the period coinciding with their abrupt release into the environment.
- Todd G.R. et al.** *Acute adrenal crisis in asthmatics treated with high-dose fluticasone propionate.* Eur Respir J. 2002; 19(6) : 1207-9.p **Abstract:** Four cases of asthma (one adult, three children) developing acute adrenal crisis after introduction of high-dose inhaled fluticasone propionate are presented. The three children, aged 7-9 yrs, had been prescribed inhaled fluticasone, dosage 500-2,000 microg x day(-1) and duration 5 months-5 yrs. All presented with convulsions due to hypoglycaemia (blood glucose 1.3-1.8 mM). The fourth case was a male of 33 yrs with difficult-to-control asthma and had been taking fluticasone propionate 1,000-2,000 microg x day(-1) for 3 yrs. He presented with fatigue, lethargy, nausea and postural hypotension. Acute adrenal crisis in each case was confirmed by investigations which included measurement of acute phase cortisol levels, short and long Synacthen stimulation tests and glucagon stimulation tests. Other cases of hypothalamic-pituitary-adrenal axis suppression were excluded.
- Todokoro M. et al.** *Childhood cough variant asthma and its relationship to classic asthma.* Ann Allergy Asthma Immunol. 2003; 90(6) : 652-9.p **Abstract:** **BACKGROUND:** In pediatrics, some patients with chronic cough who have no evidence of a causative disease are

diagnosed as having cough variant asthma (CVA). The precise prognosis of infants and children with CVA, however, is still unclear. **OBJECTIVE:** To evaluate the relationship between CVA and classic asthma in childhood. **METHODS:** To diagnose CVA, we performed a methacholine inhalation challenge with use of a transcutaneous oxygen pressure (tcPO₂) monitoring system in 100 children with chronic cough, and 75 children (45 boys and 30 girls; mean age, 5.7 years) were diagnosed as having CVA. These patients underwent follow-up monitoring for more than 3 years to ascertain whether classic asthma developed. For comparison, 53 age-matched children with classic asthma (30 boys and 23 girls; mean age, 5.6 years) and 30 age-matched control subjects (12 boys and 18 girls; mean age, 5.5 years) also participated in this study. Consecutive doses of methacholine were doubled until a 10% decrease in tcPO₂ from the baseline was reached. The cumulative dose of methacholine at the inflection point of tcPO₂ (D_{min}-PO₂) was considered to represent the sensitivity of tcPO₂ to inhaled methacholine. **RESULTS:** After 3 years or more of follow-up assessments, 52 of the 75 patients answered our questionnaire. Of the responding patients, 28 had been diagnosed as having classic asthma. A significant difference was noted in the age at onset of CVA between the children in whom classic asthma developed (the asthma-developed group) and those in whom classic asthma did not develop (the asthma-free group). No statistically significant differences in D_{min}-PO₂ between the asthma-developed group and the asthma-free group or between the girls and the boys, however, were found. **CONCLUSIONS:** This study showed that 75% of children with chronic cough had CVA, that classic asthma developed in 54% of the children with CVA, and that it is not the severity of bronchial hyperresponsiveness in CVA but the age at onset of CVA that is a risk factor for the development of classic asthma in childhood CVA.

Tomerak A.A. et al. *Inhaled beta2-agonists for treating non-specific chronic cough in children.* Cochrane Database Syst Rev. 2005; (3) : CD005373.p **Abstract:** **BACKGROUND:** The pathophysiology of so called 'cough variant asthma' has not received a great deal of research interest and opinion lies divided as to whether it is really asthma or not. The proponents of cough variant asthma suggest a therapeutic trial of medications usually used to treat asthma. **OBJECTIVES:** To determine the effectiveness of inhaled ss2 agonists in non-specific chronic cough in children over the age of 2 years. **SEARCH STRATEGY:** The Cochrane Airways Group database (including MEDLINE, EMBASE and CINAHL) and the Cochrane Controlled Trials Register (CCRT) were searched. Additional searching included hand searching of medical journals through the Cochrane Collaboration, references, references of references listed in primary sources and personal communication with authors. In addition "Grey literature" including theses, internal reports, non-peer reviewed journals were sought. **SELECTION CRITERIA:** All randomised (randomised and quasi-randomised) controlled clinical trials in which inhaled ss2 agonists were given for chronic cough in children over 2 years of age were included. Two reviewers independently assessed articles for inclusion and methodological quality. **DATA COLLECTION AND ANALYSIS:** Data for trials of salbutamol versus placebo were extracted by both reviewers and entered into the Cochrane Collaboration software program Review Manager, version 4.2. **MAIN RESULTS:** In children presenting with isolated chronic cough there was no significant difference between salbutamol treated group and placebo group. **AUTHORS' CONCLUSIONS:** Salbutamol was no different from placebo in reducing the frequency of cough measured objectively or scored subjectively.

Tomita Y. et al. *Artificial neural network approach for selection of susceptible single nucleotide polymorphisms and construction of prediction model on childhood allergic asthma.* BMC Bioinformatics. 2004; 5 : 120.p **Abstract:** **BACKGROUND:** Screening of various gene markers such as single nucleotide polymorphism (SNP) and correlation between these markers and

development of multifactorial disease have previously been studied. Here, we propose a susceptible marker-selectable artificial neural network (ANN) for predicting development of allergic disease. **RESULTS:** To predict development of childhood allergic asthma (CAA) and select susceptible SNPs, we used an ANN with a parameter decreasing method (PDM) to analyze 25 SNPs of 17 genes in 344 Japanese people, and select 10 susceptible SNPs of CAA. The accuracy of the ANN model with 10 SNPs was 97.7% for learning data and 74.4% for evaluation data. Important combinations were determined by effective combination value (ECV) defined in the present paper. Effective 2-SNP or 3-SNP combinations were found to be concentrated among the 10 selected SNPs. **CONCLUSION:** ANN can reliably select SNP combinations that are associated with CAA. Thus, the ANN can be used to characterize development of complex diseases caused by multiple factors. This is the first report of automatic selection of SNPs related to development of multifactorial disease from SNP data of more than 300 patients.

Tonelli E. *[Toxocariasis and asthma: a relevant association].* J Pediatr (Rio J). 2005; 81(2) : 95-6.p

Townley R.G. et al. *The effect of BCG vaccine at birth on the development of atopy or allergic disease in young children.* Ann Allergy Asthma Immunol. 2004; 92(3) : 350-5.p **Abstract:** **BACKGROUND:** Exposure to infectious diseases may reduce the development of asthma or allergy. In particular, the role of the BCG vaccine in modulating asthma or allergy has been a source of speculation. **OBJECTIVE:** To study newborns from 3 international sites to evaluate the prospective effect of BCG vaccine on allergic diseases or atopic development. **METHODS:** Infants were enrolled from newborn and well-infant clinics in Thailand, Argentina, and Turkey. The standard BCG vaccine for each country was given at birth. Parents who consented to have their infant included in the protocol completed an allergy family questionnaire. Infants underwent a standard purified protein derivative (PPD) test at 9 to 12 months of age, and the reaction size was measured. At the age of 2 years, the children returned to be studied. Allergy skin tests to common allergens appropriate to location and age were performed, and the parents completed the International Study of Allergy and Asthma in Childhood questionnaire. The PPD reaction size was compared with the presence of atopy and allergy questionnaire responses. **RESULTS:** A total of 1,704 infants were studied. Statistical significance was found between a negative PPD response vs any positive PPD response and the risk of having an allergic history at the age of 2 years in Turkey (relative risk, 2.11; 95% confidence interval, 1.25-3.55; P = .005) and Thailand (relative risk, 2.16; 95% confidence interval, 1.18-3.94; P = .02) but not Argentina (relative risk, 1.09; 95% confidence interval, 0.70-1.68; P = .70). **CONCLUSIONS:** This study further supports the role of infectious agents in modulating asthma and allergy development.

Toye C. et al. *Psychometric testing and refinement of the Support Needs Inventory for Parents of Asthmatic Children.* J Nurs Meas. 2004; 12(3) : 179-93.p **Abstract:** This study refined the Support Needs Inventory for Parents of Asthmatic Children (SNIPAC) (Coleman, Maltby, Kristjanson, & Robinson, 2001) to produce a more parsimonious tool to assess the importance and meet the support needs of parents of children with asthma. The original tool was completed by 145 parents of 199 children with asthma, and 74 of these also provided test-retest responses. Internal consistency reliability, construct validity, and stability over time were assessed and refinements were made. Internal consistency reliability of the revised 20-item tool ranged from .77 to .95 for the three subscales of the Parent's Priority Scale (PPS), and .92 for the full PPS. Cronbach's alphas ranged from .74 to .90 for the three subscales of the Parent's Fulfillment Scale (PFS) and was .91 for the full scale. Factor analysis results of the PPS were compatible with the tool's conceptual framework. The revised 20-item tool demonstrated adequate psychometric properties in most areas. This tool may be used for

research or clinical screening without imposing undue burden on parents. Further work is required to establish the tool's stability over time.

Trollvik A. et al. *Influence of an asthma education program on parents with children suffering from asthma.* Nurs Health Sci. 2005; 7(3) : 157-63.p **Abstract:** Several studies have evaluated the effectiveness of various methods of asthma education for parents. This study adds a qualitative and inner perspective from the families of children suffering from asthma. The aim was to illuminate the influence of an asthma education program (AEP) for parents. The study sample consisted of nine parents of five children with moderate to severe asthma in the 2-6 years age group. Data were collected by interviews and qualitative analyses were used. The main findings were that the parents experienced an increased understanding of their child's experience of asthma after having participated in the program. Three themes were revealed: sharing experiences, accepting the illness, and partnership building. In conclusion, the parents in the study expressed that they promote increased self-understanding by meeting other parents in groups.

Trollvik A. et al. *Parents' experiences of asthma: process from chaos to coping.* Nurs Health Sci. 2004; 6(2) : 93-9.p **Abstract:** The aim of the present qualitative study was to describe nine parents' everyday experiences of living with a child suffering from asthma. Data were collected by means of in-depth interviews and phenomenological content analysis. Four main themes emerged: feelings of uncertainty, helplessness and guilt; the need for support and help from healthcare professionals; adaptation to everyday life; and the development of coping strategies. In addition, two subthemes; trying out and seeking information, emerged. Trying out was found to be an important strategy for parents in managing the illness. In encounters with healthcare professionals, parents felt that they were not respected and that their competence was questioned. In conclusion, this study emphasizes the importance of a mutual dialogue between healthcare professionals and parents to enable the parents to develop the competence necessary to care for their child.

Trotter S. *Neonatal skincare: why change is vital.* RCM Midwives. 2006; 9(4) : 134-8.p **Abstract:** 'Newborn skin is thinner, more permeable and less able to withstand the sensitising effects of modern detergents. It is also important to remember that anything placed on, in or around a baby has the capacity to harm' (Trotter, 2004a). The anatomical and functional differences of neonatal skin have been thoroughly reported over the years and there is now a body of evidence to support the above statement (Fatter, 1997; Gelmetti, 2001; Lund, 2001a, 2001b; Medves, 2001; Ertel, 2003; Trotter, 2002, 2004a). The aim of this article is to inform midwives about the potential dangers of chemical ingredients used in personal care products and to suggest simpler skincare regimes. It is anticipated that doing so will reduce the risks of conditions like eczema, asthma and related allergies.

Tsakok A.D. *Comment on respiratory morbidity and lung function.* Respiriology. 2003; 8(3) : 404-5.p

Tsao C.H. et al. *Concomitant chronic sinusitis treatment in children with mild asthma: the effect on bronchial hyperresponsiveness.* Chest. 2003; 123(3) : 757-64.p **Abstract:** STUDY OBJECTIVE: Previous studies have suggested that aggressive treatment of sinusitis can decrease bronchial hyperresponsiveness (BHR). However, there is still too little evidence to draw this conclusion, and the concept remains controversial. DESIGN: A prospective, open-label study. SETTING: University children's hospital allergy and immunology center and radiologic department. PATIENTS: Sixty-one children with mild asthma and allergic rhinitis participated in the study. Forty-

one of these 61 children had sinusitis, and the remainder had no sinusitis. Ten matched, nonatopic, healthy children were used as a control group. INTERVENTION: Children with chronic sinusitis were placed into two groups. One group was treated with amoxicillin-clavulanate for 6 weeks and then with nasal saline solution irrigation for 6 weeks. For the other group, the treatment order was reversed. Children without chronic sinusitis received nasal saline solution irrigation for 12 weeks. MEASUREMENTS: Clinical symptoms and signs of sinusitis, FEV(1), and BHR were analyzed in the patients before and after treatment. RESULTS: The clinical symptoms and signs of sinusitis, but not FEV(1), showed a significant improvement after antibiotic treatment. After aggressive treatment for sinusitis, it was found that the provocative concentration of methacholine causing a 20% fall in FEV(1) of children with mild asthma and sinusitis was significantly higher after treatment. CONCLUSION: The results suggest that every asthmatic patient needs to carefully evaluate to determine whether the patient has concomitant sinusitis. Respiratory infections that meet criteria for sinusitis, even if they do not exacerbate asthma, should be treated. It is suggested that sinusitis should always be kept in mind as a possible inducible factor for BHR, and that aggressive treatment of chronic sinusitis is indicated when dealing with an asthmatic patient who shows an unpredictable response to appropriate treatment. Moreover, the findings of this study provide more evidence for an association between sinusitis and asthma with respect to BHR.

Tsunemi Y. et al. *Interleukin-13 gene polymorphism G4257A is associated with atopic dermatitis in Japanese patients.* J Dermatol Sci. 2002; 30(2) : 100-7.p **Abstract:** Interleukin (IL)-13 plays an important role in the induction of immunoglobulin E (IgE) and in the pathogenesis of atopic dermatitis (AD). We investigated the allele and genotype frequencies of three IL-13 single nucleotide polymorphisms (SNPs) (A704C and C1103T in the promoter region and G4257A in exon 4) in Japanese patients with AD. For A704C and C1103T SNPs, there were no significant differences in allele or genotype frequencies between AD patients and controls. For G4257A SNP, A allele was significantly increased in AD patients (39.5%) compared with controls (29.4%) (P = 0.016). The same proportion of each genotype and allele was observed in the patient subgroup with and without asthma. Serum IgE levels and peripheral eosinophil counts were not significantly different among genotypes in G4257A SNP. There was also no significant difference in allele or genotype frequencies between AD patients with mild disease and those with severe disease, between those with family history of AD and those without it, or between those with family history of atopic disorders and those without it. This result suggests that G4257A allele is associated with susceptibility to AD and that it may function in the pathogenesis of AD itself, presumably by other mechanisms than inducing IgE production.

Tsunemi Y. et al. *Lack of association of CCR4 single nucleotide polymorphism with atopic dermatitis in Japanese patients.* Acta Derm Venereol. 2004; 84(3) : 187-90.p **Abstract:** CCR4, a member of the CC chemokine receptor family, is believed to play an important role in the pathogenesis of atopic dermatitis. To examine whether CCR4 single nucleotide polymorphism (SNP) is associated with susceptibility to atopic dermatitis, we investigated the allele and genotype frequencies of C1014T SNP of CCR4 in 198 Japanese patients with atopic dermatitis and controls by a PCR-restriction fragment length polymorphism method. There was no significant difference in allele or genotype frequencies between patients with atopic dermatitis and controls. Serum IgE levels and peripheral blood eosinophil counts were not significantly different among genotypes. There was also no significant difference in allele or genotype frequencies between the patient subgroup with and without asthma, with mild or moderate disease, with and without family history of atopic dermatitis, or with and without family history of atopic disorders. C1014T SNP of CCR4 does not appear to be associated with susceptibility to atopic dermatitis in Japanese patients.

Tsuyuki R.T. et al. *Management of asthma among community-based primary care physicians.* J Asthma. 2005; 42(3) : 163-7.p
Abstract: BACKGROUND: Despite significant improvements in asthma treatment and the dissemination of national and international guidelines for asthma management, there are ongoing concerns that suboptimal care is being provided for patients with asthma. OBJECTIVE: To determine the current practice patterns of asthma care among primary care physicians. DESIGN: A cross-sectional study. SETTING: Province of Alberta, Canada (population: 3 million people). PARTICIPANTS: Patients, 5 years of age or older, who had a physician's diagnosis of asthma, and had at least two visits for asthma between 1996 and 2001. MEASUREMENT AND RESULTS: Charts of 3072 distinct patients (from 45 unique primary care physicians) were reviewed. Previous emergency department visits or hospitalizations were experienced by 20% of the sample. A total of 25% of patients had documented evidence that they had performed spirometry. More than half of the patients had no documented evidence that they had received any form of asthma education; only 2% of the charts indicated that patients received a written action plan. Two thirds of the patients were prescribed an inhaled steroid within 6 months of the last clinic visit. CONCLUSIONS: Our study indicates a gap in the provision of asthma education, written action plans, and spirometric testing for patients diagnosed with asthma among primary care physicians.

Turner S.W. et al. *Infants with flow limitation at 4 weeks: outcome at 6 and 11 years.* Am J Respir Crit Care Med. 2002; 165(9) : 1294-8.p
Abstract: Within a longitudinal study of lung function in 243 infants, we identified a group of 23 individuals with flow limitation in tidal expiration. In infancy, flow-limited children have reduced lung function and increased airway responsiveness (AR), and at 2 years of age they are diagnosed with asthma more frequently. We hypothesized that these observations would persist throughout childhood. Data from ages 3 to 11 years were analyzed. Only at 4 years of age did the flow-limited group have increased wheeze compared with other cohort members (odds ratio, 4.25; 95% confidence interval [CI], 1.11 to 16.2; $p = 0.04$; $n = 114$). At 6 years of age, 117 cohort members were seen. The flow-limited group ($n = 14$) had greater AR ($p = 0.009$) and reduced mean FEV₁ (131 ml; 95% CI, 16 to 246; $p = 0.03$) and FEF(25-75) (0.28 L/second; 95% CI, 0.05 to 0.52; $p = 0.02$). At 11 years of age, 183 children were seen and the flow-limited group ($n = 18$) had greater AR ($p = 0.02$) and a trend toward reduced mean FEF(25-75) (0.24 L/second; 95% CI, -0.02 to 0.49; $p = 0.08$). Atopy and parental asthma were not increased in the flow-limited group. We suggest that the physiologic abnormality that causes flow limitation in early infancy may identify an at-risk group, different from asthma, who have reduced lung function and increased airway responsiveness in later life.

Turner S.W. et al. *Reduced lung function both before bronchiolitis and at 11 years.* Arch Dis Child. 2002; 87(5) : 417-20.p
Abstract: BACKGROUND AND AIMS: We have previously shown an association between reduced premorbid lung function (V_{max}FRC) and bronchiolitis. We hypothesized that individuals with bronchiolitis will go on to have reduced lung function and increased respiratory symptoms in childhood. METHODS: V_{max}FRC was measured at 1 month of age; individuals with bronchiolitis were prospectively identified. Annual symptom questionnaires were completed from 3 to 6 years. At 11 years of age, children underwent an assessment including questionnaire, lung function, airway response to histamine (AR), and skin prick testing. RESULTS: Eighteen individuals with bronchiolitis were ascertained from 253 cohort members. Children with bronchiolitis had increased viral induced wheeze at 3 (OR 5.8, 95% CI 1.4 to 25.2; $n = 103$) and 5 years (OR 5.3, 95% CI 1.1 to 25.5; $n = 101$). At 11 years of age, 194 children were assessed including 16 with past bronchiolitis. These 16 individuals had reduced mean z scores for % V_{max}FRC compared with other

children (-0.56 and 0.06 respectively) and mean z scores for % FEF(25-75) at 11 years (-0.53 and 0.06 respectively). At 11 years, FEV₁, FVC PEF, AR, atopy, wheeze, and diagnosed asthma were not different between groups. CONCLUSIONS: Reduced lung function is present before and after bronchiolitis; the level of reduction is comparable. The mechanism for wheeze and reduced lung function after bronchiolitis appears to be related to premorbid lung function and not bronchiolitis per se.

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Udy A. *A 10-year-old child with status asthmaticus, hypercapnia and a unilateral dilated pupil.* Paediatr Anaesth. 2005; 15(12) : 1120-3.p
Abstract: This article reports the case of a 10-year-old child with an exacerbation of asthma requiring mechanical ventilation. His immediate course was complicated by significantly elevated arterial CO₂ tensions and a unilateral dilated pupil. A computed tomography scan of his brain failed to demonstrate any evidence of intracranial hypertension or cerebral edema, and he went on to make an uncomplicated recovery, with no evidence of neurological sequelae. The most likely diagnosis appeared to be local contamination with ipratropium when he was receiving frequent nebulizers prior to mechanical ventilation. Similar cases reported in the literature are reviewed, with a discussion of clinical management, implications of permissive hypercapnia and neurological complications in ventilating asthmatic patients and the importance of safe drug handling by staff members.

Ulger Z. et al. *The effect of childhood obesity on respiratory function tests and airway hyperresponsiveness.* Turk J Pediatr. 2006; 48(1) : 43-50.p
Abstract: The aims of this study were to investigate the effect of exogenous obesity on respiratory function tests, to define the relationship between the severity of obesity and respiratory function test parameters, and to detect the incidence of airway hyperresponsiveness and exercise-induced bronchospasm in an obese study group. This cross-sectional controlled study was done with 38 exogenous obese patients, aged 9 to 15 years, and 30 healthy children. Basal respiratory function test parameters were measured with spirometry. To display airway hyperresponsiveness, 4.5% hypertonic saline provocation test was used; exercise-induced bronchospasm incidence was defined with bicycle ergometry. Basal respiratory function test parameters were lower in the study group as compared with the control group. Exercise test was positive in 31.6% of the obese group and in 3.3% of the control group ($P = 0.003$). The provocation test with hypertonic saline test was positive in 18.4% of the obese group. There were strong negative correlations between body mass index (BMI), relative weight, skin fold thickness, waist/hip circumference ratio and basal forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), and peak expiratory flow (PEF) values. The diagnosis and management of exercise-induced bronchospasm may improve exercise performance and physical activity, assist with weight loss, and break the vicious circle.

Ungar W.J. et al. *Assessment of a medication-based asthma index for population research.* Am J Respir Crit Care Med. 2002; 165(2) : 190-4.p
Abstract: Asthma management guidelines recommend the use of preventive medications in sufficient amounts to control asthma symptoms. The validity of a medication use index as a proxy for asthma severity has not been established. We recruited 1,279 Ontario adults with asthma or parents of children with asthma from a community-based surveillance program in 1995-96. Participants completed a telephone questionnaire at baseline, 3 and 6 mo. The questionnaire gathered information about asthma medication use,

health care utilization, and symptoms. Asthma was classified as mild in 28%, moderate in 49%, or severe in 23% of patients based on the amount and types of medication used. There were significant differences among groups in health resource use such that adults with higher medication use visited primary care physicians and specialists more frequently, had pulmonary functions tests more frequently, and were admitted to hospital more frequently. The findings among children were similar. There were weak positive correlations between medication use and symptom frequency in adults and children. We conclude that a medication use index may be useful in population-based research where clinical asthma severity data are lacking. Such an index is distinct from but is related to disease control.

Ungar W.J. et al. *Prospective study of the patient-level cost of asthma care in children.* *Pediatr Pulmonol.* 2001; 32(2) : 101-8.p **Abstract:** 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.

Ushiyama Y. et al. *Nutrition during pregnancy may be associated with allergic diseases in infants.* *J Nutr Sci Vitaminol (Tokyo).* 2002; 48(5) : 345-51.p **Abstract:** The prevalence of allergic diseases is high in Japan, even in infants. Their risk for developing allergies is influenced by the antigens in the mother's diet during pregnancy. We hypothesized that, apart from the antigens, hypersensitivity induced through high energy and nutrient intake by mothers during pregnancy may be a factor for allergic diseases in their babies. In this study, we tried to confirm our hypothesis. Allergy histories of parents and their infants, body characteristics and food and nutrient intake were measured by a questionnaire and a food frequency questionnaire, respectively. A total of 2,642 responses were obtained (return rate, 94.7%). The major allergic diseases in the infants were atopic dermatitis (6.0%), food allergy (3.7%) and bronchial asthma or asthmatic bronchitis (3.2%). About 60% of the infants with allergies had a family history of allergies. Family history of allergy, age of infant, order of birth, head and chest circumferences of infants, BMI of mothers before pregnancy and delivery and intake of lipids (fat and vegetable oil) and vegetables by mothers related positively, and the intake of protein, carbohydrates and milk and its products correlated negatively with allergic diseases in the infants ($p < 0.05$). The results, together with previous reports, suggest that a high intake of energy and lipids (fat and vegetable oil) during pregnancy may accelerate allergic diseases in infants.

Uzel A. et al. *Evaluation of the relationship between cockroach sensitivity and house-dust-mite sensitivity in Turkish asthmatic patients.* *Respir Med.* 2005; 99(8) : 1032-7.p **Abstract:** Exposure to cockroach has been identified as an important source of indoor allergens in patients with asthma and allergic rhinitis. We evaluated the relationship between cockroach sensitivity and other allergens in patients with asthma. A total of 114 patients, defined asthma according to GINA, were enrolled in this study. A questionnaire including age, sex, duration of asthma, history of cockroach presence at home, and total IgE, blood eosinophil count, pulmonary function tests, standard skin prick test additional cockroach and shrimp allergen were performed. There were 84 (73.7%) female and 30 (26.3%) male patients with a mean age of 38.1+10.1 years. The average duration of asthma was 7.7+7.2 years. Sixty five (57%) patients were determined atopic and 49 (43%) nonatopic. Pollen allergen was the most common allergen in 59 (51.8%) patients with asthma, and second common allergen was mite allergen in 43 (37.7%) patients. Cockroach sensitivity was detected in 23 (20.2%) of 114 all asthmatics and 23 (35%) of atopic asthmatics. High rates of house-dust-mite allergy (73.9%) was determined in patients with cockroach sensitivity ($P < 0.05$), while we found no relationship with other allergens. There was no difference for cockroach sensitivity between rural and urban population. Cockroach sensitivity was more common in mild bronchial asthmatics and a female predominance was observed. In addition, there was no association between shrimp and cockroach sensitivity. As a result, a high rate of cockroach sensitivity alone or with mite sensitivity was seen in patients with bronchial asthma in Turkish population. Because of cross-reactivity between mites and cockroach, cockroach sensitivity should be investigated in patients with house-dust-mite allergy. In addition, a high rate of cockroach sensitivity, in terms of IgE sensitization, may be important for the development of new sensitizations.

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Van Dellen R.G. *Can you top this? 37-year survival of patient with Churg-Strauss syndrome.* *Ann Allergy Asthma Immunol.* 2004; 92(6) : 676.p

Van den Neucker A.M. et al. *Acid steatocrit: a reliable screening tool for steatorrhoea.* *Acta Paediatr.* 2001; 90(8) : 873-5.p **Abstract:** This study compared the acid steatocrit (AS) results of healthy children with those of sick children with and without gastrointestinal involvement. Stool samples of 166 children were investigated, comprising 50 healthy children, 26 asthma patients, and 90 patients with gastrointestinal problems divided into 34 treated cystic fibrosis (CF) patients with exocrine pancreatic insufficiency, 16 untreated coeliac disease (CD) patients and 40 patients with various gastrointestinal problems. The median values (5th-95th percentile) of AS results were 3.3% (0.0-21%) for healthy children, 4.5% (1.8-22.5%) for asthma patients, 24.7% (2.6-68.2%) for treated CF patients with exocrine pancreatic insufficiency, 19.8% (3-77.7%) for untreated CD patients and 5.5% (1.8-29%) for patients with various gastrointestinal diseases. **CONCLUSION:** The AS results of treated CF patients with exocrine pancreatic insufficiency and untreated CD patients were similar and significantly higher than those of healthy children and asthma patients. AS can be considered to be a reliable tool in screening for steatorrhoea in paediatric patients.

Van Ganse E. et al. *Level of control and hospital contacts in persistent asthma.* *J Asthma.* 2001; 38(8) : 637-43.p **Abstract:** The purpose of this study was to estimate relationships between asthma control and hospital contacts (visits to emergency rooms and hospitalizations) in a group of patients suffering from persistent asthma, after adjustment for prior use of inhaled corticosteroids. A computerized family practice database was used to identify patients

(aged 6-50 years) with persistent asthma who received asthma therapy from January 1995. The database provided information on patient demographics and drug therapy. Asthma control was estimated by a survey of patients at the end of a 12-month study period. Frequency of hospital contacts during the study period was related to demographics, asthma control, and prescribed doses of inhaled corticosteroids during a prestudy period. Review of computerized medical files of 497 family practice physicians identified 1,966 patients with persistent asthma who met the study criteria. Of these patients, 1,251 completed the survey (63.6%). Asthma control was assessed in 1,130 patients; it was moderate or poor in 42% of the cases. During the 12-month study period, 14.8% of patients reported at least one hospital contact. The level of asthma control was significantly ($p < 0.001$) associated with hospital contacts. The odds ratio (OR) for hospital contact for good and poor asthma control was 0.5 (95% confidence interval [CI] 0.2-0.7) and 2.2 (95% CI 1.2-4.4), respectively. Asthma control was related to hospital contacts independently of use of inhaled corticosteroids before the study period. Overall, control of asthma was not optimal in this population. The occurrence of hospital contacts was closely related with the level of control. This association was independent of the dose of inhaled corticosteroids prescribed before the study, suggesting that in asthma, hospital contacts are primarily related to the level of control experienced by the patients.

van Hattum E.S. et al. *Adenoidectomy and/or tonsillectomy in childhood is not associated with atopic disease later in life.* Clin Exp Allergy. 2006; 36(1) : 40-3.p **Abstract:** OBJECTIVE: To investigate the association between adenoidectomy and/or tonsillectomy in childhood and asthma, allergic rhinitis (AR), and eczema in adolescence. METHODS: Longitudinal birth cohort study of 1328 members born in the city of Nijmegen. Information on ear-nose-throat surgery was documented at 2, 4, and 8 years of age. In 1055 cohort members the incidence of asthma, AR, and eczema at 21 years of age was determined using the International Study of Asthma and Allergic disease in Childhood Core Questionnaire. To analyse the association between adenoidectomy and/or tonsillectomy in childhood and asthma, AR, and eczema at age 21 years, relative risks (RR) were calculated. RESULTS: Six hundred and ninety-three (66%) members completed the questionnaire at age 21 years, of whom 104 (15%) had undergone adenoidectomy and/or tonsillectomy and 262 (38%) reported atopic disease. Children who underwent adenoidectomy and/or tonsillectomy before the age of 8 years were not more likely to develop asthma, AR, or eczema at the age of 21 years than children who did not; RR 0.93 (95% confidence limits (CL) 0.52-1.64), RR 0.94 (CL 0.68-1.30), and RR 1.00 (CL 0.59-1.68), respectively. CONCLUSIONS: Our data show no association between adenoidectomy and/or tonsillectomy in childhood and the incidence of atopic disease in young adults.

Van Sickle D. *Perceptions of asthma among physicians: an exploratory study with the ISAAC video.* Eur Respir J. 2005; 26(5) : 829-34.p **Abstract:** The current study examined the perception and interpretation of asthma symptoms among practitioners using standardised audiovisual presentations of asthma. Two groups of practitioners ($n = 70$) in Chennai, India, were shown the International Study of Asthma and Allergies in Childhood (ISAAC) video questionnaire and asked to describe the symptoms and signs they observed and to identify possible diagnoses for each presentation. The number of practitioners who correctly described the principal symptom(s) of asthma depicted in the five video sequences ranged from 26.1% for scene 5 (wheezing and dyspnoea), to 94.2% for scene 4 (nocturnal cough). The number who identified asthma as a possible cause of the presentations ranged from 17.4% for scene 4, to 67.1% for scene 2 (wheeze after exercise). Practitioners with postgraduate medical education were significantly more likely to identify asthma as a possible cause of the presentations, as were practitioners with postgraduate training in respiratory diseases. In conclusion, the perceptions of asthma and asthma symptoms among many physicians

in Chennai, India, do not match the presentations of asthma depicted in the International Study of Asthma and Allergies in Childhood (ISAAC) video. These differences may be limiting the diagnosis and apparent prevalence of asthma, and suggest the need for additional attention to asthma in the education and training of practitioners in India.

van Staa T.P. et al. *Are inhaled corticosteroids associated with an increased risk of fracture in children?* Osteoporos Int. 2004; 15(10) : 785-91.p **Abstract:** Inhaled corticosteroids are widely used in the long-term management of asthma in children. Data on the relationship between inhaled corticosteroid therapy and osteoporotic fracture are inconsistent. We address this issue in a large population-based cohort of children aged 4-17 years in the UK (the General Practice Research Database). The incidence rates of fracture among children aged 4-17 years taking inhaled corticosteroids ($n=97,387$), taking bronchodilators only ($n=70,984$) and a reference group ($n=345,758$) were estimated. Each child with a non-vertebral fracture ($n=23,984$) was subsequently matched by age, sex, practice, and calendar time to one child without a fracture. Fracture incidence was increased in children using inhaled corticosteroids, as well as in those receiving bronchodilators alone. With an average daily beclomethasone dose of 200 microg or less, the crude fracture risk relative to nonusers was 1.10 [95% confidence interval (CI), 0.96-1.26]; with dosage of 201-400 microg, it was 1.23 (95% CI, 1.08-1.39); and with dosages over 400 microg, it was 1.36 (95% CI, 1.11-1.67). This excess risk disappeared after adjustment for indicators of asthma severity. The increased risk of fracture associated with use of inhaled corticosteroids is likely to be the result of the underlying illness, rather than being directly attributable to inhaled corticosteroid therapy.

van Strien R.T. et al. *Exposure to NO₂ and nitrous acid and respiratory symptoms in the first year of life.* Epidemiology. 2004; 15(4) : 471-8.p **Abstract:** BACKGROUND: Effects of nitrogen dioxide (NO₂) on respiratory health have been the subject of extensive research. The outcomes of these studies were not consistent. Exposure to nitrous acid, which is a primary product of combustion, and is also formed when NO₂ reacts with water, may play an important role in respiratory health. We estimate the independent effects of exposure to nitrogen dioxide and nitrous acid on respiratory symptoms during the first year of life. METHODS: Nitrogen dioxide and nitrous acid concentrations were measured once (1996-1998) in the homes of 768 infants who were at risk for developing asthma. Infants were living in southern New England. The frequency of respiratory symptoms in these children was recorded during the first year of life. RESULTS: Infants living in homes with an NO₂ concentration exceeding 17.4 ppb (highest quartile) had a higher frequency of days with wheeze (rate ratio = 2.2; 95% confidence interval = 1.4-3.4), persistent cough (1.8; 1.2-2.7), and shortness of breath (3.1; 1.8-5.6) when compared with infants in homes that had NO₂ concentrations lower than 5.1 ppb (lowest quartile), controlling for nitrous acid concentration. Nitrous acid exposure was not independently associated with respiratory symptoms. CONCLUSIONS: Among infants at risk for developing asthma, the frequency of reported respiratory symptoms in the first year of life was associated with levels of NO₂ not currently considered to be harmful.

van Veldhoven N.H. et al. *Children with asthma and physical exercise: effects of an exercise programme.* Clin Rehabil. 2001; 15(4) : 360-70.p **Abstract:** OBJECTIVE: To evaluate the effects of a physical exercise programme for children with asthma on an outpatient basis. DESIGN: Intervention study: a randomized pretest-post-test control group design. SETTING AND SUBJECTS: Forty-seven children with clinically diagnosed asthma participated in the intervention study, including 34 boys and 13 girls, from 8 to 13 years of age (mean age 10.6). INTERVENTIONS: The physical exercise programme consisted of regular group exercises and home exercises

for a period of three months. It was based on a theoretical model describing the relationships between physical competence (condition), perceived physical competence, self-esteem and coping behaviour. MAIN OUTCOME MEASURES: Maximum incremental exercise test, endurance test, the Self-Perception Profile for Children (CBSK), the Asthma Coping Test (ACBT), lung function and exercise-induced bronchoconstriction. RESULTS: The results showed significant effects of the intervention programme on physical condition. There was a significant improvement of 15 W on the maximal workload (W_{max}) ($p < 0.001$), of 7% on VO_{2max} (oxygen uptake) ($p = 0.002$) and a significant decrease on heart rate submaximal of 6% ($p = 0.001$). There was also a significant improvement of 50% in running time measured with the endurance test ($p = 0.021$). Furthermore, a significant effect of the intervention was seen on coping with asthma ($p = 0.003$). CONCLUSION: It was concluded that participation in the physical exercise programme not only enhanced physical fitness, but also improved coping behaviour with asthma.

van Woensel J.B. et al. *Bronchiolitis hospitalisations in the Netherlands from 1991 to 1999.* Arch Dis Child. 2002; 86(5) : 370-1.p Abstract: In order to analyse trends in the bronchiolitis hospitalisations in the Netherlands from 1991 to 1999 for children aged 0-4 years, the national number of bronchiolitis hospitalisations were compared with those of asthma and pneumonia hospitalisations of the same age group. The number of bronchiolitis hospitalisations significantly increased, whereas the number of asthma and pneumonia hospitalisations remained unchanged.

Vangveeravong M. *Childhood asthma: proper managements do reduce severity.* J Med Assoc Thai. 2003; 86 Suppl 3 : S648-55.p Abstract: RATIONALE: Asthma is an increasing problem, both in children and adults which is due to an increase in environmental pollution. The current management of asthmatic patients is different from the previous decade as more understanding of the mechanism of asthma pathology is known. OBJECTIVES: To study the prevalence of hospitalized asthmatic patients of different age groups in the past decade and to compare the results of different treatments during each 5-year period, 1986-1990, 1991-1995 and 1997-2001. MATERIAL AND METHOD: A retrospective review of the Out-patient Department (OPD) and In-patient Department (IPD) cases of asthma patients, sorted by International Classification of Diseases (ICD 9 & 10) at the Queen Sirikit National Institute of Child Health (QSNICH), previously known as Children's Hospital was carried out. The patients were divided into 3 groups according to the 5-year period of admissions: 1986-1990, 1991-1995 and 1997-2001. Comparison of the prevalence, age distribution, management, severity and outcomes of the patients in different groups using the standard statistical package SPSS for windows. RESULTS: The prevalence of asthma increased from 7,476 OPD visits in 1986 to the peak of 15,576 visits in 1997 and about 13,000-14,000 stable visits from 1998 through 2001. About 2-3 per cent of these OPD cases were admitted to the hospital. After the hospital charts had been reviewed, 2,927 cases of true asthma cases (81.9%) were studied and they were divided into 3 groups, group 1, 2 and 3 consisting of 1,140, 716 and 1,071 patients, respectively. About 60-80 per cent of the admitted cases were children under 5 years old. With the different management of hospitalized cases between the 3 periods, a significant reduction in the readmission rate was outstanding from 14 per cent to 5 per cent and the maximum number of readmissions was reduced from 8 times to 5 times (the majority was 2 times). The length of stay and the percentage of complicated respiratory failure cases were not different. CONCLUSION: The asthma prevalence is increasing. Young children 0-2 years of age tend to have more severe diseases that need hospitalization. Current management, inhaled beta 2 agonists, together with anti-inflammatory drugs do reduce asthma severity to a certain degree. Early intervention of controller medications and regular follow-up care do reduce the readmissions.

Further newer treatment of asthma is required for better outcomes of these asthmatic patients.

Vanin E. et al. *Anaphylactic reaction after skin-prick testing in an 8-year-old boy.* Pediatr Allergy Immunol. 2002; 13(3) : 227-8.p Abstract: This paper presents the case of an 8-year-old boy who developed an anaphylactic reaction after skin-prick testing (SPT). The tests were performed with commercial extracts and were strongly positive for dog and grass. The boy had no incidence of anaphylaxis reported in his history. At the time tests were performed, he had been admitted to the hospital because of persistent wheezing and had a dog at home for a few days. Although anaphylaxis is very rare after SPTs, these tests should always be performed in a place equipped to treat anaphylaxis.

Vargas M.H. et al. *Trends of asthma in Mexico: an 11-year analysis in a nationwide institution.* Chest. 2004; 125(6) : 1993-7.p Abstract: STUDY OBJECTIVES: Asthma prevalence is increasing in many countries. Some recent articles, however, claim that this tendency is ending. Our aim was to investigate asthma trends in Mexico. DESIGN: Annual data on health services provided to asthmatic patients were retrospectively analyzed from 1991 to 2001. SETTING: The Instituto Mexicano del Seguro Social, the largest nationwide medical institution in Mexico (approximately 24 to 32 million insured subjects). PARTICIPANTS: Health services provided to subjects of any age. INTERVENTIONS: None. MEASUREMENTS AND RESULTS: Asthma-associated health services, either expressed as absolute number or as rate per insured subjects, progressively increased until 1997 in family physician office visits (FPOVs) [newly diagnosed cases only], emergency department visits (ERVs), and hospital discharges (HDs). From that year onward, the number and rates of asthma-associated health services decreased. The same trends were observed for age groups 0 to 4 years, 5 to 14 years, 15 to 44 years, and 45 to 64 years. Using a different approach, asthma was diagnosed each year in approximately 0.4% of all FPOVs, but a decrease in this percentage was observed from 1997 onward. Likewise, asthma caused increasing percentages of all ERVs and HDs until 1997, followed by a sharp decline thereafter. CONCLUSIONS: A decline in absolute and relative numbers of asthma-associated health services occurred over recent years in all medical settings, suggesting that the epidemic of new asthma cases is ending and/or that better control of the disease has been achieved.

Veller-Fornasa C. et al. *Recurrent aphthous stomatitis and atopy.* Acta Derm Venereol. 2003; 83(6) : 469-70.p

Vellinga A. et al. *Changes in respiratory and allergic symptoms in schoolchildren from 1996 to 2002, results from the ISAAC surveys in Antwerp (Belgium).* Acta Clin Belg. 2005; 60(5) : 219-25.p Abstract: Two cross sectional surveys (1995/1996 and 2001/2002) were carried out according to the ISAAC protocol among 6-7 and 13-14 year old schoolchildren in Antwerp, Belgium. A total of 8244 children participated in 1996 and 8159 children in 2002. No significant differences in current prevalence of asthma and asthma medication was found in 6-7 year olds and 13-14 year old girls. Significantly less asthma and asthma medication was reported by 13-14 year old boys in 2002. Symptoms of wheeze had lower occurrence in all groups in 2002, which was significant for older age group. Current prevalence of rash was significantly higher in the 6-7 year olds in 2002. No such increase was found for rash in the older age groups but they reported significantly more rhinitis. No differences were found between urban and suburban Antwerp in either survey. No clear changes in the occurrence of asthma were found for school children in Antwerp while wheeze was reported less in 2002 compared to 1996. Allergic disorders had higher occurrences in schoolchildren in 2002.

Velsor-Friedrich B. et al. *A practitioner-based asthma intervention program with African American inner-city school children.* J Pediatr Health Care. 2005; 19(3) : 163-71.p **Abstract:** INTRODUCTION: Asthma is the most prevalent chronic illness, affecting more than 7 million children younger than 17 years. Asthma has become a leading public health concern because of the dramatic rise in the incidence of this disease during the past 15 years, particularly in minority populations. This study tested a two-part intervention on selected psychosocial and health outcomes of 8- to 13-year-old inner city minority students with asthma. METHOD: The intervention consisted of participation in an asthma education program (Open Airways) followed by 5 monthly visits with a nurse practitioner. The total sample of 52 children was composed of 28 children in the treatment group who received the intervention and 24 children who served as a control group. RESULTS: Students in the treatment group scored significantly higher than the control group over time on measures of asthma knowledge, asthma self-efficacy, general self-care practices, and asthma self-care practices. No significant differences were found between the two groups on health outcomes. DISCUSSION: A school-based intervention program can improve psychosocial outcomes for inner-city minority children with asthma. Recommendations for future research and clinical practice are discussed.

Venanzi S. et al. *Linkage to atopy on chromosome 19 in north-eastern Italian families with allergic asthma.* Clin Exp Allergy. 2001; 31(8) : 1220-4.p **Abstract:** BACKGROUND: Allergic asthma is a multifactorial disease for which there is a widely assessed, although poorly understood, genetic involvement. Genome-wide screens reported evidence for linkage of allergic asthma-related phenotypes to several chromosomal locations. Markers on chromosome 19 have been linked to allergic asthma phenotypes in different populations in independent studies. OBJECTIVE: The aim of this study was to perform a genetic linkage analysis on chromosome 19 to search for DNA markers linked to phenotypes related to allergic asthma. METHODS: Using non-parametric multipoint linkage analysis on a total of 22 random DNA markers in 2 stages, a sample of 111 families (542 subjects) from north-eastern Italy, recruited through an asthmatic allergic proband, was investigated. Phenotypes examined were: clinical asthma, total serum elevated IgE, skin prick test positivity, bronchial hyper-responsiveness, and atopy defined as skin prick test positivity and/or elevated IgE. Simulation studies were performed to confirm the significance of the results. RESULTS: A novel linkage of atopy and skin prick test positivity to marker D19S601 (19q13.3) was found. Modest evidence for linkage of atopy, skin prick test positivity, and IgE was also found to marker D19S591 (19p13.3). Simulation analysis for atopy gave an NPL-Z > 3.326 in 2 replicates out of 1000 (P = 0.002) for D19S601, and an NPL-Z > 2.56 in 16 replicates out of 1000 (P = 0.016) for D19S591. CONCLUSIONS: On chromosome 19, suggestive linkage of atopy and skin prick test positivity with marker D19S601 (19q13.3) and modest evidence of linkage of marker D19S591 (19p13.3) to the atopic phenotypes investigated were found. These results suggest that these regions may contain susceptibility loci associated to atopic phenotypes.

Ventegodt S. et al. *Clinical holistic medicine: developing from asthma, allergy, and eczema.* ScientificWorldJournal. 2004; 4 : 936-42.p **Abstract:** This paper shows how consciousness-based holistic medicine can be used in the case of asthma, allergy, and eczema. We have many fine drugs to relieve patients from the worst of these symptoms, where many children and adults suffer health problems related to hyper-reactivity of the immune system. Many symptoms remain throughout life because the drugs do not cure the allergy and allergy today is the sixth leading cause of chronic illness. The etiology of the immune disturbances is mostly unknown from a biomedical perspective. Consciousness-based holistic medicine could

therefore be used to treat these diseases if the patient is willing to confront hidden existential pain, is motivated to work hard, and is dedicated to improve quality of life, quality of working life, and personal relationships. Improving quality of life is not always an easy job for the patient, but it can be done with coaching from the physician. An increased physical health is often observed after only a few sessions with a physician skilled in using holistic medical tools and able to coach the patient successfully through a few weeks of dedicated homework. Children with allergy and asthma can also be helped if their parents are able to do work on personal development, to improve the general quality of life in the family and their relationship with the child.

Verheijden M.W. et al. *Respiratory morbidity and lung function in two Aboriginal communities in Western Australia.* Respiriology. 2002; 7(3) : 247-53.p **Abstract:** OBJECTIVE: To examine differences in the rates of respiratory symptoms, asthma and levels of lung function in two remote Aboriginal communities. METHODOLOGY: Respiratory symptoms, smoking history, skin prick test responses to common allergens, serum IgE, lung function, airway responsiveness to methacholine and white blood cell counts were compared in two Aboriginal communities, one from the central desert (n = 84) and another from the tropical north (n = 209) of Western Australia. RESULTS: Compared with the tropical community, chest tightness and dyspnoea were more frequent and forced expiratory volume in 1 s and forced vital capacity were lower in the desert community, despite similar levels of wheeze, doctor-diagnosed asthma and skin prick test responses and lower levels of airway responsiveness and smoking. The total white cell and neutrophil counts were greater in the desert community. Serum IgE was very high and similar in both communities. CONCLUSIONS: Our findings show a low prevalence of asthma in children, a high prevalence of respiratory symptoms and low levels of lung function in remote Aboriginal communities. The greater prevalence of respiratory morbidity in the desert community was not explained by diagnosed asthma, airway hyperresponsiveness or cigarette smoking. The role of infection requires further investigation. The results suggest that the lower lung function observed in Aboriginal communities (compared with non-Aboriginal communities) results at least partly from environmental factors.

Verona E. et al. *Fluticasone propionate in asthma: a long term dose comparison study.* Arch Dis Child. 2003; 88(6) : 503-9.p **Abstract:** BACKGROUND: Few dose ranging studies have investigated optimal dosing with inhaled corticosteroids in children with asthma. AIMS: To compare the efficacy and tolerability of fluticasone propionate 100 or 200 microg twice daily in children with moderate to severe asthma for one year. METHODS: One year, randomised, double blind, parallel group, multicentre study. Children aged 4-11 years (n = 528) with moderate to severe asthma who had previously received high dose inhaled corticosteroids were given fluticasone propionate 100 or 200 microg twice daily for the 52 week treatment period. Efficacy (exacerbations, lung function, and symptoms) and tolerability (adverse events and cortisol levels) were measured. RESULTS: There was a non-significant decreased risk of experiencing an exacerbation at any time with fluticasone propionate 200 microg twice daily compared with fluticasone propionate 100 microg twice daily. This difference reached significance among patients with more severe asthma (defined by previous inhaled corticosteroid dose >800 microg/day). Daily record card morning peak expiratory flow (PEF) in the total population improved significantly more with the higher dose of fluticasone propionate (between group difference, weeks 1-52: 11.4 l/min). Clinic visit mean PEF improved from baseline with both doses, but the response was significantly greater with the higher dose (between group difference, week 52: 17.8 l/min). Both doses were equally well tolerated and overnight urinary cortisol concentrations were unchanged or slightly increased during treatment with either dose. CONCLUSION: This long term dose comparison study shows that treatment with fluticasone propionate 200 micro g twice daily may

offer benefits over a lower dose, particularly in children with more severe asthma.

Vichyanond P. et al. *Exercise-induced asthma among Thai asthmatic children.* J Med Assoc Thai. 2002; 85 Suppl 2 : S579-85.p
Abstract: BACKGROUND: Approximately seventy per cent of asthmatic children from temperate climates, with normal lung function, have exercise-induced asthma (EIA). There is certain evidence to suggest that EIA may be less frequently encountered among children who live in tropical climates. Prevalence of EIA in Asian asthmatic children has never been thoroughly studied. OBJECTIVE: To study the prevalence of EIA among Thai asthmatic children. METHOD: A prospective study was performed to determine the prevalence of EIA in 44 Thai asthmatic children who were able to perform the spirometric maneuver. Subjects were randomly selected asthmatic children from the Pediatric Allergy Clinic, Department of Pediatrics, Siriraj Hospital. They were subjected to exercise testing on a steady state, motor-driven treadmill for 6 minutes (mean speed +/- SD = 3.7 +/- 0.4 km/h, mean level of inclination + SD = 15.0 +/- 5.2 degrees). The testing was conducted in a temperature-controlled (mean temperature +/- SD = 24.4 +/- 0.8 degrees C) and humidity-controlled environment (mean relative humidity +/- SD = 41.7 +/- 2.1%). Lung function tests were performed before exercise, immediately after and at 3, 5, 10, 15, 20 and 30 minutes after exercise. Results of the lung function test were calculated as per cent falls of forced expiratory volume in 1 sec (FEV1), peak expiratory flow rate (PEFR), and forced expiratory flow at 25 per cent-75 per cent (FEF50) from baselines. EIAs were diagnosed when drops of FEV1, PEFR and FEF50 were greater than 20 per cent, 25 per cent and 25 per cent from baseline values, respectively. RESULTS: Of the 44 patients studied (31 boys and 13 girls; mean age 11.9 years), 34 per cent had mild asthma. Fifty-nine per cent had moderate asthma and 7 per cent had severe asthma. Eleven patients (25%) had EIA diagnosed by significant falls of FEV1's (26 +/- 12.6%), whereas, 13 patients (30%) and 20 patients (45%) had EIA defined by significant drops of PEFR's and FEF50's, respectively. A total of 23 patients (52%) had EIA by one or more diagnostic criteria. Peak times for EIA as diagnosed by FEV1, PEFR and FEF50 occurred at 3, 10, and 10 minutes respectively, after exercise. Most EIA episodes observed were of mild degree. CONCLUSIONS: The prevalence of EIA in Thai children is much lower than figures reported in studies from Western countries. By using a significant fall of FEV1's as the diagnostic criteria, only 25 per cent were diagnosed as having EIA. By PEFR and FEF50 criteria, percentages of EIA increased to 30 per cent and 45 per cent respectively. Screening for EIA, therefore, may not be an appropriate diagnostic tool for the diagnosis of childhood asthma in tropical climates.

Villeneuve P.J. et al. *Frequency of emergency room visits for childhood asthma in Ottawa, Canada: the role of weather.* Int J Biometeorol. 2005; 50(1) : 48-56.p
Abstract: The aim of this study was to evaluate associations between meteorological conditions and the number of emergency department visits for asthma in a children's hospital in Ottawa, Canada. A case-crossover study design was used. Hospital emergency department visits for asthma between 1992 and 2000 were identified based on patients' presenting complaints. We obtained hourly measures for the following meteorological variables: wind speed, temperature, atmospheric pressure, relative humidity, and visibility. Particular emphasis was placed on exploring the association between asthma visits and fog, thunderstorms, snow, and liquid and freezing forms of precipitation. In total, there were 18,970 asthma visits among children between 2 and 15 years of age. The number of visits and weather characteristics were grouped into 6 h case and control intervals. The occurrence of fog or liquid precipitation was associated with an increased number of asthma visits, while snow was associated with a reduced number (P<0.05). Stratified analyses by season found no association in any of the four calendar intervals between the number of asthma visits and visibility,

change in relative humidity and change in temperature. In contrast, summertime thunderstorm activity was associated with an odds ratio of 1.35 (95% CI=1.02-1.77) relative to summer periods with no activity. Models that incorporate calendar and meteorological data may help emergency departments to more efficiently allocate resources needed to treat children presenting with respiratory distress.

Vilozni D. et al. *The role of computer games in measuring spirometry in healthy and "asthmatic" preschool children.* Chest. 2005; 128(3) : 1146-55.p
Abstract : STUDY OBJECTIVES: To explore the role of respiratory interactive computer games in teaching spirometry to preschool children, and to examine whether the spirometry data achieved are compatible with acceptable criteria for adults and with published data for healthy preschool children, and whether spirometry at this age can assess airway obstruction. DESIGN: Feasibility study. SETTINGS: Community kindergartens around Israel and a tertiary pediatric pulmonary clinic. PARTICIPANTS: Healthy and asthmatic preschool children (age range, 2.0 to 6.5 years). INTERVENTION: Multi-target interactive spirometry games including three targets: full inspiration before expiration, instant forced expiration, and long expiration to residual volume. MEASUREMENTS AND RESULTS: One hundred nine healthy and 157 asthmatic children succeeded in performing adequate spirometry using a multi-target interactive spirometry game. American Thoracic Society (ATS)/European Respiratory Society spirometry criteria for adults for the start of the test, and repeatability were met. Expiration time increased with age (1.3 +/- 0.3 s at 3 years to 1.9 +/- 0.3 s at 6 years [+/- SD], p < 0.05). FVC and flow rates increased with age, while FEV1/FVC decreased. Healthy children had FVC and FEV1 values similar to those of previous preschool studies, but flows were significantly higher (> 1.5 SD for forced expiratory flow at 50% of vital capacity [FEF50] and forced expiratory flow at 75% of vital capacity [FEF75], p < 0.005). The descending part of the flow/volume curve was convex in 2.5- to 3.5-year-old patients, resembling that of infants, while in 5- to 6-year-old patients, there was linear decay. Asthma severity by Global Initiative for Asthma guidelines correlated with longer expiration time (1.7 +/- 0.4 s; p < 0.03) and lower FEF50 (32 to 63%; p < 0.001) compared to healthy children. Bronchodilators improved FEV1 by 10 to 13% and FEF50 by 38 to 56% of baseline. CONCLUSIONS: Interactive respiratory games can facilitate spirometry in very young children, yielding results that conform to most of the ATS criteria established for adults and published data for healthy preschool children. Spirometric indexes correlated with degree of asthma severity.

Violano P. et al. *Targeting educational initiatives.* Nurs Econ. 2005; 23(5) : 248-52, 211.p
Abstract: The nursing education department of a large teaching hospital faced the challenge of prioritizing the delivery of staff education programs after reductions in personnel and resources. Patient population data were used to guide curricula development. Results included improved clinical practice in a cost-effective manner.

Violante R. et al. *Obesity risk factors in the ISAAC (International Study of Asthma and Allergies in Childhood) in Mexico City.* Rev Alerg Mex. 2005; 52(4) : 141-5.p
Abstract: BACKGROUND: The International Study of Asthma and Allergies in Childhood (ISAAC) has promoted surveys in asthma and allergic diseases using standardized methodologies including validated questionnaires. Many items in the questionnaires have also been implied in the overweight and obesity etiology. OBJECTIVE: To describe the factors associated with obesity in subjects of 6-7 years and 13-14 years in the ISAAC survey in Mexico City. MATERIAL AND METHODS: Data were obtained from questionnaires of children participating in a phase 3b ISAAC survey. Logistic regression was used to determine the obesity risks factors. RESULTS: The factors related to obesity were weekly consumption of meat (+, positive

relationship), vegetables, pasta, rice (+) and quartiles of birth weight (+) in boys of 6-7 years. Having suffered eczema at any time, weekly consumption of fruit, pasta, butter, nuts, potato (+), fast food (+), daily TV viewing (+) in girls of 6-7 years. Having suffered eczema at any time, weekly consumption of pasta (+), butter, potato, weekly physical exercise in boys of 13-14 years; weekly consumption of pasta, margarine, milk, fast food (+), currently smoking in girls of 13-14 years. CONCLUSIONS: There were not common factor patterns for the different groups, birth weight, fast food, TV viewing and lack of exercise have been previously related to pediatric obesity. Asthma was not associated with a higher risk of obesity but medical history of eczema was associated with lower risk of obesity in the 6-7 years girls, and 13-14 years boys. The present study provides the bases for future epidemiological studies and gives some clues on possible public health actions.

Virkki R. et al. *Radiographic follow-up of pneumonia in children.* *Pediatr Pulmonol.* 2005; 40(3) : 223-7.p **Abstract:** This study assessed the clinical value of routine follow-up chest radiographs in hospitalized children with community-acquired pneumonia. The study population consisted of 196 children hospitalized for community-acquired pneumonia diagnosed between 1993-1995. Seventeen infective agents (10 viruses and 7 bacteria) were sought. Chest radiographs were taken on admission and 3-7 weeks later. All children were treated with antibiotics. Data on the course of illness over the following 8-10 years were obtained from patient files and questionnaires sent to parents. A potential causative agent was found in 165 (84%) of 196 cases. On follow-up chest radiographs, residual or new changes were seen in 30% of cases. The residual changes tended to be more common after mixed viral-bacterial infection (43%) than after sole viral (25%) or sole bacterial (20%) infection. Interstitial infiltrates (66%), atelectasis (46%), and enlarged lymph nodes were the most common sequelae seen on follow-up. Residual findings on follow-up radiographs did not affect the treatment of the children. No further chest radiographs were taken. During the 8-10-year follow-up of 194 children, no illnesses appeared that were associated with previous pneumonia. Twenty-six children had a new episode of pneumonia, 7 of them had asthma, and 6 had different underlying illnesses. In conclusion, routine follow-up chest radiographs are not needed in childhood community-acquired pneumonia if the child has a clinically uneventful recovery.

Visitsunthorn N. et al. *Linear growth of prepubertal asthmatic Thai children receiving long-term inhaled corticosteroids.* *J Med Assoc Thai.* 2002; 85 Suppl 2 : S599-606.p **Abstract:** BACKGROUND: Long-term inhaled corticosteroids are recommended in persistent asthma in children. The aim of this study was to determine the growth rate of asthmatic Thai children who received long-term inhaled corticosteroids. METHOD: This controlled clinical trial was carried out on 145 prepubertal asthmatic Thai children, 81 in the study group (the group who received long-term inhaled corticosteroids) and 64 in the control group. RESULTS: The mean age of the patients when the study began was 5.9 years in the study group and 4.7 years in the control group. The average dose of inhaled corticosteroids used was 300 microg/day. The average duration overtime of inhaled corticosteroid usage was 2 years (9 months-5 years). The study showed that inhaled corticosteroids (300 microg/day for 9-60 months) have no significant effects on growth rate. From linear regression analysis, the factors that influenced the growth rate of asthmatic patients were the severity of the asthma and the age of the patients when nasal corticosteroids were started. Insulin-like Growth Factor 1 (IGF 1) and Insulin-like Growth Factor Binding Protein 3 (IGFBP 3), were measured in 7 patients in the study group and 5 in the control group. All were normal, the height standard deviation score (Ht.SDS) was below average. CONCLUSIONS: The average dose of inhaled corticosteroids (300 microg/day for 9 months) has no significant effects on the growth rate of prepubertal asthmatic Thai children.

Visser M.J. et al. *One-year treatment with different dosing schedules of fluticasone propionate in childhood asthma. Effects on hyperresponsiveness, lung function, and height.* *Am J Respir Crit Care Med.* 2001; 164(11) : 2073-7.p **Abstract :** Dose-dependent effects of inhaled corticosteroids have been described. Although it has been advised to start treatment with inhaled corticosteroids with a high dose tapering off subsequently (stepdown approach), no clinical studies have assessed this strategy. We compared two different dosage schedules of inhaled fluticasone propionate (FP) in chronic persistent childhood asthma with respect to efficacy (airways hyperresponsiveness [PD(20)], lung function, exhaled nitric oxide [eNO]) and safety (height). During this double-blind study, children with asthma (aged 6-10 yr) were randomized to receive either FP 200 microg/d (constant dose approach) or to start with 1000 microg/d with two monthly reductions to 500, 200, and 100 microg/d (stepdown approach). PD(20) improved in both approaches during treatment with FP, with a significantly better PD(20) after 2 mo of 1000 microg/d followed by 500 microg/d in the stepdown approach versus 200 microg/d in the constant dose approach. No significant differences in PD(20) or other efficacy parameters were found after 1 yr. Changes in standing height were similar in both treatment approaches. This study showed no superior clinical effect of a stepdown approach compared with a constant dose strategy of FP for 1 yr in children with chronic persistent asthma.

Vogelberg C. et al. *Clinical evaluation of the peak inspiratory flow generated by asthmatic children through the Novolizer.* *Respir Med.* 2004; 98(10) : 924-31.p **Abstract:** STUDY OBJECTIVE: To assess whether asthmatic children may generate sufficient peak inspiratory flow through the Novolizer, a novel multiple dose dry powder inhaler with acoustic and optical feedback mechanisms for correct inhalation. PATIENTS AND METHODS: 137 children (median age 7 years, range 4-2) with mild to moderate persistent asthma (FEV1 < 90% predicted or pre-treated with low-dose steroids) participated in this open, multi-centre study. After assessment of FEV1 and peak inspiratory flow (without inhalator device, PIF), the children were instructed to inhale with the Novolizer (PIF through inhaler, PIF-N). All assessments were done in triplicate and the mean out of three attempts analysed. RESULTS: Mean PIF was 128 +/- 61 l/min and mean PIF-N was 69 +/- 18 l/min. This is distinctly above the rate necessary to overcome the Novolizer's trigger threshold. PIF performance through the Novolizer was linear in the age interval of 4-8 years, no further increase was observed beyond 8 years. CONCLUSIONS: The medium to low intrinsic resistance of the Novolizer permits a relatively high PIF through this device. Together with the feedback mechanisms, this makes the Novolizer particularly valuable for inhalation therapy in asthmatic children with drugs such as salbutamol, formoterol, or budesonide.

Vogelmeier C. et al. *Budesonide/formoterol maintenance and reliever therapy: an effective asthma treatment option?* *Eur Respir J.* 2005; 26(5) : 819-28.p **Abstract:** This 12-month dose-titration study assessed the effectiveness of budesonide/formoterol for maintenance plus relief with a control group using salmeterol/fluticasone for maintenance plus salbutamol for relief. Adolescents and adults (n = 2,143; mean forced expiratory volume in one second (FEV1) 73% predicted; mean inhaled corticosteroid (ICS) 884 microg.day(-1)) were randomised to budesonide/formoterol 160/4.5 microg two inhalations b.i.d. plus additional inhalations as needed, or salmeterol/fluticasone 50/250 microg b.i.d. plus salbutamol as needed. Treatment was prescribed open label; after 4 weeks, physicians could titrate maintenance doses in accordance with normal clinical practice. Maintenance plus as-needed budesonide/formoterol prolonged the time to first severe exacerbation versus salmeterol/fluticasone (25% risk reduction). The total number of severe exacerbations was significantly reduced in the budesonide/formoterol group (255 versus 329). Both regimens provided sustained improvements in symptoms, as-needed use,

quality of life and FEV1, with differences in favour of the budesonide/formoterol group for as-needed use (0.58 versus 0.93 inhalations.day(-1)) and FEV1 (post-beta2-agonist values). Mean ICS dose during treatment was similar in both groups (653 microg budesonide.day(-1) (maintenance plus as-needed) versus 583 microg fluticasone.day(-1)). The simplified strategy using budesonide/formoterol for maintenance and reliever therapy is feasible, safe and at least as effective as salmeterol/fluticasone plus salbutamol.

Vollmert C. et al. *Single nucleotide polymorphism screening and association analysis--exclusion of integrin beta 7 and vitamin D receptor (chromosome 12q) as candidate genes for asthma.* Clin Exp Allergy. 2004; 34(12) : 1841-50.p **Abstract** : **BACKGROUND**: The human genes coding for integrin beta 7 (ITGB7) and vitamin D receptor (VDR) are two of the several candidate genes for asthma and related phenotypes found in a promising candidate region on chromosome 12q that has been identified in multiple genomewide screens and candidate gene approaches. **METHODS**: All exons, including parts of the neighbouring introns, and the predicted promoter region of the ITGB7 gene were screened for common polymorphisms in 32 independent asthmatic and healthy probands, resulting in the detection of two single nucleotide polymorphisms (SNPs) unknown so far. In addition to these SNPs, five already described SNPs of the ITGB7 and one in the human VDR gene were analysed in a Caucasian sib pair study of 176 families with at least two affected children, using matrix assisted laser desorption/ionization time of flight mass spectrometry. All confirmed SNPs were tested for linkage/association with asthma and related traits (total serum IgE level, eosinophil cell count and slope of the dose-response curve after bronchial challenge). **RESULTS**: Two new variations in the ITGB7 gene were identified. The coding SNP in exon 4 causes a substitution of the amino acid GLU by VAL, whereas the other variation is non-coding (intron 3). None of the eight analysed SNPs, of either the ITGB7 or the VDR genes, showed significant linkage/association with asthma or related phenotypes in the family study. **CONCLUSIONS**: These findings indicate that neither the human ITGB7 nor the VDR gene seem to be associated with the pathogenesis of asthma or the expression of related allergic phenotypes such as eosinophilia and changes in total IgE level.

Volovitz B. et al. *Increasing asthma awareness among physicians: impact on patient management and satisfaction.* J Asthma. 2003; 40(8) : 901-8.p **Abstract**: Our objective was to investigate the impact of increased asthma awareness among primary care physicians on the asthma control and satisfaction of their patients. Physicians attended an asthma education session with emphasis on patient-physician partnership followed by 4 month monitored follow-up of patients aged 5-44 years with mild to moderate asthma. Findings were compared with a group of patients whose physician attended the session but did not participate in the follow-up and two other control groups. The study included pediatricians and general practitioners of Maccabi Healthcare Services and their patients. Asthma symptoms were rated by patients and physicians. Data on drug prescription and use were derived from the Maccabi central database. Patient response and satisfaction and physician satisfaction were evaluated by telephone interviews. Mean asthma symptom score improved from 2.0 to 1.1 in the study group of patients ($p < 0.001$). The use of reliever drugs decreased concomitantly with a rise in controller drugs in all patients. An improvement in asthma status was reported by 64% of the study patients and 39% of non-participating patients ($p = 0.007$). Fifty-eight percent of the patients rated their competence to deal with asthma as high before the intervention compared to 62% of the participating and 55% of the non-participating patients after the intervention ($p = 0.002$). Most physicians claimed that simply increasing their awareness on asthma led to beneficial results in their patients. Physician education followed by monitored follow-up enhanced asthma control and patient satisfaction. Nevertheless,

physician education alone appears to have a significant isolated impact on asthma control.

Volovitz B. et al. *Effect of high starting dose of budesonide inhalation suspension on serum cortisol concentration in young children with recurrent wheezing episodes.* J Asthma. 2003; 40(6) : 625-9.p **Abstract**: **INTRODUCTION**: There are no available data on the safety of recommended schedules for the initiation of treatment with budesonide inhalation suspension in children with recurrent wheezing episodes. We compared the safety of high and low starting dose of budesonide by measuring their effect on plasma cortisol concentration. **METHODS**: A randomized double-blind, placebo-controlled design was used. Twenty-nine children ages 6 months to 3 years were divided into three groups: (1) high starting dose: 1 mg budesonide inhalation suspension twice daily followed by a stepwise decrease of 25% every second day for 8 days ($n = 11$); (2) low starting dose: 0.25 mg twice daily for 8 days ($n = 11$); (3) placebo ($n = 7$). The 8 AM (fasting) and 1-hour post-ACTH stimulation plasma cortisol concentrations were measured before and 10 days after initiation of budesonide treatment. **RESULTS**: Before treatment and after 8-10 days of treatment, there was no significant difference in mean serum cortisol concentration in the high starting dose, low-dose and placebo groups, either at 8 AM or at 1 hour after ACTH stimulation. **CONCLUSION**: The administration of nebulized suspension of budesonide at a high starting dose (2 mg/day for 2 days) followed by a rapid stepwise decrease over 8 days was safe, causing similar changes in serum cortisol levels to low-dose budesonide suspension or placebo.

von Berg A. et al. *Fluticasone for the treatment of symptomatic bronchial asthma in children treated with sodium cromoglycate--a prospective, randomised trial.* Eur J Med Res. 2002; 7(6) : 257-64.p **Abstract**: **BACKGROUND**: Children with persistent mild to moderate bronchial asthma require anti-inflammatory therapy. According to current treatment guidelines both sodium cromoglycate (SCG) and inhaled corticosteroids can be used. If children remain symptomatic despite regular SCG therapy, corticosteroids are the next therapeutic option. **AIMS**: To determine whether combined SCG and fluticasone (inhaled corticosteroid) therapy is of additional benefit in children who are symptomatic on SCG compared with simply switching to fluticasone. **PATIENTS AND METHODS**: Children with mild or moderate persistent asthma aged 6 to 16 years who had been treated with inhaled SCG for at least 3 months prior to the study received either 2 mg SCG four times daily from a metered dose inhaler plus fluticasone propionate powder 50 microg b.i.d. from the Diskus inhaler (group FS) or fluticasone 50 microg b.i.d. only (group F). The randomised, controlled, parallel-group study had a 2 week run-in phase and an 8 week treatment period. Morning and evening peak expiratory flow rates (PEFR) were measured daily by patients and recorded in diaries. Asthma symptoms, use of rescue medication and spirometry were also documented. **RESULTS**: Paediatricians from 21 study centres recruited 124 children with asthma, of whom 104 fulfilled randomisation criteria and were allocated to study medication. Morning PEFR increased by 47 l/min and by 45 l/min after 8 weeks of treatment in groups F and FS, respectively. The adjusted difference between groups was 0.84% of predicted (95% CI, -7.3 to 5.6, $p=0.80$). Asthma symptoms and lung function also improved with no significant differences between treatment groups ($p>0.24$). Frequency and severity of adverse events was similar in both groups. **CONCLUSION**: In children who are symptomatic while taking sodium cromoglycate four times daily, the combination of inhaled fluticasone and SCG is not superior to fluticasone alone. SCG can safely be withdrawn when commencing fluticasone, thus facilitating asthma treatment.

von Berg A. et al. *Efficacy and safety of ipratropium bromide plus fenoterol inhaled via Respimat Soft Mist Inhaler vs. a conventional metered dose inhaler plus spacer in children with asthma.* Pediatr

Pulmonol. 2004; 37(3) : 264-72.p **Abstract:** The objective of this study was to compare the efficacy and safety of ipratropium bromide/fenoterol hydrobromide (IB/FEN; Berodual) delivered from the novel propellant-free Respimat Soft Mist Inhaler (SMI) with that from a chlorofluorocarbon (CFC) metered-dose inhaler (MDI) plus spacer in children with asthma. The study followed a multicenter, randomized, double-blind (within Respimat SMI), parallel-group design. During the 2-week run-in period, patients received two actuations of CFC-MDI tid (IB 20 microg/FEN 50 microg per actuation) via a spacer (Aerochamber) (MDI 40/100). Patients (n=535) were then randomized to: Respimat SMI containing IB 10 microg/FEN 25 microg (Respimat SMI 10/25), IB 20 microg/FEN 50 microg (Respimat SMI 20/50), one actuation tid or CFC-MDI containing IB 20 microg/FEN 50 microg per actuation (in total IB 40 microg/FEN 100 microg), or two actuations tid via Aerochamber (MDI 40/100), for 4 weeks. The primary endpoint was the change in forced expiratory volume in 1 second (FEV1) during the first 60 min after dosing (area under the curve from 0-1 h [AUC(0-1 h)]) on day 29. Analysis of the primary endpoint demonstrated that the efficacy of Respimat SMI 10/25 and 20/50 was equivalent to or greater than that of MDI 40/100. Similar results indicating that Respimat SMI 10/25 and 20/50 were not inferior to MDI 40/100 were also found on days 1 and 15. Analyses of other secondary endpoints supported these results. The safety profile of Respimat SMI was comparable to that of the CFC-MDI plus spacer. In conclusion, IB/FEN delivered via Respimat SMI is at least as effective as, and is as safe as, when delivered via CFC-MDI plus Aerochamber in children with asthma. Use of Respimat SMI thus enables a 2-4-fold reduction in the nominal dose of IB/FEN, and obviates the need for a spacer.

Von Berg A. et al. *Efficacy and tolerability of formoterol Turbuhaler in children.* Int J Clin Pract. 2003; 57(10) : 852-6.p **Abstract:** A randomised, double-blind trial was undertaken to investigate the efficacy and tolerability of formoterol Turbuhaler in children with mild to moderate asthma. After a two-week run-in, 248 children aged 6-17 years were randomised to receive formoterol 4.5 and 9 pmicro b.i.d. or placebo for 12 weeks. Morning PEF (primary variable), was significantly improved versus placebo only in the formoterol 9 pmicro b.i.d. group (13 l/min, 95% CCI 1.9, 24.2%; p = 0 .02). Both formoterol 4.5 and 9 pmicro significantly increased the pre-bronchodilator FEV1 by 5.2-6.7% (p < 0 .05) and reduced use of daytime relief medication versus placebo (p < 0 .05). Formoterol 9 pmicro significantly reduced night-time reliever use and awakenings due to asthma versus placebo (p < 0.05). Both doses of formoterol were as well tolerated as placebo. In conclusion, formoterol 4.5 and 9 micro b.i.d. is effective and well tolerated as maintenance therapy in children with mild to moderate asthma.

von Maffei J. et al. *Risk factors for asthma prevalence among urban and nonurban African American children.* J Asthma. 2001; 38(7) : 555-64.p **Abstract:** Urban residence is a risk factor for asthma. We examined multiple risk factors simultaneously among African American children. We interviewed 2409 African American mothers of newborns who had at least 1 child at home under 18 years of age. Sixteen percent reported at least 1 child with physician-diagnosed asthma. Significantly associated with an asthmatic child were maternal asthma and allergies, maternal cigarette smoking, a humidifying device, and a gas range or oven in the home. Urban residence was related to asthma but became nonsignificant once other factors were controlled for. Asthma associated with urban residence may be explained by identifiable factors.

von Mutius E. *Childhood experiences take away your breath as a young adult.* Am J Respir Crit Care Med. 2002; 165(11) : 1467-8.p

Vonk J.M. et al. *Perinatal risk factors for bronchial hyperresponsiveness and atopy after a follow-up of 20 years.* J Allergy Clin Immunol.

2004; 114(2) : 270-6.p **Abstract:** BACKGROUND: Perinatal risk factors are associated with lung function and respiratory symptoms in adult life. Whether the same holds for distinctive asthma features, such as bronchial hyperresponsiveness (BHR) and atopy, has scarcely been studied. OBJECTIVE: We sought to identify the perinatal risk factors for the development of BHR and atopy. METHODS: BHR and atopy were measured after 20 years' follow-up in 597 of 3162 babies born from 1975 through 1978. Factors directly related to delivery of these children were studied in association with the presence of BHR and atopy. RESULTS: Twenty-five percent had BHR, and 47% had atopy. Delivery duration of longer than 12 hours was associated with the development of atopy (odds ratio [OR], 2.24; 95% CI, 1.30-3.86), and severe respiratory infection in the first year of life was associated with the development of BHR (OR, 2.69; 95% CI, 1.41-5.16). Nonatopic subjects born after induced labor and current smokers were more likely to have BHR (ORs of 2.41 [95% CI, 1.07-5.41] and 2.50 [95% CI, 1.12-5.59], respectively). Prenatal smoke exposure and childhood pet keeping decreased the risk for atopy, especially in BHR-positive subjects (ORs of 0.51 [95% CI, 0.27-0.99] and 0.46 [95% CI, 0.24-0.88], respectively). CONCLUSIONS: It has been shown that events before or during birth still have an effect on respiratory health 20 years later. We put forward that an extreme hormonal status during delivery primes the fetal immune system toward atopy development. Furthermore, a severe respiratory infection in the first year of life appears associated with BHR development, and prenatal smoke exposure might be protective for the development of atopy, yet explanatory mechanisms are lacking thus far.

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Wagner C.W. *The ongoing evaluation of the impact of depression on asthma.* Ann Allergy Asthma Immunol. 2002; 89(6) : 540-1.p

Wagner V.L. et al. *Asthma in Medicaid managed care enrollees residing in New York City: results from a post-World Trade Center disaster survey.* J Urban Health. 2005; 82(1) : 76-89.p **Abstract:** The collapse of the World Trade Center on September 11, 2001, released a substantial amount of respiratory irritants into the air. To assess the asthma status of Medicaid managed care enrollees who may have been exposed, the New York State Department of Health, Office of Managed Care, conducted a mail survey among enrollees residing in New York City. All enrollees, aged 5-56 with persistent asthma before September 11, 2001, were surveyed during summer 2002. Administrative health service utilization data from the Medicaid Encounter Data System were used to validate and supplement survey responses. A total of 3,664 enrollees responded. Multivariate logistic regression models were developed to examine factors associated with self-reported worsened asthma post September 11, 2001, and with emergency department/inpatient hospitalizations related to asthma from September 11, 2001, through December 31, 2001. Forty-five percent of survey respondents reported worsened asthma post 9/11. Respondents who reported worsened asthma were significantly more likely to have utilized health services for asthma than those who reported stable or improved asthma. Residence in both lower Manhattan (adjusted OR = 2.28) and Western Brooklyn (adjusted OR = 2.40) were associated with self-reported worsened asthma. However, only residents of Western Brooklyn had an elevated odds ratio for emergency department/inpatient hospitalizations with diagnoses of asthma post 9/11 (adjusted OR = 1.52). Worsened asthma was reported by a significant proportion of this low-income, largely minority population and was associated with the location of residence. Results from this study provide guidance to health care organizations in the development of plans to ensure the health of people with asthma during disaster situations.

- Wakefield M. et al.** *Effect of feedback regarding urinary cotinine and brief tailored advice on home smoking restrictions among low-income parents of children with asthma: a controlled trial.* *Prev Med.* 2002; 34(1) : 58-65.p **Abstract:** BACKGROUND: Since most smoker parents of children with asthma are unable to quit, an alternative measure that would reduce their children's exposure to environmental tobacco smoke (ETS) is to ban smoking in the home. METHODS: Compared with 136 usual-care controls, 128 intervention-group parents recruited from South Australian pediatric hospital outpatient waiting rooms were given written and verbal feedback about their 1- to 11-year-old child's urinary cotinine-to-creatinine level, information booklets, and two telephone calls encouraging a ban on smoking at home. RESULTS: At 6 months, 49.2% of the intervention group reported having banned smoking in the home compared with 41.9% of controls, but the differential rate of change from baseline was not significant (P = 0.40). At follow-up, there were no significant differences between groups in the percentage reporting bans on smoking in the car, the mean reduction from baseline in total daily consumption or consumption in front of the child, children's urinary cotinine level, or parental smoking cessation. CONCLUSIONS: The intervention did not change parents' propensity to create or maintain bans on smoking in their homes or otherwise change smoking habits to reduce their children's exposure to ETS. More intensive interventions may be required to achieve change among low-income smoker parents of children with asthma.
- Walders N. et al.** *Asthma knowledge, awareness, and training among head start and early head start staff.* *J Sch Health.* 2004; 74(1) : 32-4.p
- Waldman H.B. et al.** *Health of children at the turn of the century.* *J Dent Child (Chic).* 2003; 70(3) : 189-93.p **Abstract:** A summary is presented of the highlights from the 1999 National Health Interview Survey of Children with comparisons to previous reports, including a consideration of general health status, prevalence of asthma, attention deficit disorder and other learning disabilities, contact with health professionals, need for and use of dental services, use of prescription medications, and health care risk factors.
- Waldron D.L. et al.** *Paediatric asthma education programmes: impact and future directions.* *Ir Med J.* 2004; 97(6) : 183-5.p
- Walters C.S. et al.** *Bystander T cells participate in specific response to cockroach antigen (CR) in vitro.* *Immunol Invest.* 2003; 32(1-2) : 105-18.p **Abstract:** Allergic reactions due to whole body, body parts and fecal products of cockroach (CR) are characterized by inflammatory reaction that may lead to symptoms of rhinitis or asthma in atopic individuals. Although the majority of T cells at the site of CR hypersensitivity are not antigen specific, the cellular subset and cytokine receptors that participate and control the outcome of the reaction have not been fully studied. In this study, we have used fluorescent activated cell sorter (FACS) analysis to characterize the activation marker and cytokine profile of antigen specific and bystander T cells after in vitro stimulation of peripheral blood lymphocytes with whole body extract of CR antigen. There was significant enhancement of CD69 on blast and bystander T cells in all atopic subjects compared to non-atopics. Both antigen specific and bystander T cells showed increased expression of HLA-DR, CD25 and CD71 in 9 of 11 atopic patients compared to control. There was also an increase in CD45RA+ and a decrease in CD45RO+ cells following antigen stimulation. These results correlated with the increase in the early apoptotic cells observed in patients as measured by Annexin V stain. Our data revealed that there was no difference in the expression of CD95 in both stimulated and bystander T cells. However, there was enhancement of FasL by CR antigen, suggesting that the increased apoptosis that was observed was probably due to the Fas/FasL interaction. Positive intracellular IL2, IL-4 and IFN-gamma in T cells were observed in only the antigen specific blast cells in 83% of patients studied. These results suggest interplay of memory T cell response, apoptosis, and activated bystander T cells activities in maintaining cellular homeostasis during allergic reaction in cockroach sensitive atopic subjects.
- Wamboldt F.S. et al.** *Prevalence and correlates of household exposures to tobacco smoke and pets in children with asthma.* *J Pediatr.* 2002; 141(1) : 109-15.p **Abstract:** OBJECTIVES: To examine the prevalence rates of household smoking and ownership of a furred or feathered pet, the intercorrelation of these home environment measures, and their association with sociodemographic, family, and child asthma variables. STUDY DESIGN: Children with asthma (n = 152, aged 7-18 years) with asthma and their primary parent were evaluated through the use of reliable and valid questionnaires focusing on exposure to household smoke and furred or feathered pets as well as sociodemographic, family, and asthma variables. RESULTS: Prevalence of household smoking and pet ownership were high and comparable to normal levels in the US population. Smoking and pet ownership were not correlated with each other or with asthma medication adherence. Sociodemographic, family, and asthma variables showed distinct patterns of correlation with smoking and pet status. Household smoking was associated with poorer family resources and greater stress; pet ownership was associated with greater resources. CONCLUSIONS: Smoke exposure and pet ownership are not related to one another in children with asthma and will require independent counseling strategies because they relate in different and opposite ways to socioeconomic status.
- Wamboldt F.S. et al.** *Reliability and validity of a system for coding asthma outcomes from medical records.* *J Asthma.* 2002; 39(4) : 299-305.p **Abstract:** To evaluate the reliability and validity of a standardized asthma outcome coding system, we obtained medical records for 182 asthmatic children. Records were coded by trained staff using explicit and detailed criteria. Outcome variables coded included number of corticosteroid bursts, asthma-related physician contacts, emergency room visits, hospitalizations, and number of asthma episodes. Interrater reliability was excellent. Patterns of associations between the coded variables and other independently obtained outcome measures supported concurrent and construct validity. Given the intense scrutiny of health outcomes in the current managed-care marketplace, use of this system may foster further clinical research examining asthma outcomes.
- Wang H. et al.** *A nonsense mutation of PEPD in four Amish children with prolidase deficiency.* *Am J Med Genet A.* 2006; 140(6) : 580-5.p **Abstract:** Encoded by the peptidase D (PEPD) gene located at 19q12-q13.11, prolidase is a ubiquitous cytosolic enzyme that catalyzes hydrolysis of oligopeptides with a C-terminal proline or hydroxyproline. We describe here four Amish children with a severe phenotype of prolidase deficiency in the Geauga settlements of Ohio as the first report of prolidase deficiency in the Amish population as well as in the United States. The patients presented with infection, hepatosplenomegaly, or thrombocytopenia, in contrast to most cases previously reported in the literature, presenting with skin ulcers. All four patients had typical facial features, classic skin ulcers, and multisystem involvement. Recurrent infections, asthma-like chronic reactive airway disease, hyperimmunoglobulins, hepatosplenomegaly with mildly elevated aspartate transaminase (AST), anemia, and thrombocytopenia were common and massive imidodipeptiduria was universal. Prolidase activity in our patients is nearly undetectable. Direct sequencing of PCR-amplified genomic DNA for all of the exons from the four patients revealed the same homozygous single nucleotide mutation c.793 T > C in exon 11, resulting in a premature stop-codon at amino acid residue 265 (p.R265X). It is speculated that the severe phenotype in these patients might be associated with the type of the PEPD gene mutation.

- Wang J.Y. et al.** *Discovery of genetic difference between asthmatic children with high IgE level and normal IgE level by whole genome linkage disequilibrium mapping using 763 autosomal STR markers.* *J Hum Genet.* 2005; 50(5) : 249-58.p **Abstract:** The genome-wide linkage disequilibrium screen for loci associated with genetic difference between allergic and nonallergic asthma was conducted with 763 autosomal STR markers and included 190 asthmatic children. Evidence for association with differences between the two forms of asthma was observed for 36 STR markers. Marker-to-marker synergetic effect and by simulation resampling tests revealed D5S2011, D6S305, and D9S286 were important loci in allergic asthma while D6S1574, D8S1769, and D19S226 were important in nonallergic asthma. Our results show strong genetic evidence that these markers play an important role in defining allergic and nonallergic asthma and provides important candidates of susceptible genes in these two categories of asthma. This study further shows that asthma is, indeed, a heterogeneous group of underlying diseases and, although with similar clinical phenotypes, may have different clinical severities, outcomes, and need more tailor-made management.
- Wang J.Y. et al.** *Association study using combination analysis of SNP and STRP markers: CD14 promoter polymorphism and IgE level in Taiwanese asthma children.* *J Hum Genet.* 2005; 50(1) : 36-41.p **Abstract:** Chromosome 5, especially the 5q31-33 region, may contain one or more loci to control total serum IgE as well as asthma and bronchial hyperresponsiveness. To investigate the regions related with IgE level in chromosome 5, we performed a case-control association study on 105 high-IgE-level and 85 normal-IgE-level asthmatic children using 43 microsatellite markers that span the whole chromosome 5 with 5 cM intervals. One of microsatellite marker, D5S2011, had significantly different allele frequency between the two asthmatic groups. E allele (143 bp) of the D5S2011 marker was more frequent in high-IgE asthmatics. CD14 is the candidate gene of atopy and asthma and is distant from D5S2011 by about 1 Mb. We analyzed the SNP genotypes in the CD14 gene region alone and in combination with microsatellite marker D5S2011. The CD14/-2984 polymorphism but not the CD14/-159 is associated with IgE level in Taiwanese asthmatic children. The CD14/-159 allele was observed only to be associated with IgE level when -159T was part of a haplotype containing a D5S2011 E allele. The combination analysis using SNP and STRP markers provided a novel method for increasing detection power in candidate gene association studies.
- Wang T.N. et al.** *Familial risk of asthma among adolescents and their relatives in Taiwan.* *J Asthma.* 2001; 38(6) : 485-94.p **Abstract:** Although family studies have established that asthma has a hereditary basis, little evidence has been presented about the family risk of simple asthma (AS or nonatopic asthma) and asthma with other atopic diseases (AWAD or atopic asthma) after adjusting for potential risk factors. In this study, data were collected on demographic variables and a wide range of known risk factors for asthma. Study participants were asthmatic adolescents and controls, and their relatives. The role of a familial history of asthma and atopic diseases in predicting asthma risk among asthmatic adolescents and their relatives was evaluated in a population-based family study conducted in southern Taiwan. Asthma risk factor data were collected through telephone interviews with students' parents for 207 asthmatic adolescents 11-16 years of age, their 1600 relatives, and 207 nonasthmatic adolescents in the control group and their 1638 relatives. The results show (after adjusting potential confounders) that a family history of asthma is highly associated with asthma in adolescents. Having two or more family members with asthma was associated with a 3.4-fold (95% confidence interval [CI] = 1.0-12.0) increased risk of asthma among adolescents. Logistic regression was used to assess the effects of having an asthmatic relative and the effect of atopic diseases among relatives of cases. Having a family history of asthma and other atopic conditions, such as rhinitis and atopic dermatitis (adjusted odds ratio [AOR] = 3.64, 95% CI = 2.29-5.74 and AOR = 1.94, 95% CI = 1.53-2.46, respectively), was found to be a significant predictor of asthma in children. Along with a history of allergic rhinitis or atopic dermatitis, familial risks of asthma occurring in adolescents with and without other atopic diseases will be analyzed separately. A critical finding was the significant difference in a risk of asthma and atopic diseases among the relatives of asthma cases with atopic diseases and controls. However, for relatives of asthma cases without atopic diseases compared to control probands, AORs were highly significant for family history of asthma, but not for the family history of atopic diseases. These findings suggest that both forms of asthma may be hereditary, but there are differences in their modes of inheritance. Atopic status itself did not predispose a child to AS. A concomitant inheritance of a predisposition to asthma and atopic condition for AWAD cases was suggested.
- Ward D.J. et al.** *Effects of daily variation in outdoor particulates and ambient acid species in normal and asthmatic children.* *Thorax.* 2002; 57(6) : 489-502.p **Abstract:** BACKGROUND: Evidence suggests that the respiratory health of children may be adversely affected by daily variation in outdoor pollutants, particularly ozone and particulates. However, data from the UK are sparse and the contribution of different particulate fractions and acid species, together with the identification of those individuals most at risk, are not clear. METHODS: One hundred and sixty two 9 year old children were enrolled from two inner city locations and recorded daily symptoms and twice daily peak expiratory flow (PEF) over 8 week periods in the winter and summer. Their results were analysed with daily pollutant levels at appropriate lags using regression models which corrected for trends, weather, pollen, and autocorrelation. RESULTS: Pollutant levels were generally low, especially in the summer. Multiple statistically significant associations were noted between health outcomes and pollutant concentrations, but no consistent patterns in identified effects were apparent between pollutants, lags, direction of observed effect, or location. There was no evidence to suggest that subgroups with atopy or pre-existing wheeze are more sensitive to pollutant effects. CONCLUSION: These data do not suggest that adverse health outcomes are associated with daily variations in pollutants [corrected]. No evidence was found to indicate that particulates or individual acid and anion species are more closely related to adverse health outcomes than other pollutants.
- Warke T.J. et al.** *Exhaled nitric oxide correlates with airway eosinophils in childhood asthma.* *Thorax.* 2002; 57(5) : 383-7.p **Abstract:** BACKGROUND: Exhaled nitric oxide has been proposed as a marker for airway inflammation in asthma. The aim of this study was to compare exhaled nitric oxide levels with inflammatory cells and mediators in bronchoalveolar lavage fluid from asthmatic and normal children. METHODS: Children were recruited from elective surgical lists and a non-bronchoscopic bronchoalveolar lavage (BAL) was performed after induction of anaesthesia. Exhaled nitric oxide (parts per billion) was measured by two techniques: tidal breathing and restricted breath. RESULTS: Median (interquartile range) exhaled nitric oxide measured by restricted breath was increased in asthmatics compared with normal children (24.3 (10.5-66.5) v 9.7 (6.5-16.5), difference between medians 14.6 (95% CI 5.1 to 29.9), p=0.001). In asthmatic children exhaled nitric oxide correlated significantly with percentage eosinophils (r=0.78, p<0.001 (tidal breathing) and r=0.78, p<0.001 (restricted breath)) and with eosinophilic cationic protein (r=0.53, p<0.01 (restricted breath)), but not with other inflammatory cells in the BAL fluid. The area under the receiver operator characteristic curves for the prediction of the presence of eosinophilic airways inflammation by exhaled nitric oxide (tidal and restricted) was 0.80 and 0.87, respectively. CONCLUSIONS: Exhaled nitric oxide correlates closely with percentage eosinophils in BAL fluid in asthmatic children and is

therefore likely to be a useful non-invasive marker of airway inflammation.

Warner J.O. *The blood lung function test: does it exist for asthma?* Am J Respir Crit Care Med. 2003; 167(11): 1465-6.p

Warner J.O. *A double-blinded, randomized, placebo-controlled trial of cetirizine in preventing the onset of asthma in children with atopic dermatitis: 18 months' treatment and 18 months' posttreatment follow-up.* J Allergy Clin Immunol. 2001; 108(6) : 929-37.p
Abstract: BACKGROUND: Because asthma is not a curable condition, the development of strategies for prevention of the disease has a high priority. Atopic dermatitis is a common precursor to the development of asthma, and 2 studies have suggested that the use of an H(1) receptor antagonist might reduce the development of asthma while the treatment is being administered, at least in subgroups with evidence of high IgE levels. However, no trial to date has conducted follow-up after the initial treatment has been stopped to establish whether the intervention has merely suppressed symptoms or truly prevented disease. OBJECTIVE: We sought to establish whether the use of cetirizine compared with placebo for 18 months in infants with atopic dermatitis suppressed or truly delayed the onset of asthma, even after cessation of therapy. METHODS: The Early Treatment of the Atopic Child study was a double-blinded, parallel-group, randomized trial of 0.25 mg/kg body weight cetirizine administered twice daily compared with placebo given to infants between 1 and 2 years of age with atopic dermatitis. After 18 months of treatment, follow-up continued for a further 18 months. This article reports the outcome over the full 3 years of follow-up and relates the outcomes to the allergic status on the basis of IgE antibody measurements at recruitment. RESULTS: Although there was no difference in cumulative prevalence of asthma between active and placebo treatment in the intention-to-treat population ($P = .7$), those infants with evidence of sensitivity to house dust mite, grass pollen, or both who were treated with cetirizine were significantly less likely to have asthma compared with those treated with placebo over the 18 months of treatment ($P = .005$ and $.002$, respectively), and this effect was sustained for the grass pollen-sensitized infants over the full 36 months ($P = .008$). In the house dust mite-sensitized group there was a gradual narrowing of the difference between active and placebo treatment in terms of cumulative prevalence of asthma at the end of 36 months but no evidence of a rebound immediately after the treatment stopped ($P = .04$). In the placebo population there was a significantly higher risk of development of asthma in those sensitized at baseline to egg (relative risk, 1.4 [95% CI, 1.1-1.7]), house dust mite (relative risk, 1.6 [95% CI, 1.3-1.9]), grass pollen (relative risk, 1.7 [95% CI, 1.4-2.1]), or cat (relative risk, 1.5 [95% CI, 1.2-1.9]). Early and persistent sensitization conferred a higher risk than transient or later sensitization. CONCLUSIONS: Cetirizine compared with placebo truly delays or, in some cases, prevents the development of asthma in a subgroup of infants with atopic dermatitis sensitized to grass pollen and, to a lesser extent, house dust mite. Further studies are required focusing specifically on sensitized groups to substantiate this finding. The study also highlights risk factors for asthma in infants with atopic dermatitis and indicates that early and persistent aeroallergen sensitization confers a higher risk than later development of sensitivity.

Warner J.O. *The early life origins of asthma and related allergic disorders.* Arch Dis Child. 2004; 89(2): 97-102.p

Warschburger P. et al. *Health-related quality of life in children assessed by their parents: evaluation of the psychometric properties of the CHQ-PF50 in two German clinical samples.* Qual Life Res. 2003; 12(3) : 291-301.p
Abstract: The aim of the study was to evaluate the psychometric properties of the German translation of the Child Health Questionnaire (CHQ). Parents of two clinical samples were asked to rate the quality of life of their children using the German

version of the CHQ. Item internal consistency (item-scale correlation) and internal consistency of scales were tested; quartiles and factor analysis were conducted. The results of the German clinical samples were compared with US clinical samples (t-test). The two clinical German sub-groups were compared using multivariate analysis (MANOVA). The psychometric testing of the CHQ showed good results. Internal consistency of the hypothesized scales were all higher than 0.70. The results of the factor analysis confirmed the results of the US norm sample: As expected, the subscales loaded on two factors explaining 57.4% of the total variance. The group comparison supported the discriminative properties of the CHQ. Preliminary psychometric findings support use of the German version of the CHQ. The next step will be the testing of healthy German samples and development of norm scores.

Warschburger P. et al. *An educational program for parents of asthmatic preschool children: short- and medium-term effects.* Patient Educ Couns. 2003; 51(1) : 83-91.p
Abstract: Parent education has proven to be effective in improving parents coping with their child's asthma. Little is known about its effectiveness neither during inpatient rehabilitation nor about the different effectiveness of different approaches. A controlled clinical trial was conducted with 242 parents of asthmatic children aged less than 8 years. The aims were to develop a cognitive-behavioral training program for parents and compare its differential effectiveness with an information-centered standard-program as part of rehabilitation. Both groups reported a highly significant increase in their knowledge, self-efficacy and quality of life over time in a follow-up just after the end of their inpatient stay. There was a further increase from discharge to the 6-month follow-up for self-efficacy and quality of life. In respect to the functional severity of asthma, children of both groups showed a significant improvement. Whether these effects have long-term stability and which parents benefit from which type of intervention will be the objective of an ongoing 12-month follow-up.

Waser M. et al. *Determinants of endotoxin levels in living environments of farmers' children and their peers from rural areas.* Clin Exp Allergy. 2004; 34(3) : 389-97.p
Abstract: BACKGROUND: Lower frequencies of asthma and hayfever have been observed in children with contact to livestock. At school age, the amount of endotoxin measured in the dust of children's mattresses is inversely related to the occurrence of atopic asthma, hayfever and atopic sensitization both in children from farming and non-farming households. OBJECTIVE: The aim of the present study was to investigate which home and lifestyle characteristics of farm and non-farm families contribute to endotoxin levels measured in different indoor home environments. METHODS: In the framework of the Allergy and Endotoxin (ALEX) Study, endotoxin was measured in dust samples from the living room floor and the child's mattress of 319 farmers' families and 493 non-farming families, and in settled dust from stables. Endotoxin content of all dust samples was determined by a kinetic Limulus assay (Limulus-Amebocyte-Lysate test). Information about the child's activities on farms, home characteristics and cleaning behaviours was obtained from parental questionnaires. RESULTS: Endotoxin levels in stables did not predict the amount of endotoxin measured in floors or mattresses. However, a dose-dependent association between the child's activity on the farm and indoor home endotoxin levels was observed, both in farm and non-farm children. In non-farm children pet keeping and the frequency of floor cleaning were additionally associated with endotoxin levels, whereas in farm children parental farm activities, study area, time since last cleaning, the mattress type as well as younger age of the children contributed to increased microbial exposure. CONCLUSION: These results demonstrate that regular contact to farm animals increases indoor home endotoxin concentrations, both in farm and non-farm children, and might thus explain the protective effect of contact to livestock on atopic outcomes. To assess children's individual exposure to a microbial environment, measures of

mattress dust exposure are needed as stable endotoxin concentrations were not associated with indoor home levels.

Waser M. et al. *Exposure to pets, and the association with hay fever, asthma, and atopic sensitization in rural children.* Allergy. 2005; 60(2) : 177-84.p **Abstract:** BACKGROUND: An increasing number of studies report pet exposure to be associated with lower risk of asthma and allergies. This 'protective pet effect' has been suggested to result from a modified T-helper (Th)2-cell response, or because of increased microbial load in homes where pets are kept. We examined the associations between pet contact and the occurrence of asthma and allergies in children of the rural Allergy and Endotoxin (ALEX) population, taking farm animal contact, endotoxin and cat allergen levels in mattress dust into account. METHODS: Information about contact with pets and farm animals, asthma and allergy were collected for 812 children by a standardized parents' questionnaire and an interview. Mattress dust endotoxin and cat allergen levels as well as specific IgE and IgG4 antibodies to Fel d1 were determined. RESULTS: Current contact with dogs was inversely associated with diagnosed hay fever (OR 0.26, 95% CI 0.11-0.57), diagnosed asthma (OR 0.29, 95% CI 0.12-0.71), sensitization to cat allergen (OR 0.48, 95% CI 0.23-0.99) and to grass pollen (OR 0.55, 95% CI 0.33-0.94), but not with increased IgG4 levels. Early and current contact with cats were associated with reduced risk of wheezing (OR 0.48, 95% CI 0.23-1.00, and OR 0.49, 95% CI 0.26-0.92, respectively) and grass pollen sensitization. Adjustment for farm animal contact but not for endotoxin and cat allergen exposure attenuated these associations and the effect of pet was stronger among farmers' children. CONCLUSION: Although pet exposure was very frequent in this rural population, the inverse relation between current dog contact, asthma and allergy was mostly explained by simultaneously occurring exposure to stable animals or was restricted to farm children. In addition, a subtle form of pet avoidance may contribute to the protective effect of pet.

Watson L. et al. *Obtaining optimal control in mild asthma: theory and practice.* Fam Pract. 2005; 22(3) : 305-10.p **Abstract:** BACKGROUND: Studies have shown that asthma severity is easily under-estimated and as a result, patients may be under-treated with reduced asthma control. OBJECTIVE: This study, performed in the General Practice Research Database (GPRD), investigates asthma control in patients treated as intermittent asthmatics (short-acting beta agonist (SABA) alone), or persistent asthmatics (additional inhaled cortico-steroid (ICS), no other medication). METHODS: Patients (0-45 years) diagnosed with asthma between 1 January 1995 and 31 December 2001 taking > or =2 scripts for SABA (SABA only group) or > or =3 scripts for ICS (ICS group) in the first six months following diagnosis were selected. Factors associated with drug prescriptions were assessed. RESULTS: SABA script rates were 3.6 and 5.1 per year in the SABA and ICS group respectively, i.e. >1 dose/day. 10.5% of SABA group and 13.4% of ICS group used oral steroids. Within the SABA group, 37% were stepped up to ICS, the time to first ICS script being significantly associated with prior hospitalization (RR 2.26, CI 1.65-3.10) and atopy (RR 1.47, CI 1.33-1.63). A higher rate of oral steroid use was significantly associated with using ICS, being female, adult and smoking. Smokers and atopic individuals had increased risk of obtaining an earlier script for oral steroid (RR 1.32, CI 1.10-1.59 and RR 1.28, CI 1.10-1.49, respectively). CONCLUSIONS: Asthma control was sub-optimal in a substantial proportion of patients using relatively high doses of SABA, or SABA and ICS from the outset of asthma treatment in general practice. Being female, atopic, a smoker and prior hospitalization were all associated with lack of asthma control and could guide physicians in treatment prescribing.

Webber M.P. et al. *Prevalence of asthma and asthma-like symptoms in inner-city elementary schoolchildren.* Pediatr Pulmonol. 2002; 34(2) : 105-11.p **Abstract:** American inner-city children are

disproportionately affected by asthma. During the 1999-2000 school year, we conducted a survey of 6 Bronx, New York City elementary schools to assess the prevalence of asthma and asthma-like symptoms as reported by parents. Children with probable asthma had symptoms within the last 12 months and parents who indicated that their child had asthma. Children with possible asthma had symptoms within the last 12 months but lacked a diagnosis. Overall, 74% (4,775/6,433) of parents returned completed surveys, identifying 20% (949/4,775) of children as probable asthmatics, and 12% (589/4,775) as possible asthmatics. In multivariate analyses, probable asthma was associated with: Puerto Rican, Black, and white race/ethnicity, male gender, having health insurance, and registration at the poorest school. Possible asthma was associated with lack of health insurance and female gender, but was not associated with any specific race/ethnicity. Our findings support the effectiveness of school-based surveys to identify children at high risk for asthma. The challenge remains to engage children and families in appropriate follow-up care and to manage their illness, either through the use of school-based health centers or stronger links to community services.

Webber M.P. et al. *Impact of asthma intervention in two elementary school-based health centers in the Bronx, New York City.* Pediatr Pulmonol. 2005; 40(6) : 487-93.p **Abstract:** This study examines healthcare utilization over time in Bronx, New York schoolchildren with asthma who were previously identified via parent surveys in six elementary schools. Four of the schools have on-site school-based health centers (SBHCs), and two do not have on-site health services (control schools). At baseline, we reported an asthma prevalence of 20%, and high rates of emergency department (ED) use (46%) in the previous year. To determine if asthma morbidity (specifically, ED use, community provider use, and hospitalizations for asthma) could be reduced by incorporating an aggressive intervention at two schools with SBHCs, we prospectively followed children for up to 3 years. Parents were scheduled for interviews every 6 months, and were queried about their children's use of health services for asthma in the prior 6 months. In multivariate models, children in the two intervention SBHC schools were less likely to have visited a community provider for asthma (relative rate ratio, 0.52; 95% confidence interval (CI), 0.30-0.88) or an emergency department for asthma (odds ratio, 0.44; 95% CI, 0.14-1.38; P = 0.059) in the prior 6 months compared to children attending control schools. There was no difference in community provider use or emergency department use for asthma between children attending nonintervention SBHCs and control schools. However, school type did not affect asthma hospitalization rates, which declined in all groups. Our findings support the effectiveness of aggressive school-based asthma services provided by SBHCs to reduce asthma morbidity and complement community health services.

Weber R.W. *Dermatophagoides pteronyssinus.* Ann Allergy Asthma Immunol. 2001; 87(6) : A-4.p

Weber R.W. *Species of Cladosporium.* Ann Allergy Asthma Immunol. 2002; 89(6) : A-6.p

Weghofer M. et al. *Comparison of purified Dermatophagoides pteronyssinus allergens and extract by two-dimensional immunoblotting and quantitative immunoglobulin E inhibitions.* Clin Exp Allergy. 2005; 35(10) : 1384-91.p **Abstract:** BACKGROUND: The allergens of the house dust mite (*Dermatophagoides pteronyssinus*, Der p), one of the most important indoor allergen sources, occur as isoallergens that differ in their amino acid sequence. These variations may influence allergenic activity and thus may have impact on diagnostic tests and specific immunotherapy. OBJECTIVE: We investigated whether single purified recombinant mite allergens contain the IgE epitopes of the natural Der p isoallergens. METHODS: A panel of purified recombinant (rDer p 2, 5, 7, 8, 10 and 14) and two natural (nDer p 1

and 4) mite allergens were used to establish IgE reactivity profiles of Der p allergic patients and to inhibit IgE reactivity to two-dimensionally separated Der p isoallergens. In addition, we determined the percentage of Der p extract-specific IgE which could be preadsorbed with a mixture of purified mite allergens (nDer p 1, rDer p 2, 5, 7, 8 and 10) from sera of mite-allergic patients (n=18) in a non-denaturing RAST-based inhibition. RESULTS: We demonstrate that single recombinant mite allergens inhibit IgE reactivity to the corresponding natural isoallergens. A mixture of purified mite allergens (nDer p 1, rDer p 2, 5, 7, 8 and 10) bound on an average 76% of Der p-specific IgE antibodies. CONCLUSION: The studied recombinant and natural mite allergens contain a large portion of Der p-specific IgE and may be used for diagnostic tests and therapy of Der p allergy.

Weiland S.K. et al. *Phase II of the International Study of Asthma and Allergies in Childhood (ISAAC II): rationale and methods.* Eur Respir J. 2004; 24(3) : 406-12.p Abstract: International comparative studies, investigating whether disease incidence or prevalence rates differ between populations and, if so, which factors explain the observed differences, have made important contributions to the understanding of disease aetiology in many areas. In Phase I of the International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence rates of symptoms of asthma, allergic rhinitis and atopic eczema in 13-14-yr-olds, assessed by standardised questionnaires, were found to differ >20-fold between the 155 study centres around the world. Phase II of ISAAC aims to identify determinants of these differences by studying informative populations. A detailed study protocol was developed for use in community-based random samples of children aged 9-11 yrs. The study modules include standardised questionnaires with detailed questions on the occurrence and severity of symptoms of asthma, allergic rhinitis and atopic eczema, their clinical management, and a broad range of previous and current exposure conditions. In addition, standardised protocols were applied for examination of flexural dermatitis, skin-prick testing, bronchial challenge with hypertonic saline, blood sampling for immunoglobulin E analyses and genotyping, and dust sampling for assessment of indoor exposures to allergens and endotoxin. To date, ISAAC II field work had been completed or started in 30 study centres in 22 countries. The majority of centres are in countries that participated in International Study of Asthma and Allergies in Childhood Phase I and reflect almost the full range of the observed variability in Phase I prevalence rates.

Weiland S.K. et al. *Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children.* Occup Environ Med. 2004; 61(7) : 609-15.p Abstract: AIMS: To investigate the association between climate and atopic diseases using worldwide data from 146 centres of the International Study of Asthma and Allergies in Childhood (ISAAC). METHODS: Between 1992 and 1996, each centre studied random samples of children aged 13-14 and 6-7 years (approx. 3000 per age group and centre) using standardised written and video questionnaires on symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema during the past 12 months. Data on long term climatic conditions in the centres were abstracted from one standardised source, and mixed linear regression models calculated to take the clustering of centres within countries into account. RESULTS: In Western Europe (57 centres in 12 countries), the prevalence of asthma symptoms, assessed by written questionnaire, increased by 2.7% (95% CI 1.0% to 4.5%) with an increase in the estimated annual mean of indoor relative humidity of 10%. Similar associations were seen for the video questionnaire and the younger age group. Altitude and the annual variation of temperature and relative humidity outdoors were negatively associated with asthma symptoms. The prevalence of eczema symptoms correlated with latitude (positively) and mean annual outdoor temperature (negatively). CONCLUSIONS: Results suggest that climate may affect the prevalence of asthma and atopic eczema in children.

Weinberger M. *Exercise induced dyspnoea: if not asthma, then what?* Arch Dis Child. 2006; 91(6) : 543-4.p

Weinberger M. *Inhaled corticosteroids for infants.* J Pediatr. 2006; 148(2) : 284; author reply 284-5.p

Weinmann S. et al. *The costs of atopy and asthma in children: assessment of direct costs and their determinants in a birth cohort.* Pediatr Allergy Immunol. 2003; 14(1) : 18-26.p Abstract: The aim of this study was to estimate costs accrued by the health care of children with asthma in comparison to children with atopic eczema and seasonal rhinitis and to investigate cost determinants. From the multicenter cohort study (MAS-90), we selected children with an asthma, atopic eczema and/or seasonal rhinitis diagnosis during the first 8 years of life, and overall 8-year health care utilization was estimated retrospectively by reviewing medical records. Asthma treatment (n = 76) incurs an average cost of 627 US dollars per year, 44% due to hospital stays. Atopic eczema treatment (n = 91) cost on average 219 US dollars and seasonal rhinitis (n = 69) 57 US dollars per year. In asthma and atopic eczema, costs increase significantly with disease severity. Allergy diagnostics use accounts for only 1% of total costs. Costs for asthma and atopic eczema treatment are highest in those years when topical steroids are used for the first time, but decrease with every further year of steroid use. A remarkable 25% of asthmatic children with severe symptoms were not treated according to national guidelines, so that most steroid treatment was initiated during the first hospital stay. In the case of asthma, total direct costs increased until the 3rd year of the disease, and then decreased with further years of diagnosis, while steroid use continued to increase. These results indicate a 'learning effect' in the treatment of asthma and atopic eczema for each patient as well as considerable cost-saving potential by preventing severe asthma. Moreover, the importance of considering cost-driving factors and using cohort or longitudinal designs in cost-of-illness approaches is emphasized.

Welsh L. et al. *Fitness and physical activity in children with asthma.* Sports Med. 2004; 34(13) : 861-70.p Abstract: Asthma remains the most common chronic disease in childhood, reportedly affecting up to 25% of children in Western urban environmental settings. There seems to be a common perception that asthmatic children have a reduced capacity for exercise. Surprisingly, there is conflicting evidence in the literature in relation to this position. In this review, we present an overview of the literature in which habitual physical activity and fitness levels, including aerobic fitness, of asthmatic and non-asthmatic children are compared. There is contradictory evidence regarding the aerobic fitness levels of asthmatic children and adolescents, and it remains unclear whether significant differences exist between asthmatic children and their non-asthmatic counterparts. There is limited information concerning the relative anaerobic fitness of asthmatic children and adolescents; however, this is also conflicting. During childhood and adolescence, asthmatic individuals seem to have physical activity levels comparable with those of the normal paediatric population. However, differences in physical activity levels may develop during the time of maturation from adolescence into adulthood. Accordingly, it is not possible to establish a definitive conclusion about the issue in either children or adults. Further research with well designed methodologies is needed in order to determine whether asthmatic children and adolescents have different aerobic fitness, anaerobic fitness and physical activity levels when compared with the normal paediatric population.

Weng H.C. *Impacts of a government-sponsored outpatient-based disease management program for patients with asthma: a preliminary analysis of national data from Taiwan.* Dis Manag. 2005; 8(1) : 48-58.p Abstract: In response to the high prevalence rates, mortality

rates, and rising medical cost of asthma, the Bureau of National Health Insurance (BNHI) initiated a Healthcare Quality Improvement Program (HQIP) for people with asthma. The aim of this study was to investigate a preliminary analysis of the impact of a government-sponsored, outpatient-based disease management programs for people with asthma on the economic outcomes, the physician's and the patient's satisfaction. Using a retrospective design, a 1:4 (intervention vs. control group) matched cohort study design was used. Comparison of 1-year pre/post tests of utilizations of healthcare resources were conducted for 854 already diagnosed cases of patients with asthma. Comparison of independent tests between the intervention group and control group were performed for already diagnosed cases (n = 854) and newly-diagnosed cases (n = 231). Valid surveys were received from 212 physicians who participated the program, for a response rate of 46.0%, and 642 patients who enrolled in the program, for a response rate of 27.70%. Results indicated that the intervention group of already diagnosed cases had 39.94% fewer ED visits, 46.31% fewer inpatient visits, and 51.74% shorter length of stay, at a significant level. Though the HQIP program for people with asthma appeared to reduce medical care resource utilization for the intervention group, the control groups showed similar reductions but in different magnitude. For the newly diagnosed group, the intervention group had 197.43% more outpatient visits and 61.19% fewer ED visits of than those of the control group at a significant level. A majority of physicians (70%-85%) had positive opinions toward the HQIP program, but they admitted that the HQIP program prolonged the consultation time in outpatient visits (79.1%), and only 29.7% physicians did not feel interfered with while carrying out the HQIP. More than 80% of the patients showed positive feedback to the HQIP. The majority of the patients substantially adhered to physicians' suggestions, and had more accurate knowledge of and better self-care skills concerning asthma. These results have significance for the design of future programs aimed at improving the care of people with asthma and other chronic diseases in BNHI, Taiwan.

Wennergren G. et al. *Asthma hospitalizations continue to decrease in schoolchildren but hospitalization rates for wheezing illnesses remain high in young children.* Acta Paediatr. 2002; 91(11) : 1239-45.p **Abstract:** AIM: To analyse changes in hospitalization rates for asthma in children during recent years. METHODS: In a population-based analysis, changes in asthma hospitalization rates were studied in children in Goteborg (Gothenburg), the second largest city in Sweden, during 1985-2000. The changes in different age groups have been correlated with the delivery of inhaled corticosteroids to the age groups. RESULTS: In the 5 to 18-y age group, there was a continuous, significant decrease in number of hospital days, admissions and individual patients admitted for asthma not only for the entire study period, 1985-2000, but also during the past 10-y period. The number of hospital days in the year 2000 was only 6% of the figure for 1985. An inverse correlation between delivery of inhaled corticosteroids and hospitalization for asthma was seen not only during 1985-1995, when use of inhaled corticosteroids became widespread ($r(s) = -0.95$, $p = 0.007$ for hospital days), but also when the entire period from 1985 to 2000 was analysed. Conversely, in the 0 to 1-y and 2 to 4-y age groups, there was no decrease in hospitalizations for wheezing illnesses or asthma-like symptoms during the past 10-y period, 1991-2000. CONCLUSION: During the period 1985-2000 the number of hospital days owing to asthma decreased by more than 90% in the 5 to 18-y age group. The marked decrease in asthma hospitalization rates among schoolchildren represents a great advance in paediatric respiratory medicine, which has been continuous during the past 10-y period. However, in young children admissions for wheezing have apparently not decreased.

Werner M. et al. *Asthma is associated with single-nucleotide polymorphisms in ADAM33.* Clin Exp Allergy. 2004; 34(1) : 26-31.p **Abstract:** BACKGROUND : The ADAM33 gene has recently been associated with asthma and bronchial hyper-reactivity. It codes

for a disintegrin and metalloproteinase that triggers intra- and extracellular signalling by protein shedding. OBJECTIVE : We examined whether polymorphisms in ADAM33 are associated with asthma and related traits in two German populations. METHODS : We genotyped 15 intragenic single-nucleotide polymorphisms (SNPs) by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry of allele-specific primer extension products. The transmission disequilibrium test was used for association analysis in the German asthma family study. Additionally, we tested for association of these SNPs in a case-control sample from the European Community Respiratory Health Study using Armitage's trend test. RESULTS : In both studies, we found SNPs that were significantly associated with asthma and related traits. In the family study, significant associations were observed for the SNPs F+1, ST+4 and ST+5 (with the lowest P-value for F+1, $P=0.005$). Remarkably, this association is seen even in the absence of linkage with two microsatellite markers from a previous genome scan either 3.1 million bases (Mb) up- or 5.6 Mb downstream. In the case-control study, SNP ST+7 ($P=0.008$) was significantly associated with asthma. Some of these SNPs overlapped with those found to be associated with elevated total IgE levels and bronchial hyper-responsiveness. CONCLUSION : This study replicates the recently published association between asthma and ADAM33 gene variants. However, most of the associated SNPs were at non-identical positions in the German, UK and US samples. As linkage disequilibrium is high among the tested SNPs, and there is no known functional polymorphism, either not-tested variants in ADAM33, unknown regulatory elements or a gene in close proximity is responsible for this association.

White A. et al. *Individualised homeopathy as an adjunct in the treatment of childhood asthma: a randomised placebo controlled trial.* Thorax. 2003; 58(4) : 317-21.p **Abstract:** BACKGROUND: Homeopathy is frequently used to treat asthma in children. In the common classical form of homeopathy, prescriptions are individualised for each patient. There has been no rigorous investigation into this form of treatment for asthma. METHODS: In a randomised, double blind, placebo controlled trial the effects of individualised homeopathic remedies were compared with placebo medication in 96 children with mild to moderate asthma as an adjunct to conventional treatment. The main outcome measure was the active quality of living subscale of the Childhood Asthma Questionnaire administered at baseline and follow up at 12 months. Other outcome measures included other subscales of the same questionnaire, peak flow rates, use of medication, symptom scores, days off school, asthma events, global assessment of change, and adverse reactions. RESULTS: There were no clinically relevant or statistically significant changes in the active quality of life score. Other subscales, notably those measuring severity, indicated relative improvements but the sizes of the effects were small. There were no differences between the groups for other measures. CONCLUSIONS: This study provides no evidence that adjunctive homeopathic remedies, as prescribed by experienced homeopathic practitioners, are superior to placebo in improving the quality of life of children with mild to moderate asthma in addition to conventional treatment in primary care.

Wickens K. et al. *The determinants of dust mite allergen and its relationship to the prevalence of symptoms of asthma in the Asia-Pacific region.* Pediatr Allergy Immunol. 2004; 15(1) : 55-61.p **Abstract:** The role that house dust mites play in the primary causation of asthma is controversial. Approximately thirty-six 10-year-old children in each of 10 centres in the Asia-Pacific region participated. Researchers collected dust from mattresses and living room floors using standardized procedures. Der p1 and Der f1 were analysed using a double monoclonal antibody enzyme-linked immunosorbent assay. Geometric mean allergen levels were calculated for each centre. An ecological analysis was conducted to show the regression of the geometric mean allergen level, using the highest household level, against asthma symptom and severity

prevalence data from the International Study of Asthma and Allergies in Childhood, Phase I. Among children aged 13-14 yr, the change in asthma symptom prevalence was associated with per unit change in Der p1 microg/g (1.08, 95% CI 0.10-2.06) and Der 1 microg/g (Der p1 + Der f1) (0.64, 95% CI 0.02-1.26). The change in having four or more attacks of asthma in the last 12 months was associated with per unit change in Der p 1 microg/g (0.29, 95% CI -0.02 to 0.60) and Der 1 microg/g (0.20, 95% CI 0.01-0.38). There was no effect for total Der p1 or Der f1 (total or microg/g). Among children aged 6-7 yr, neither allergen was related to symptoms or severity prevalence. While our findings suggest that *Dermatophagoides pteronyssinus* may have a role in the primary causation of asthma, the complexity of this association reinforces the need for prospective studies.

Wickens K. et al. *Determinants of endotoxin levels in carpets in New Zealand homes.* *Indoor Air.* 2003; 13(2) : 128-35.p **Abstract:** Endotoxin in house dust has been shown to be associated with asthma severity. Little is known about the influence of housing characteristics on endotoxin distribution. Using standardized methods, dust was sampled from a 1m(2) site and the whole accessible carpet area in selected Wellington, New Zealand homes (n = 77). Endotoxin was measured using a *Limulus Amoebocyte Lysate* assay. Relative humidity and temperature were recorded using sensors placed in carpet bases. Questionnaires were used to collect information on housing characteristics. All analyses were performed for endotoxin units (EU)/mg and EU/m2 for each site. Geometric mean endotoxin levels were 22.7 EU/mg [geometric standard deviation (GSD) = 2.4] or 30,544 EU/m2 (GSD = 3.2) from the 1m(2) site, and 28.4 EU/mg (GSD = 3.4) or 5653 EU/m2 (GSD = 6.4) from the whole room. After controlling for confounding, endotoxin was positively associated with dogs inside [geometric mean ratio (GMR): 0.9-2.0], total household occupants (GMR: 1.7-2.0, for 1 m2 sample only), vacuum cleaners <1-year old (GMR: 2.3-2.7), reusing vacuum dust collection bags (GMR: 1.4-3.1), steamcleaning or shampooing the carpet (GMR: 1.4-2.2) and high relative humidity (GMR: 1.4-1.6). Lower endotoxin was associated with floor insulation (GMR: 0.4-0.8), and north-facing living rooms (GMR: 0.4-0.8). This study has identified home characteristics that could be modified to reduce endotoxin exposure.

Wickman M. et al. *Strategies for preventing wheezing and asthma in small children.* *Allergy.* 2003; 58(8) : 742-7.p **Abstract:** **OBJECTIVE:** To assess the effects of living in agreement with allergy preventive guidelines on wheezing and asthma at 2 years of age. **DESIGN:** Prospective birth cohort study (BAMSE). Questionnaires on heredity and environmental factors were answered when the child was 2 months, and detailed questionnaires on symptoms at 1 and 2 years of age. **PARTICIPANTS:** 4089 children, born during 1994-1996. **SETTING:** Child Health Centres in central and north-western parts of Stockholm, Sweden. **MAIN OUTCOME MEASURES:** Wheezing and asthma up to the age of 2. **RESULTS:** The effects of preventive guidelines regarding breastfeeding, maternal tobacco smoke and home dampness on wheezing and asthma were assessed in multiple logistic regression models. The cumulative incidence of recurrent wheezing at 2 years of age was 12.6% and of asthma 6.8% among those with a lifestyle in agreement with all guidelines and 24.1 and 17.9%, respectively, in families exposed to at least two of the three risk factors. Among children with no heredity, family lifestyle according to the guidelines gave a twofold reduction of asthma (5.3 vs. 10.5%), while the group with heredity had a threefold reduction (9.1 vs. 27.3%). The attributable fraction for asthma associated with the guidelines was 23% in total and 33% among those with heredity. **CONCLUSION:** In this observational study, family lifestyle according to preventive guidelines is associated with an important reduction of recurrent wheezing and asthma at 2 years of age, especially among children with allergic heredity. A follow-up will determine whether there still a risk reduction of both symptoms and disease.

Wijga A.H. et al. *Breast milk fatty acids and allergic disease in preschool children: the Prevention and Incidence of Asthma and Mite Allergy birth cohort study.* *J Allergy Clin Immunol.* 2006; 117(2) : 440-7.p **Abstract:** **BACKGROUND:** Better understanding of the association between early life lipid intakes and the development of allergic diseases is needed. **OBJECTIVE:** We prospectively studied breast milk content of n-6, n-3, and trans fatty acids in relation to allergic symptoms at the ages of 1 and 4 years. **METHODS:** Fatty acid content was determined in breast milk samples of 265 (158 allergic and 107 nonallergic) mothers of children participating in the Prevention and Incidence of Asthma and Mite Allergy study. Outcome variables studied were parental reported eczema at age 1 year, eczema at age 4 years, asthma at age 4 years, and, in a subgroup of 133 children, sensitization at age 4 years. **RESULTS:** In children of mothers with allergy, breast milk n-3 long chain polyunsaturated fatty acids and the ratio between n-3 and n-6 long chain polyunsaturated fatty acids were inversely associated with asthma and with persistent symptoms (eczema at age 1 year and eczema at age 4 years and/or asthma at age 4 years), but no associations between breast milk fatty acids and sensitization were observed. In children of mothers with allergy, also trans fatty acids tended to be inversely associated with allergic symptoms. In children of mothers without allergy, no associations between breast milk fatty acids and allergic symptoms were observed, but alpha-linolenic acid (18:3n-3) was positively associated with sensitization. **CONCLUSION:** In susceptible infants, the risk to develop allergic symptoms, but not the risk of sensitization, was modified by intake of n-3 long chain polyunsaturated fatty acids through breast milk.

Wildhaber J.H. et al. *Comparison of subjective and objective measures in recurrently wheezy infants.* *Respiration.* 2002; 69(5) : 397-405.p **Abstract:** **OBJECTIVES:** The aim of this study was to compare subjective measures (overall health assessment both by the study physician and the child's mother) with objective measurements of forced expiratory volumes (FEV(t)) and maximal flow at functional residual capacity V(max)FRC) in recurrently wheezy infants. **METHODS:** Sixteen wheezy infants (12 boys) aged 8-26 months were studied. A clinical assessment at visit 1 was followed by the run-in period during which day- and nighttime asthma symptom scores were obtained. The actual study period consisted of 2 visits when patient's lung function was assessed. The first of which was during an acute exacerbation (visit 2), while the second was when the infant was asymptomatic (visit 3). FEV(t) were obtained by the raised volume rapid thoracic compression technique (RVRTC) and V(max)FRC by the tidal volume rapid thoracic compression technique (TVRTC). **RESULTS:** Mean FEV(t) but not mean V(max)FRC were significantly lower at visit 2 compared to visit 3 (FEV(0.5): p = 0.005, and FEV(0.75): p = 0.002; V(max)FRC: p = 0.15) and correlated well with overall health assessment by the study physician (FEV(0.5): r = 0.82, and FEV(0.75): r = 0.84), but not with the overall health assessment by the mother. **CONCLUSIONS:** We have shown in the present study that objective measurements of FEV(t) from a raised lung volume correlate well with the overall health assessment by the study physician; this was in contrast to measurements of V(max)FRC in the tidal volume range. We therefore conclude that the RVRTC technique is a feasible method to assess and monitor obstructive lung disease in infancy.

Willers S. et al. *Assessment of environmental tobacco smoke exposure: urinary cotinine concentrations in children are strongly associated with the house dust concentrations of nicotine at home.* *Indoor Air.* 2004; 14(2) : 83-6.p **Abstract:** In the present study the possibility of using nicotine in house dust as an index of environmental tobacco smoke (ETS) exposure was evaluated in an environmental investigation of 23 children with asthma. A standardized procedure for house dust sampling of nicotine with a filter holder connected to a vacuum cleaner, for a defined time and area was developed (F-

nicotine). Also, house dust sampling was carried out from the vacuum cleaner bags of the homes (VC-nicotine). There was a larger variation in VC-nicotine (13-655, median 66 microg/g) compared with F-nicotine (15-393 median 156 microg/g). There were statistically significant associations between an inquiry data based ETS exposure index on the one hand, and urinary cotinine concentrations in children (U-cotinine), F-nicotine and VC-nicotine of their homes, on the other. The strong correlation between U-cotinine and F-nicotine ($r_s = 0.93$; $P < 0.0001$) indicates that the new standardized house dust sampling method should be useful in ETS exposure assessment. However, further validation by a larger sample size with repeated measurements in the same homes is needed.

Williams D. et al. *Preferential prescribing of oral corticosteroids in Irish male asthmatic children.* Br J Clin Pharmacol. 2001; 52(3) : 319-21.p **Abstract:** AIMS: To determine if there is a gender difference in the prescription of oral corticosteroids in asthmatic children (< 15 years). METHODS: 8072 asthmatics were identified on the basis that they received a prescription for either an inhaled beta-adrenoceptor agonist, an inhaled corticosteroid, inhaled cromoglycate/nedocromil sodium, oral xanthines or leukotriene antagonist. Odds ratios (OR) and 95% confidence intervals (CI) were determined for the different asthma treatments for males compared with females. RESULTS AND CONCLUSIONS: Male asthmatic children were more likely (OR = 1.37, 95% CI = 1.21,1.55, $P < 0.001$) to receive a prescription for an oral corticosteroid compared with their female counterparts suggesting a possible increased severity of their condition, rather than a different management of their disease. Male asthmatic children were less likely to be prescribed an antibiotic over the study period (OR = 0.85, 95% CI = 0.77, 0.93, $P < 0.001$).

Williams J. et al. *Asthma-specific quality of life questionnaires in children: are they useful and feasible in routine clinical practice?* Pediatr Pulmonol. 2003; 35(2) : 114-8.p **Abstract:** This study used well-validated quality of life (QOL) instruments to compare the QOL scores achieved by children aged 7-17 years with the views of their parents of the effects of their child's asthma on family life. Also, a comparison was made between the child's QOL scores and the judgment of the clinician in charge in regard to asthma control. There was poor correlation between the overall scores of the children and the overall caregiver's score ($r = 0.19$, $P = 0.18$), and no correlation between the child's score and assessment of control given by the clinician in charge of the case ($r = 0.02$, $P = 0.98$). It is important to recognize that there may be little relationship between the concerns of the child regarding his or her asthma, the effects on the family as reported by a parent, and the clinician's view of asthma control. This recognition may significantly affect treatment planning with the family. The administration of the QOL instrument used in this study was straightforward and quite quick, with a mean time to completion of about 8 min.

Willwerth B.M. et al. *Prenatal, perinatal, and heritable influences on cord blood immune responses.* Ann Allergy Asthma Immunol. 2006; 96(3) : 445-53.p **Abstract:** BACKGROUND: Maternal and perinatal environmental exposures, as well as inherited factors, may influence neonatal immune responses. OBJECTIVE: To determine relations of maternal and perinatal exposures to antigen-specific cord blood lymphoproliferative responses. METHODS: In 427 newborns from a Boston pregnancy/birth cohort, lymphoproliferative responses in cord blood mononuclear cells to stimulation with cockroach (Bla g 2), house dust mite (Der f 1), ovalbumin, and mitogen phytohemagglutinin were measured as stimulation index (SI). We used the Wilcoxon rank sum and chi2 tests to evaluate predictors of ovalbumin SI as a continuous ranked or dichotomous outcome. We used t test and Spearman correlation for univariate testing and linear regression to evaluate predictors of natural log-transformed Bla g 2, Der f 1, and phytohemagglutinin SI. Logistic multivariate regression was applied to evaluate predictors of Bla g 2, Der f 1, and

phytohemagglutinin SI dichotomized at 2 or at the median for phytohemagglutinin. RESULTS: Maternal smoking during pregnancy, inadequate or excessive maternal weight gain during pregnancy, neonate black race/ethnicity (compared with white), and Apgar score less than 8 were each independently associated with increased cord blood mononuclear cell proliferative responses to stimulation with Bla g 2 and/or Der f 1. Maternal history of asthma was associated only with increased lymphoproliferative response to ovalbumin stimulation. CONCLUSIONS: Distinct fetal and perinatal exposures and black race/ethnicity may be associated with increased cord blood lymphoproliferative responses. The implications of these findings for future development of allergy or asthma are, as yet, unknown.

Wilson A.M. et al. *Air pollution, weather, and respiratory emergency room visits in two northern New England cities: an ecological time-series study.* Environ Res. 2005; 97(3) : 312-21.p **Abstract:** Daily emergency room (ER) visits for all respiratory (ICD-9 460-519) and asthma (ICD-9 493) were compared with daily sulfur dioxide (SO₂), ozone (O₃), and weather variables over the period 1998-2000 in Portland, Maine (population 248,000), and 1996-2000 in Manchester, New Hampshire (population 176,000). Seasonal variability was removed from all variables using nonparametric smoothed function (LOESS) of day of study. Generalized additive models were used to estimate the effect of elevated levels of pollutants on ER visits. Relative risks of pollutants are reported over their interquartile range (IQR, the 75th -25th percentile pollutant values). In Portland, an IQR increase in SO₂ was associated with a 5% (95% CI 2-7%) increase in all respiratory ER visits and a 6% (95% CI 1-12%) increase in asthma visits. An IQR increase in O₃ was associated with a 5% (95% CI 1-10%) increase in Portland asthmatic ER visits. No significant associations were found in Manchester, New Hampshire, possibly due to statistical limitations of analyzing a smaller population. The absence of statistical evidence for a relationship should not be used as evidence of no relationship. This analysis reveals that, on a daily basis, elevated SO₂ and O₃ have a significant impact on public health in Portland, Maine.

Wilson S.E. et al. *Racial differences in exposure to environmental tobacco smoke among children.* Environ Health Perspect. 2005; 113(3) : 362-7.p **Abstract:** Exposure to environmental tobacco smoke (ETS) is a major cause of morbidity and mortality among U.S. children. Despite African-American children's having a lower reported exposure to tobacco compared to whites, they suffer disproportionately from tobacco-related illnesses and have higher levels of serum cotinine than white children. The goal of this study was to test whether African-American children have higher levels of serum and hair cotinine, after accounting for ETS exposure and various housing characteristics. We investigated the level of cotinine in both hair and serum in a sample of 222 children with asthma. Using a previously validated survey for adult smokers, we assessed each child's exposure to ETS. We collected detailed information on the primary residence, including home volume, ventilation, and overall home configuration. Despite a lower reported ETS exposure, African-American children had higher mean levels of serum cotinine (1.41 ng/mL vs. 0.97 ng/mL; $p = 0.03$) and hair cotinine (0.25 ng/mg vs. 0.07 ng/mg; $p < 0.001$) compared with white children. After adjusting for ETS exposure, housing size, and other demographic characteristics, serum and hair cotinine levels remained significantly higher in African-American children ($ss = 0.34$, $p = 0.03$) than in white children ($ss = 1.06$, $p < 0.001$). Housing volume was significantly associated with both serum and hair cotinine but did not fully explain the race difference. Our results demonstrate that, despite a lower reported exposure to ETS, African-American children with asthma had significantly higher levels of both serum and hair cotinine than did white children. Identifying causes and consequences of increased cotinine may help explain the striking differences in tobacco-related illnesses.

Wilson S.E. et al. *Underuse of controller medications among children with persistent asthma in the Ohio medicaid population: evolving differences with new medications.* *Ambul Pediatr.* 2005; 5(2) : 83-9.p **Abstract:** BACKGROUND: Despite innovations in asthma care, morbidity and mortality have increased significantly. Underuse of controller medications is a major contributor to increased morbidity and mortality. OBJECTIVE: To determine the extent of underuse of asthma controller medications among Ohio Medicaid children and to determine if there are racial differences in controller medication claims. METHODS: We conducted a retrospective analysis of Ohio Medicaid claims data. The source data included all institutional, medical service, and pharmacy claims for fee-for-service patients between January 1, 1997, and December 31, 2001. We identified children with persistent asthma using Health Employer Data Information System criteria. The primary outcome was a controller medication claim. We used multivariable logistic regression to identify risk factors for underutilizing asthma controller medications and applied generalized estimating equations to account for repeated measures. RESULTS: The proportion of children with claims for a controller medication increased from 53% in 1997 to 67% in 2001. Although there were no racial differences in medication claims in 1997, a smaller proportion of African American children had a claim for a controller medication in 2001 (64.8% vs 67.8%, $P < .001$). Leukotriene antagonists (LTAs) were driving this difference. Individuals residing in urban areas were significantly less likely to have claims for LTAs when compared with those who resided in nonurban areas. CONCLUSIONS: Overall use of asthma controller medications among Ohio Medicaid children was poor. There was a widening racial difference in controller medication claims over the 5-year study. Regional differences in LTA claims were driving this racial difference.

Wogelius P. et al. *Asthma, ear problems, and dental anxiety among 6- to 8-yr-olds in Denmark: a population-based cross-sectional study.* *Eur J Oral Sci.* 2003; 111(6) : 472-6.p **Abstract:** The aim of this study was to examine the association between asthma, ear problems, and dental anxiety in children in a population-based cross-sectional study. The population included four municipalities in the County of North Jutland, Denmark, in 2001. A total of 1235 children aged 6-8 yr, and their parents, were identified. Data were obtained from a prescription database, from parental-answered questionnaires, and from dental records. Children with asthma were defined as children that had received prescriptions for both inhaled beta2-agonists and corticosteroids during the past year. Data on ear problems and dental anxiety were obtained from the questionnaires. Dental anxiety was measured using the Children's Fear Survey Schedule-Dental Subscale (CFSS-DS). Use of asthma-drugs was associated with dental anxiety (odds ratio = 1.70; 95% confidence interval 0.90-3.22). A history of often ear problems was also associated with dental anxiety (odds ratio = 1.83; 95% confidence interval 1.20-2.80). It is concluded that asthma and ear problems may be risk factors for dental anxiety in children.

Wogelius P. et al. *Use of asthma-drugs and risk of dental caries among 5 to 7 year old Danish children: a cohort study.* *Community Dent Health.* 2004; 21(3) : 207-11.p **Abstract:** OBJECTIVE: To estimate the risk of dental caries in 5-7 year old Danish children who received prescriptions for asthma-drugs. DESIGN: Population-based cohort-study based on data from a prescription registry and dental database. Setting The County of North Jutland, Denmark. PARTICIPANTS: 4,920 children born in 1993, and followed to the end of 2000. Main outcome measures Dental caries in primary canines and molars, and permanent teeth. RESULTS: Between the age 3 and 5 years 30.4% of the children received one or more prescriptions for asthma-drugs compared to 18.8% between 5 and 7 years of age. Children often received two or more drugs in combination. Approximately 6% of the children received both inhaled cortico-steroids and inhaled beta2-agonists between 3 and 7 years of age. No increased risk of caries could be shown in the

primary teeth, while the relative risk of caries in the permanent teeth was estimated at 1.45 (95% C.I.: 0.99-2.11) in children who received prescriptions of both inhaled beta2-agonists and corticosteroids between 5 and 7 years. Of the 169 children who received prescriptions of both inhaled beta2-agonists and cortico-steroids between the ages of 3 and 7 years, the relative risk was estimated at 1.62 (95% C.I.: 1.03-2.56). CONCLUSIONS: Asthma-drugs may increase the risk of caries in newly erupted permanent molars.

Wogelius P. et al. *Validity of parental-reported questionnaire data on Danish children's use of asthma-drugs: a comparison with a population-based prescription database.* *Eur J Epidemiol.* 2005; 20(1) : 17-22.p **Abstract:** The aim of this study was to examine the validity--estimated as the sensitivity, specificity, and predictive values--of questionnaire-based parental reporting on Danish children's use of asthma drugs. Within a population-based cross-sectional study on the association between asthma and dental anxiety, we compared parental answers on their children's use of asthma drugs during the past 12 months with National Health Service (NHS) data from a prescription database on prescriptions of inhaled beta 2-agonists, inhaled corticosteroids, or both for a period of 14 months preceding the date of posting the parental questionnaires. In four municipalities in North Jutland County, Denmark, in 2001, parents of 1273 children between the ages of 6 and 8 years completed the questionnaire. For frequency of use, the sensitivity increased from 57.9% (95% confidence interval [CI]: 47.8-67.3%) for the answer 'Every day' to 91.6% (95% CI: 84.3-95.7%) when the answers 'Every day', 'Often', and 'Sometimes' were combined. The specificity exceeded 95.9% (95% CI: 94.6-96.9%) for all answers. The positive predictive value (PPV) increased from 64.4% (95% CI: 56.1-72.0%) when the answers 'Every day', 'Often', and 'Sometimes' were combined to 94.8% (95% CI: 85.9-98.2%) for the answer 'Every day'. The negative predictive value (NPV) both exceeded 96.7% (95% CI: 95.5-97.6%) for all answers. Questionnaire-based parental reporting on children's one-year asthma-drug use appears to be valid in epidemiological research depending on the study question and design.

Woitsch B. et al. *A comprehensive analysis of interleukin-4 receptor polymorphisms and their association with atopy and IgE regulation in childhood.* *Int Arch Allergy Immunol.* 2004; 135(4) : 319-24.p **Abstract:** BACKGROUND: The interleukin (IL) 4/IL13 pathway is involved in the regulation of IgE production associated with atopic diseases. Numerous polymorphisms have been identified in the coding region of the IL4 receptor alpha chain (IL4Ra) and previous association studies have shown conflicting results. Based on their putative functional role, polymorphisms A148G, T1432C and A1652G, located in the coding region of IL4Ra, were selected for association and haplotype studies in a large German population sample (n = 1,120). METHODS: Genotyping was performed using allele-specific PCR and restriction-enzyme-based assays. Haplotypes were estimated, and population-derived IgE percentiles (50% IgE >60 IU/ml, 66% IgE >115 IU/ml and 90% IgE >457 IU/ml) were calculated as outcome variables in a haplotype trend regression analysis. RESULTS: In our population, only polymorphism T1432C showed a trend for a protective effect against atopic rhinitis (odds ratio, OR: 0.52, 95% confidence interval, CI: 0.26-1.02, $p = 0.05$). When haplotypes were calculated, one haplotype was significantly associated with elevated serum IgE levels at the 50th percentile (OR 1.60, 95% CI 1.08-2.37, $p = 0.02$). CONCLUSIONS: These data indicate that IL4Ra polymorphisms, although suggested to be functionally relevant by in vitro studies, have only a minor influence on IgE regulation in our large population sample.

Wolf R.L. et al. *Development and validation of a brief pediatric screen for asthma and allergies among children.* *Ann Allergy Asthma Immunol.* 2003; 90(5) : 500-7.p **Abstract:** BACKGROUND: Asthma is the most common disease of childhood, but the

recognition and detection remain poor, especially among schoolchildren. There has been an increase in the number of instruments available to detect the risk of asthma earlier in children. We have previously validated a simple, self-reported screen, the Brief Pediatric Asthma Screen (BPAS). OBJECTIVE: To develop a new screen for asthma and allergies based on the BPAS (BPAS+) with the intent of keeping the screen brief and simple, while including allergy detection. METHODS: Questions from the BPAS were extensively revised, and questions regarding allergic rhinitis were added. A panel of parents of asthmatic children reviewed and critiqued the questions. The final BPAS + was distributed in elementary schools, and a cohort of 129 participated in a validation against the gold standard of evaluation by an expert in asthma. RESULTS: For asthma the best items were wheeze, persistent cough, night cough, and response to change in air temperature. The simplest scoring, any 1 of the 4 items, yielded the best balance of specificity (73.6%) and sensitivity (73.3%). For allergy, using all six items, having any one or any two of the items had sensitivity of 71.4% and specificity of 77.3%. CONCLUSIONS: The BPAS+ provides a rapid and valid method for the detection of potential allergy and asthma in schoolchildren. Sensitivity and specificity are acceptable for both asthma and allergies.

Wolthers O.D. et al. *Inhaled corticosteroids, growth, and compliance.* N Engl J Med. 2002; 347(15) : 1210-1.p

Wong E.Y. et al. *Assessing the health benefits of air pollution reduction for children.* Environ Health Perspect. 2004; 112(2) : 226-32.p
Abstract: Benefit-cost analyses of environmental regulations are increasingly mandated in the United States. Evaluations of criteria air pollutants have focused on benefits and costs associated with adverse health effects. Children are significantly affected by the health benefits of improved air quality, yet key environmental health policy analyses have not previously focused specifically on children's effects. In this article we present a "meta-analysis" approach to child-specific health impacts derived from the U.S. Clean Air Act (CAA). On the basis of data from existing studies, reductions in criteria air pollutants predicted to occur by 2010 because of CAA regulations are estimated to produce the following impacts: 200 fewer expected cases of postneonatal mortality; 10,000 fewer asthma hospitalizations in children 1-16 years old, with estimated benefits ranging from 20 million U.S. dollars to 46 million U.S. dollars (1990 U.S. dollars); 40,000 fewer emergency department visits in children 1-16 years old, with estimated benefits ranging from 1.3 million U.S. dollars to 5.8 million U.S. dollars; 20 million school absences avoided by children 6-11 years old, with estimated benefits of 0.7-1.8 billion U.S. dollars; and 10,000 fewer infants of low birth weight, with estimated benefits of 230 million U.S. dollars. Inclusion of limited child-specific data on hospitalizations, emergency department visits, school absences, and low birth weight could be expected to add 1-2 billion U.S. dollars (1990 U.S. dollars) to the 8 billion U.S. dollars in health benefits currently estimated to result from decreased morbidity, and 600 million U.S. dollars to the 100 billion U.S. dollars estimated to result from decreased mortality. These estimates highlight the need for increased consideration of children's health effects. Key needs for environmental health policy analyses include improved information for children's health effects, additional life-stage-specific information, and improved health economics information specific for children.

Wong G.C. et al. *Children's exposure to environmental tobacco smoke in the home: comparison of urine cotinine and parental reports.* Arch Environ Health. 2002; 57(6) : 584-90.p
Abstract: The authors examined the relationship between parent-reported estimates of children's exposure to environmental tobacco smoke (ETS) in the home and children's urinary cotinine levels. Data were collected from a largely ethnic minority, low-income, urban sample of households in which a child had asthma and at least 1 household member smoked. Information about level of household smoking restriction, parental

smoking status, and number of cigarettes smoked per day accounted for approximately 45% of the variance in cotinine concentration. Detailed information about the duration of household smoking or children's ETS exposure added no additional significant information. Questionnaires eliciting detailed information about smoking habits and children's ETS exposure may be no better at predicting children's urinary cotinine levels than simpler surveys that inquire about smoking restrictions in the home, parental smoking status, and number of cigarettes smoked at home per day.

Wong G.W. et al. *Individual allergens as risk factors for asthma and bronchial hyperresponsiveness in Chinese children.* Eur Respir J. 2002; 19(2) : 288-93.p
Abstract: The role of allergen sensitization in the development of asthma in the Chinese is not clear. This study aims to determine the relationship of sensitization to individual allergens, and the development of asthma and bronchial hyperresponsiveness (BHR) in schoolchildren from three Chinese cities: Hong Kong, Beijing and Guangzhou. Community-based random samples of 10-yr-old schoolchildren from three Chinese cities were recruited for study using the International Study of Asthma and Allergies in Childhood (ISAAC) Phase II protocol. Subjects were studied by parental questionnaires (n=10,902), skin-prick tests (n=3,479), and methacholine challenge tests (n=608). The prevalence rates of wheeze in the past 12 months (Hong Kong, 5.8%; Beijing, 3.8%; Guangzhou, 3.4%) and atopy (Hong Kong, 41.2%; Beijing, 23.9%; Guangzhou, 30.8%) were highest in schoolchildren from Hong Kong. Multivariate logistic regression analyses revealed that sensitization to *Dermatophagoides pteronyssinus* (odds ratio (OR)=4.48; 95% confidence interval (CI): 3.02-6.66), cat (2.59; 1.67-4.03), *Dermatophagoides farinae* (2.41; 1.65-3.51) and mixed grass pollen (2.85; 1.24-6.50) were significantly associated with current wheeze. Atopy, defined as having > or = 1 positive skin-prick tests, was not an independent risk factor for current wheeze in children from any of the three cities. Furthermore, atopy (OR=2.53; 95% CI: 1.07-5.97), sensitization to cat (3.01; 1.39-6.52) and *D. farinae* (3.67; 1.93-6.97) were significantly associated with BHR. The authors confirmed that sensitization to house dust mite and cat was significantly associated with current wheeze and bronchial hyperresponsiveness in Chinese schoolchildren. However, the difference in the prevalence rate of atopic sensitization cannot explain the higher prevalence of childhood asthma in Hong Kong, when compared with those children from Beijing and Guangzhou.

Wong G.W. et al. *High levels and gender difference of exhaled nitric oxide in Chinese schoolchildren.* Clin Exp Allergy. 2005; 35(7) : 889-93.p
Abstract: BACKGROUND: Exhaled nitric oxide (eNO) may represent a useful noninvasive marker of airway inflammation, but data on the reference population values in schoolchildren are limited. No reference eNO study in Asian children has been published. METHODS: Levels of eNO in a sample of 531 schoolchildren aged 11-18 years recruited from five schools (three international schools) in Hong Kong were measured online by a chemiluminescence analyser according to ERS/ATS standard. Each student also completed an International Study of Asthma and Allergic disease in Childhood questionnaire. RESULTS: Among the children without a physician's diagnosis of asthma or symptoms of wheeze, rhinitis and eczema, there were 258 Chinese and 33 Caucasians. In control Chinese children, the eNO level (median: interquartile range) was significantly higher (P<0.001) in males (17.0 parts per billion (p.p.b.); 10.7-36.6) than in females (10.8 p.p.b.; 7.8-17.6). When compared with Caucasian control males (11.6 p.p.b.; 8.2-19.3) and females (9.1 p.p.b.; 7.5-11.9), the Chinese children had significantly higher eNO levels for both males (P=0.011) and females (P=0.037). For Chinese asthmatic males, the median eNO (interquartile range) was 39.8 p.p.b. (12.5-73.8), and for asthmatic females, 18.0 (9.6-56.3). After controlling for sex in Chinese controls, eNO did not have any significant correlation with height, weight and body mass index or body surface area. CONCLUSIONS: This study demonstrates a gender difference of

eNO level in healthy Chinese schoolchildren. When compared with Caucasians, Chinese children have significantly higher eNO levels.

Wong J.Y. et al. *Growth and adrenal suppression in asthmatic children on moderate to high doses of fluticasone propionate.* J Paediatr Child Health. 2002; 38(1) : 59-62.p **Abstract:** OBJECTIVE: Growth and adrenal suppression have been reported in asthmatic children using high-dose inhaled fluticasone propionate (FP). Inhaled FP, given at moderate doses (250-750 microg/day), has not been documented to be associated with growth or adrenal suppression in asthmatic children until recently. We report three cases illustrating these side effects. METHODS: Growth and adrenal suppression, after the introduction of inhaled FP, were observed in three prepubertal young asthmatic children referred to our asthma clinic and growth clinic. Growth centile and velocity were assessed by longitudinal stadiometry height measurements. Early morning plasma cortisol levels, and glucagon stimulation tests were used to assess the pituitary adrenal axis. RESULTS: Severe growth and adrenal suppression were noted in three children while they were on moderate doses of inhaled FP. Improvements in growth and adrenal function were observed following cessation or dose reduction of inhaled FP. CONCLUSIONS: Unexpected growth and adrenal suppression may occur in young asthmatic children using moderate doses of inhaled FP.

Woo J.G. et al. *The -159 C-->T polymorphism of CD14 is associated with nonatopic asthma and food allergy.* J Allergy Clin Immunol. 2003; 112(2) : 438-44.p **Abstract:** BACKGROUND: CD14, the receptor for LPS, plays an important role in innate immunity. A polymorphism in the promoter for CD14, -159 C-->T, has been implicated in atopy. OBJECTIVE: We explored the relationship of this polymorphism with both atopic and nonatopic asthma, as well as with food allergy. METHODS: Patients with asthma and food allergy were recruited along with nonatopic, nonasthmatic control subjects. The -159 C-->T polymorphism was genotyped by using the PCR-based RFLP assay. RESULTS: The -159 T allele was more common among patients with nonatopic asthma and food allergy than among control subjects ($\chi^2 = 6.03$, $P = .01$ and $\chi^2 = 4.94$; $P = .03$, respectively). Patients with food allergy had a 4-fold increased odds of having the TT genotype versus carriers of the C allele compared with control subjects (odds ratio [OR] = 3.9, 95% CI = 1.5-10.3), whereas patients with nonatopic asthma had a 3-fold increased odds of having the TT genotype (OR = 3.1 [95% CI = 1.1-9.1]). Controlling for sex differences between groups did not alter this relationship, which remained significant for patients with food allergy (OR = 3.7 [95% CI = 1.4-10.1]) or nonatopic asthma (OR = 2.7 [95% CI = 0.9-8.0]). We performed a stratified analysis, limited to white patients, to reduce population stratification. The relationship with the TT genotype was stronger in white patients with nonatopic asthma (OR = 4.4 [95% CI = 1.3-14.8]) and patients with food allergy (OR = 5.1 [95% CI = 1.6-16.2]), even adjusting for sex differences (OR = 3.9 [95% CI = 1.1-13.5] and OR = 4.6 [95% CI = 1.4-14.8], respectively). CONCLUSIONS: The TT genotype of -159 C-->T CD14 is associated with nonatopic asthma and food allergy, particularly in white subjects. Thus CD14 is a candidate gene specifically for nonatopic asthma and not for asthma in general. This indicates that atopic and nonatopic asthma might be distinct conditions in their genetic predisposition, despite the fact that they are very similar once they have been established.

Wright N.P. et al. *The incidence of hypoglycaemia in children with type 1 diabetes and treated asthma.* Arch Dis Child. 2003; 88(2) : 155-6.p **Abstract:** AIMS: To investigate whether treatment of coexisting asthma has any effect on the incidence of hypoglycaemia and on glycaemic control in children with type 1 diabetes. METHODS: An observational study of children attending the paediatric diabetes clinics of five hospitals in the North Trent Region. Information on the frequency of hypoglycaemia in the preceding three months,

treatment for asthma, and the individual's latest HbA1c, was recorded when they attended for review. RESULTS: Data were collected on 226 children, of whom 27 (12%) had treated asthma. Only 11/27 children with asthma were taking their prescribed inhaled steroids. All used beta agonists at least once a week. There was a reduction of 20% in the incidence of hypoglycaemia in the diabetic children with treated asthma. Of the children with diabetes and treated asthma, 52% reported an episode of hypoglycaemia in the previous three months compared to 72% of those with only diabetes. There was no difference in the proportion of children experiencing nocturnal or severe hypoglycaemia. Although not significant, those with asthma and diabetes also had better overall control (HbA1c 8.8%) compared to those with diabetes alone (HbA1c 9.3%). CONCLUSIONS: Diabetic children with treated asthma have significantly fewer episodes of hypoglycaemia and better glycaemic control compared to children with diabetes alone. This observation needs further investigation but raises an interesting question. Do the drugs used to treat asthma, in particular beta agonists, have the therapeutic potential to reduce hypoglycaemia and facilitate an improvement in glycaemic control?

Wright R.J. et al. *Chronic caregiver stress and IgE expression, allergen-induced proliferation, and cytokine profiles in a birth cohort predisposed to atopy.* J Allergy Clin Immunol. 2004; 113(6) : 1051-7.p **Abstract:** BACKGROUND: Psychologic stress modifies immune function and cytokine production. OBJECTIVE: We examined relationships between caregiver stress on the following markers of early childhood immune response: (1) IgE expression (n=215); (2) mitogen-induced and allergen-specific (Dermatophagoides farinae [Der f 1] and cockroach [Bla g 2]) proliferative response (n=114); and (3) subsequent cytokine expression (INF-gamma, TNF-alpha, IL-10, and IL-13) in a prospective birth cohort predisposed to atopy. METHODS: Caregiver stress was measured at 2-month intervals for the first 2 years of life and yearly thereafter by using the Perceived Stress Scale. A subsequent blood sample obtained from the children (median age, 2.1 years; range, 18-32 months) was analyzed for total serum IgE level and allergen-induced proliferation quantified as the stimulation index (SI; mean thymidine incorporation of the stimulated sample divided by that of the unstimulated sample). The relationship between stress and the proliferative response (SI >3 vs SI < or =3), and total IgE level (< or =100 IU/mL vs >100 IU/mL) was examined by using logistic regression. The relationship between cytokine levels and stress was analyzed by using linear regression. RESULTS: In adjusted analyses higher caregiver stress in the first 6 months after birth was associated with a Der f 1 SI of greater than 3 (odds ratio [OR], 1.5; 95% CI, 1.0-2.3) and nominally associated with a Bla g 2 SI of greater than 3 (OR, 1.13; 95% CI, 0.7-1.8). Higher stress between ages 6 and 18 months was associated with a high total IgE level (OR, 2.03; 95% CI, 1.1-3.6). Higher stress was significantly associated with increased production of TNF-alpha, with a suggested trend between higher stress and reduced INF-gamma production. CONCLUSION: Increased stress in early childhood was associated with an atopic immune profile in these children predisposed to atopy-asthma.

Wright R.J. et al. *Community violence and asthma morbidity: the Inner-City Asthma Study.* Am J Public Health. 2004; 94(4) : 625-32.p **Abstract:** OBJECTIVES: We examined the association between exposure to violence and asthma among urban children. METHODS: We obtained reports from caretakers (n = 851) of violence, negative life events, unwanted memories (rumination), caretaker-perceived stress, and caretaker behaviors (keeping children indoors, smoking, and medication adherence). Outcomes included caretaker-reported wheezing, sleep disruption, interference with play because of asthma, and effects on the caretaker (nights caretaker lost sleep because of child's asthma). RESULTS: Increased exposure to violence predicted higher number of symptom days ($P = .0008$) and more nights that caretakers lost sleep ($P = .02$) in a graded fashion after control for

socioeconomic status, housing deterioration, and negative life events. Control for stress and behaviors partially attenuated this gradient, although these variables had little effect on the association between the highest level of exposure to morbidity, which suggests there are other mechanisms. CONCLUSIONS: Mechanisms linking violence and asthma morbidity need to be further explored.

Wright R.J. et al. *Violence: an unrecognized environmental exposure that may contribute to greater asthma morbidity in high risk inner-city populations.* Environ Health Perspect. 2001; 109(10) : 1085-9.p **Abstract:** In the United States, rising trends in asthma prevalence and severity, which disproportionately impact minorities and the urban poor, have not been fully explained by traditional physical environmental risk factors. Exigencies of inner-city living can increase psychosocial risk factors (e.g., stress) that confer increased asthma morbidity. In the United States, chronic exposure to violence is a unique stressor existing in many high-risk urban neighborhoods. In this paper, we describe a series of cases that exemplify a temporal association between exposure to violence and the precipitation of asthma exacerbations in four urban pediatric patients. In the first three cases, the nature of the exposure is characterized by the proximity to violence, which ranged from direct victimization (through either the threat of physical assault or actual assault) to learning of the death of a peer. The fourth case characterizes a scenario in which a child was exposed to severe parental conflict (i.e., domestic violence) in the hospital setting. Increasingly, studies have begun to explore the effect of living in a violent environment, with a chronic pervasive atmosphere of fear and the perceived or real threat of violence, on health outcomes in population-based studies. Violence exposure may contribute to environmental demands that tax both the individual and the communities in which they live to impact the inner-city asthma burden. At the individual level, intervention strategies aimed to reduce violence exposure, to reduce stress, or to counsel victims or witnesses to violence may be complementary to more traditional asthma treatment in these populations. Change in policies that address the social, economic, and political factors that contribute to crime and violence in urban America may have broader impact.

Wu C.F. et al. *Evaluation and quality control of personal nephelometers in indoor, outdoor and personal environments.* J Expo Anal Environ Epidemiol. 2005; 15(1) : 99-110.p **Abstract:** Personal nephelometers provide useful real-time measurements of airborne particulate matter (PM). Recent studies have applied this tool to assess personal exposures and related health effects. However, a thorough quality control (QC) procedure for data collected from such a device in a large-scale exposure assessment study is lacking. We have evaluated the performance of a personal nephelometer (personal DataRAM or pDR) in the field. We present here a series of post hoc QC procedures for improving the quality of the pDR data. The correlations and the ratios between the pDRs and the collocated gravimetric measurements were used as indices of the pDR data quality. The pDR was operated in four modes: passive (no pump), active (with personal sampling pumps), active with a heated inlet, and a humidistat. The pDRs were worn by 21 asthmatic children, placed at their residences indoors and outdoors, as well as at a central site. All fixed-site pDRs were collocated with Harvard Impactors for PM_{2.5} (HI_{2.5}). By examining the differences between the time-weighted average concentrations calculated from the real-time pDRs' readings and recorded internally by the pDRs, we identified 9.1% of the pDRs' measurements suffered from negative drifts. By comparing the pDRs' daily base level with the HI_{2.5} measurements, we identified 5.7% of the pDRs' measurements suffered from positive drifts. High relative humidity (RH) affected outdoor pDR measurements, even when a heater was used. Results from a series of chamber experiments suggest that the heated air stream cooled significantly after leaving the heater and entering the pDR light-scattering chamber. An RH correction equation was applied to the pDR measurements to remove the RH effect. The final R² values

between the fixed-site pDRs and the collocated HI_{2.5} measurements ranged between 0.53 and 0.72. We concluded that with a carefully developed QC procedure, personal nephelometers can provide high-quality data for assessing PM exposures on subjects and at fixed locations. We also recommend that outdoor pDRs be operated in the active mode without a heater and that the RH effect be corrected with an RH correction equation.

Wuthrich B. *[Epidemiology of allergies in Switzerland].* Ther Umsch. 2001; 58(5) : 253-8.p **Abstract:** The Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) was carried out during 1991-1993 in eight Swiss areas with different environmental characteristics. The cross-sectional examination included 9651 adults, aged 18-60 years, who all participated in a detailed interview. In 8357 subjects complete allergy skin and in-vitro tests were available in addition. The prevalence of atopic sensitization (positive skin prick test to any of the tested inhalant allergens and/or a positive Phadiatop as an in-vitro screening test for atopy) was 32.3%, with a higher prevalence in males (35.7%) than in females (28.8%). Skin sensitization was predominantly caused by grass pollen (12.7%), followed by house dust mite (8.9%), silver birch pollen (7.9%) and cat epithelia (3.8%). 11.1% suffered from current hay fever, 6.8% from asthma, 4.5% from atopic asthma. Smokers had statistically significant ($p < 0.001$) higher mean serum IgE concentrations (geometric mean 39.7 kU/l) than nonsmokers (27.2 kU/l). In Phadiatop positive subjects, the IgE levels were highest, with a mean of 104.3 kU/l (99.0-109.8). The SCARPOL Study (Swiss Study on Childhood Allergy and Respiratory Symptoms with respect to Air Pollution and Climate) is based on a sample of 4470 children from 10 different areas who completed parental questionnaire. 35.7% of the 2879 children who underwent skin prick testing were sensitized to at least one tested aeroallergen, 22.5% to grass pollen, 12.4% to house dust mites, 11.4% to birch pollen and 6.4% to cat epithelia. 17% of the 13- to 15-year-old (8th grade) suffered from hayfever. The prevalence of asthma (ever) for the whole sample was 9%, without differences between the age groups. The lifetime prevalence of atopic dermatitis was 13% and the current prevalence 8%. The risk of eczema was higher in Swiss children than in children of immigrants, in infants with a birthweight below 2500 g, in children with a positive family history of atopic dermatitis, and in children from higher socioeconomic classes. Farm children ($n = 133$) living in a rural area suffer less frequently from pollinosis (2.4%) and bronchial asthma (1.6%) than children ($n = 966$) with no direct contact to agriculture, but living in the same area (prevalence of hayfever 18.3%, of asthma 9.1%). This figures are similar to results from former East and Western Germany and from the former USSR and Baltic areas. These large Swiss epidemiologic studies confirmed both, the high prevalence of atopy and atopic diseases, and the health impact of moderate air pollution levels and of factors associated with the 'western lifestyle'.

Xu B. et al. *Body build from birth to adulthood and risk of asthma.* Eur J Public Health. 2002; 12(3) : 166-70.p **Abstract:** BACKGROUND: Few reports aimed at the study of adulthood obesity and asthma have taken into account the effects of size at birth and obesity in adolescence. This paper examines the combined effect of size at birth and obesity in both adolescence and adulthood on the risk of asthma at age 31 years. METHODS: The study was derived from a prospectively population-based Finnish birth cohort born in 1966, for which data were collected in pregnancy and at various ages. Adulthood doctor-diagnosed asthma with current symptoms and results of skin prick tests were obtained in 1997. The analysis was limited to 4719 subjects with complete information on asthma and atopy and anthropometric measures at various ages. RESULTS: Ponderal index at birth had a U-shaped association with adult atopy, OR 1.30 (95% CI: 1.11-1.52) for the lowest tertile and OR 1.33 (95% CI: 1.13-1.55) for the highest tertile, as compared to the middle tertile. The association was independent of obesity later in life. Those obese (BMI \geq 30) in adolescence (OR 2.09, 95%

CI: 1.23-3.57) and in adulthood (OR 1.99, 95% CI: 1.14-3.47) had a higher occurrence of adult asthma than those with BMI < 85th percentile. Both estimates were reduced after mutual adjustment. CONCLUSIONS: Size at birth has a long-lasting effect on atopy in adulthood, which is independent of weight in adolescence and adulthood. Those who were obese in adolescence and adulthood tended to have a higher risk of asthma in adulthood. These findings underline the importance of considering the life course of obesity in the analyses of asthma and atopy.

Xu G. *Prof. Xiao Shaoqin's experience in acupuncture treatment.* J Tradit Chin Med. 2001; 21(4) : 273-6.p

Xuan W. et al. *Risk factors for onset and remission of atopy, wheeze, and airway hyperresponsiveness.* Thorax. 2002; 57(2) : 104-9.p
Abstract: BACKGROUND: Although many children with asthma may have a remission as they grow and other children who did not have asthma may develop asthma in adult life, knowledge about the factors that influence the onset and prognosis of asthma during adolescence and young adulthood is very limited. METHODS: A cohort of 8-10 year old children (n=718) living in Belmont, New South Wales, Australia were surveyed six times at 2 yearly intervals from 1982 to 1992, and then again 5 years later in 1997. From this cohort, 498 subjects had between three and seven assessments and were included in the analysis. Atopy, airway hyperresponsiveness (AHR), and wheeze in the last 12 months were measured at each survey. Late onset, remission, and persistence were defined based on characteristics at the initial survey and the changes in characteristics at the follow up surveys. RESULTS: The proportion of subjects with late onset atopy (13.7%) and wheeze (12.4%) was greater than the proportion with remission of atopy (3.2%) and wheeze (5.6%). Having atopy at age 8-12 years (OR 2.8, 95% CI 1.5 to 5.1) and having a parental history of asthma (OR 2.0, 95% CI 1.02 to 4.13) were significant risk factors for the onset of wheeze. Having AHR at age 8-12 years was a significant risk factor for the persistence of wheeze (OR 4.3, 95% CI 1.3 to 15.0). Female sex (OR 1.9, 95% CI 1.01 to 3.60) was a significant risk factor for late onset AHR whereas male sex (OR 1.9, 95% CI 1.1 to 2.8) was a significant risk factor for late onset atopy. CONCLUSIONS: The onset of AHR is uncommon during adolescence, but the risk of acquiring atopy and recent wheeze for the first time continues during this period. Atopy, particularly present at the age of 8-10 years, predicts the subsequent onset of wheeze.

Yamada Y. et al. *Creola bodies in wheezing infants predict the development of asthma.* Pediatr Allergy Immunol. 2004; 15(2) : 159-62.p
Abstract: Creola bodies (CrBs) have been shown to be present specifically in the sputum of adults with asthma, and are clinically useful in the estimation of airway hyper-responsiveness through correlation with the levels of eosinophil cationic protein in the sputum. Our aim was to investigate whether CrBs can be detected in the sputum of wheezing infants, and the clinical significance of CrBs in wheezing infants in the development of asthma. Twenty-three wheezing infant patients, mean age 5.3 months, were studied. The presence of CrBs in the sputum was determined by Papanicolaou's stain. The patients were divided into two groups: CrB positive [CrB(+)] and CrB negative [CrB(-)]. In addition, we examined the relationship between the presence of CrBs and the asthma symptom scores that occurred during a 1-month post-discharge period. The following results were obtained: (i) CrBs were detected in 15 of 23 (65%) wheezing infants; (ii) the asthma symptom scores after discharge was significantly higher in the CrB(+) group than in the CrB(-) group ($p < 0.001$); (iii) in the infants experiencing their first episode of wheezing, the asthma symptom scores during the post-discharge period was also significantly higher in the CrB(+) group than in the CrB(-) group ($p < 0.05$). Furthermore, infantile asthma was diagnosed in 12 (80.0%) infants in the CrB(+) group during the following 2-yr period, but none in the CrB(-) group. These findings

suggest that CrBs detected in the sputum of wheezing infants may be used to identify the progression to infantile asthma.

Yamagami S. et al. *Chemokine receptor gene expression in giant papillae of atopic keratoconjunctivitis.* Mol Vis. 2005; 11 : 192-200.p
Abstract: PURPOSE: Major chemokine receptors in the giant papillae of atopic keratoconjunctivitis (AKC) have yet to be determined. We evaluated chemokine receptor genes and their ligand expressions in upper tarsal conjunctival giant papillae of AKC with atopic dermatitis and/or asthma. METHODS: CC, CXCR4, and CX3CR1 chemokine receptor (R) gene expression levels in giant papillae of five clinically active AKC patients and in three age matched non-allergic control conjunctiva were measured with a multi-probe ribonuclease protection assay (RPA) system. The ligands of abundant chemokine receptors in the giant papillae were examined by immunohistochemistry or reverse transcription-polymerase chain reaction. Interleukin (IL)-4 and IL-13 gene expression levels were measured with RPA. Ligand expression in cultured human conjunctival fibroblasts was examined by reverse transcription-polymerase chain reaction. RESULTS: High CXCR4 and CCR4 gene expression levels were detected in the giant papillae of all (CXCR4) and four out of five (CCR4) patients. As a CCR4-ligand, thymus and activation regulated cytokine (TARC/CCL17) rather than macrophage derived chemokine (MDC/CCL22), was predominant immunohistochemically in the giant papillae. Giant papillae with high CCR4 gene expression levels showed high IL-4 and IL-13 expression. Cultured human conjunctival fibroblasts express stromal cell derived factor-1 (SDF-1/CXCL12) in vitro. CONCLUSIONS: CXCR4 and CCR4 are the major chemokine receptor genes expressed in the giant papillae of AKC with atopic dermatitis and/or asthma. Our findings suggest a role for CXCR4 and CCR4 in the formation of giant papillae.

Yao T.C. et al. *MCP-1 gene regulatory region polymorphism in Chinese children with mild, moderate and near-fatal asthma.* Allergy. 2004; 59(4) : 436-41.p
Abstract: BACKGROUND: A polymorphism in the monocyte chemoattractant protein 1 (MCP-1) gene regulatory region has been associated with asthma in Caucasians. This polymorphism is possibly endemic to the Asian region, but its impact on Asian populations is unclear. In addition, the relationship of this marker with life-threatening asthma has not been clarified. The aim of this study was to test the genetic association between the MCP-1 -2518A/G polymorphism and asthma/atopy in a cohort of Chinese children, with particular emphasis on those patients who had experienced life-threatening asthma attacks. METHODS: Forty-eight children with near-fatal asthma, 134 mild-to-moderate asthmatics, 69 allergic-disorder cases without asthma, and 107 nonasthmatic, nonatopic control children were genotyped by a polymerase chain reaction-based assay. RESULTS: Comparison of the four groups of children (n = 358) revealed no detectable differences in genotype or allele frequencies of the MCP-1 -2518A/G polymorphism. There was no evidence of association between the polymorphism and any of the outcomes of interest including clinical severity, blood eosinophil count, atopy, total serum IgE levels, and degree of bronchial hyper-responsiveness. CONCLUSION: These results suggest that the MCP-1 -2518A/G polymorphism is not a risk factor for near-fatal asthma. Furthermore, this polymorphism seems to play no role in the development of asthma or atopy in Chinese subjects, possibly as a result of the genetic heterogeneity between Asian and Caucasian populations with respect to regulation of MCP-1 expression. Our results underscore the necessity of accounting for ethnic background in the investigation of asthma-predisposition genes.

Yasui K. et al. *Neutrophilic inflammation in childhood bronchial asthma.* Thorax. 2005; 60(8) : 704-5.p

Yawn B.P. et al. *Asthma severity: the patient's perspective.* J Asthma. 2004; 41(6) : 623-30.p **Abstract:** BACKGROUND: Although asthma is a common condition, limited epidemiological data exists on the distribution or course of asthma severity. We know even less about how patients or parents rate the severity of their or their child's asthma or what factors they associate with more severe asthma. A large nationally diverse sample of asthma patients' self-assessment of severity is available but has not been analyzed to look at asthma severity from the patients' perspective. METHOD: Data from the "household" and "event" files from the 1999 Medical Expenditure Panel Survey were combined to obtain a distribution of patient-reported asthma severity and the health care utilization, medication usage, and personal characteristics associated with different levels of self-reported severity for that subgroup that answered the chronic disease portion of the survey. RESULTS: Almost two thirds of patients (63% of adults) or parents (65% of children) described their or their child's asthma as very or somewhat serious. Among both children and adults, more severe asthma was associated with greater numbers of missed school and workdays, and lower overall health status. The associated differences in health utilization varied by age. Models of severity based on available NAEP criteria explained less than 10% of the participant's variation in self-reported asthma severity. CONCLUSION: Parents and patients with asthma appear to use different metrics than physicians and researchers to define the more severe categories of asthma. This disparity suggests the need for an asthma measure that is more widely understood, and accepted by patients and clinicians to serve as a tool to improve asthma-related communications and the achievement of mutually determined therapy goals.

Yawn B.P. et al. *Using the ecology model to describe the impact of asthma on patterns of health care.* BMC Pulm Med. 2005; 5 : 7.p **Abstract:** BACKGROUND: Asthma changes both the volume and patterns of healthcare of affected people. Most studies of asthma health care utilization have been done in selected insured populations or in a single site such as the emergency department. Asthma is an ambulatory sensitive care condition making it important to understand the relationship between care in all sites across the health service spectrum. Asthma is also more common in people with fewer economic resources making it important to include people across all types of insurance and no insurance categories. The ecology of medical care model may provide a useful framework to describe the use of health services in people with asthma compared to those without asthma and identify subgroups with apparent gaps in care. METHODS: This is a case-control study using the 1999 U.S. Medical Expenditure Panel Survey. Cases are school-aged children (6 to 17 years) and young adults (18 to 44 years) with self-reported asthma. Controls are from the same age groups who have no self-reported asthma. Descriptive analyses and risk ratios are placed within the ecology of medical care model and used to describe and compare the healthcare contact of cases and controls across multiple settings. RESULTS: In 1999, the presence of asthma significantly increased the likelihood of an ambulatory care visit by 20 to 30% and more than doubled the likelihood of making one or more visits to the emergency department (ED). Yet, 18.8% of children and 14.5% of adults with asthma (over a million Americans) had no ambulatory care visits for asthma. About one in 20 to 35 people with asthma (5.2% of children and 3.6% of adults) were seen in the ED or hospital but had no prior or follow-up ambulatory care visits. These Americans were more likely to be uninsured, have no usual source of care and live in metropolitan areas. CONCLUSION: The ecology model confirmed that having asthma changes the likelihood and pattern of care for Americans. More importantly, the ecology model identified a subgroup with asthma who sought only emergent or hospital services.

Yawn B.P. et al. *Outcome results of a school-based screening program for undertreated asthma.* Ann Allergy Asthma Immunol. 2003; 90(5) : 508-15.p **Abstract:** BACKGROUND: Undertreatment of asthma is

associated with significant potentially preventable morbidity, including frequent school absences. Guideline dissemination and clinician education have met with variable success. School-based identification of children with potentially undertreated asthma may provide an alternative strategy for improving asthma management in children. OBJECTIVE: To evaluate the effectiveness of school-based identification of potentially undertreated asthma. METHODS: A controlled trial of school-based identification of children with known but symptomatic asthma using mailed parent surveys, letters recommending medical follow-up, and medical record review to evaluate changes in asthma treatment after referral. RESULTS: Most parents (79.9%, n = 5,116 respondents) responded to the survey and 19.4% (n = 994) of children were reported to have a physician diagnosis of asthma or reactive airway disease. Letters of referral were sent to 489 children with parent-reported asthma who were identified as having potentially undertreated asthma. Approximately one-third (31.2%, n = 153) of these children had physician visits, and 92 (18.8% of all referred) had documented medication changes. In addition, there were 20 new physician diagnoses in this group of children. In the control group of 604 children with asthma, there were significantly fewer children with asthma-related visits (131, 21.7%, P = 0.0004) and children with medication changes (74, 12.3%, P = 0.002) in a comparable 6-month window. CONCLUSIONS: School-based screening or case identification increased the number of physician asthma-related visits and changes in asthma therapy.

Yazicioglu M. et al. *Sensitization to common allergens, especially pollens, among children with respiratory allergy in the Trakya region of Turkey.* Asian Pac J Allergy Immunol. 2004; 22(4) : 183-90.p **Abstract:** Asthma and allergic rhinitis are common problems in children and the causative pollen allergens vary according to the geographical area. The aim of this study was to investigate patterns of sensitization to common inhalant allergens, especially pollens, in Turkish children living in the Trakya region and to determine differences between rural and urban areas. Allergen skin testing was prospectively performed on 539 children aged between 4 and 17 years with respiratory allergy. The reaction was considered to be positive if the mean wheal diameter was at least 3 mm greater than that of the negative controls. We detected positive skin reactions in 420 (77.9%) children. Two hundred and eighty-one (52.1%) mite, 277 (51.4%) pollen, 174 (32.3%) mold, 65 (12.1%) animal dander, 12 (2.2%) cockroach and 6 (1.1%) latex skin sensitivities were detected. Among the pollen allergies 173 were cereal pollen (32.1%), 170 grass pollen (31.5%) and 144 tree pollen allergies (26.7%). The most common positive skin test among the pollens was to cultivated wheat (*Triticum vulgare*) (n = 116, 21.5%), followed by rye grass (*Lolium perenne*) and orchard grass (*Dactylis glomerata*). Positive skin reactions to *Alternaria*, to *Candida albicans*, and to all pollens except *Ulmus competris*, *Pinus sylvestris*, *Platanus vulgaris* and *Tilia platyphyllos*, were higher in children with allergic rhinitis than in those with asthma. In children from rural areas, allergic skin reactivity was found to be more common against *Candida albicans*, sheep dander and all pollens except *Corylus avellana*, *Fraxinus excelsior*, *Populus alba*, *Pinus sylvestris*, *Platanus vulgaris* and *Chenopodium album*, than in urban children. Although Trakya is close to Greece and other Mediterranean countries, this study suggests that the pollens, which sensitize children, are not similar.

Yeatts K. et al. *Health consequences associated with frequent wheezing in adolescents without asthma diagnosis.* Eur Respir J. 2003; 22(5) : 781-6.p **Abstract:** Using questions from the International Study of Asthma and Allergies in Childhood, this study evaluated the association between undiagnosed frequent wheezing and health consequences in adolescents. The North Carolina School Asthma Survey provided self-reported questionnaire data on respiratory health from 122,829 children aged 12-14 yrs. The frequency of health consequences were compared among undiagnosed frequent wheezers, diagnosed asthmatics, and children with no wheezing

symptoms or diagnosed asthma. The odds of wheezing-related sleep disturbances, limited activities, and missed school were higher among undiagnosed frequent wheezers, relative to diagnosed asthmatics. The frequency of emergency room visits and hospitalisations did not differ substantially between the undiagnosed wheezing and diagnosed asthma groups, though the undiagnosed group was less likely to have visited a physician for wheezing in the past year. Children with frequent wheezing symptoms but no asthma diagnosis experience substantial illness-related morbidity similar to that of diagnosed asthmatics. Undiagnosed frequent wheezers require more recognition from primary care physicians and need active disease management to reduce health consequences.

Yeatts K. et al. *Health consequences for children with undiagnosed asthma-like symptoms.* Arch Pediatr Adolesc Med. 2003; 157(6) : 540-4.p **Abstract:** **BACKGROUND:** A growing body of evidence indicates that there are a substantial number of children who report asthma-like symptoms and are not diagnosed with asthma. However, there is little information on the health consequences of asthma-like symptoms for children with these symptoms and no asthma diagnosis. **OBJECTIVE:** To assess the prevalence and health consequences (school absences, sleep disturbances, activity limitations, physician visits, emergency department visits, and hospitalizations) of asthma-like symptoms among children with and without physician diagnosis. **STUDY DESIGN:** We surveyed 122 829 children aged 12 to 14 years in 499 North Carolina public middle schools. A standardized questionnaire (International Study of Asthma and Allergies in Childhood [ISAAC]) containing video scenes of adolescents experiencing asthma-like symptoms was adapted to include questions on health consequences. **RESULTS:** Seventeen percent (n = 21 184) reported current asthma-like symptoms with no diagnosis of asthma (during the last 12 months.) Eleven percent (n = 13 619) of the children reported physician-diagnosed asthma with current asthma-like symptoms. Of the children with asthma-like symptoms and no diagnosis of asthma, 20% missed a half day or more of school per month because of wheeze, 25% had limited activities because of wheeze once or more per month, and 32% had sleep disturbances because of wheeze in the last 4 weeks. Seven percent of children with current asthma-like symptoms but no diagnosis reported 1 or more emergency department visits for asthma-like symptoms, and 5% reported wheeze-related hospitalizations in the last year. Of children with physician-diagnosed asthma, almost half (47%) reported missing a half day or more of school in the last month. Thirty percent of physician-diagnosed children reported 1 or more emergency department visits in the last year for asthma-like symptoms. **CONCLUSIONS:** The health consequences of asthma-like symptoms in children with no diagnosis are substantial; these children are essentially untreated. Better detection of this disease group by the medical community has the potential to improve health consequences for these children.

Yeatts K.B. et al. *Prevalence and consequences of asthma and wheezing in African-American and White adolescents.* J Adolesc Health. 2001; 29(5) : 314-9.p **Abstract:** **PURPOSE:** To describe the functional consequences of health care utilization for wheezing symptoms and diagnosed asthma in a multiracial school-based population. **METHODS:** Wheezing symptoms and physician-diagnosed asthma were measured in 2059 eighth graders with the International Study of Asthma and Allergies in Children video questionnaire. The sample site population was 40% African-American, 53% White, and 49% girls. Thirty-two percent of the children were on the free school lunch program. Adolescents self-reported their wheezing symptoms and physician diagnosis in response to the video wheezing scenes. They also answered questions on activity limitations, school attendance, and sleep disturbances owing to their wheezing symptoms. Multiple logistic regression was used to calculate odds ratios and adjust for potential confounders. **RESULTS:** Nine percent of the adolescents reported physician-diagnosed asthma with current symptoms and 27% reported current wheezing with no diagnosis of

asthma. Physician-diagnosed asthmatics and wheezers were 2.6 (95% confidence interval [CI] 1.9, 3.6) and 1.8 (95% CI 1.4, 2.2) times more likely, respectively, to miss school days because of wheezing symptoms than asymptomatic adolescents. Diagnosed asthmatics were 7.8 (95% CI 5.5, 11.2) times and wheezers 4.7 (95% CI 3.5, 6.1) times more likely to have sleep disturbances than asymptomatic adolescents. Diagnosed asthmatics were 49 (95% CI 30.0, 79.8) times and wheezers 4.8 (95% CI 3.0, 7.5) times as likely to report a clinic visit for wheezing than asymptomatic adolescents. African-Americans had similar prevalence of wheezing, compared with Whites, although African-Americans were 1.4 (95% CI 1.1, 1.9) times as likely to have physician-diagnosed asthma. Girls were twice as likely to report physician-diagnosed asthma and wheezing symptoms as were boys. **CONCLUSIONS:** Adolescents with wheezing experienced functional consequences comparable to those of adolescents with physician-diagnosed asthma. Although wheezers may have less severe asthma than diagnosed asthmatics, the functional consequences of wheezing are likely to impair school performance and limit activity.

Yeoh S.M. et al. *Sensitization profiles of Malaysian and Singaporean subjects to allergens from Dermatophagoides pteronyssinus and Blomia tropicalis.* Int Arch Allergy Immunol. 2003; 132(3) : 215-20.p **Abstract:** **BACKGROUND:** The house dust mites Dermatophagoides pteronyssinus (Der p) and Blomia tropicalis (Blo t) are the most common house dust mite species in Southeast Asia. To date, there have only been a few studies on the sensitization profile of the general populations in Southeast Asia to house dust mites. The aim of this study was to determine the profiles of Der p and Blo t sensitization among Singaporean and Malaysian subjects. **METHODS:** Enzyme-linked immunosorbent assay was used to detect specific IgE to Der p and Blo t mite crude extracts as well as purified Der p 1, Der p 2 and Blo t 5 allergens. Sera used were from 229 Singaporean subjects (124 with rhinitis, 105 without rhinitis) and 143 Malaysian subjects (94 adults and 49 children with asthma). **RESULTS:** The sensitization profile of rhinitis subjects to the dust mite allergens used in this study was as follows: Blo t extract positive: 91/124 (73%); Blo t 5 positive: 62/124 (50%); Der p extract positive: 61/124 (49%); Der p 1 positive: 53/124 (43%); Der p 2 positive: 45/124 (36%). The nonrhinitis subjects' sensitization profile was as follows: Blo t extract positive: 60/105 (57%); Blo t 5 positive: 24/105 (23%); Der p extract positive: 38/105 (36%); Der p 1 positive: 14/105 (13%); Der p 2 positive: 17/105 (16%). The study of Malaysian asthmatic adults showed that 39% of them were sensitized to Der p 1, 32% to Der p 2 and 37% to Blo t 5. Among the asthmatic children, sensitization to Blo t 5, Der p 1 and Der p 2 was 90, 57 and 39%, respectively. **CONCLUSION:** This study clearly revealed that dual sensitization to B. tropicalis and D. pteronyssinus is common in the general populations of Singapore and Malaysia. Sensitization to Blo t 5 is more prevalent than to Der p 1 and Der p 2.

Yilmaz A. et al. *Cockroach allergy in a group of Turkish children with respiratory allergies.* Turk J Pediatr. 2004; 46(4) : 344-9.p **Abstract:** Exposure to cockroach may lead to exacerbations of bronchial asthma and/or allergic rhinitis in sensitized patients. Although there is a widespread belief that cockroach allergy is a common problem in patients with respiratory allergies, little is known in Turkish children. In order to investigate the prevalence and characteristics of cockroach allergy in respiratory allergic children, we performed a study in newly referred children with respiratory allergies. All patients underwent questionnaire-interview and skin prick tested with common inhalant allergens in addition to two cockroach allergens: Blatella germanica (Bg) and Periplaneta americana (Pa). A subgroup of patients was also serologically investigated for specific IgE against Bg and house dust mite. Three hundred- and thirty-seven children aged 2-16 years were recruited for the study and 77.7% of these were atopic, with the most common indoor and outdoor allergens of house dust mite (47.5%) and grass pollens (45.1%), respectively. According to the prick test results,

allergies to Bg and Pa were 11.9% and 7.4%, respectively, and there was a weak correlation between size of the prick test and specific IgE levels for Bg allergen. Almost 30% of the cockroach-sensitive patients were allergic to both cockroach antigens. Seventy percent of cockroach-sensitive patients were also sensitive to house dust mite, and only 1% were monosensitive. Dwellings in the Middle Anatolia and Black Sea regions were less commonly infested by cockroach compared to the dwellings in other regions. In conclusion, our preliminary study showed that cockroach sensitization is common among children with respiratory allergies irrespective of infestation history, suggesting that addition of cockroach allergen to the routine allergy screening panel is critical.

- Yoo Y. et al.** *Birth month and sensitization to house dust mites in asthmatic children.* Allergy. 2005; 60(10) : 1327-30.p Abstract: BACKGROUND: Early exposure to high quantities of allergen has an important role in the incidence of atopic sensitization. In fact, subjects sensitized to house dust mites (HDMs) have a significantly higher proportion of births in the season when HDMs are most abundant. OBJECTIVE: The aim of this study was to investigate whether birth month patterns differ for asthmatic patients sensitized only to HDMs and for those sensitized to HDMs and other allergen(s). METHODS: Among 2225 patients with asthma, aged 10-16 years, 1642 sensitized to HDMs were identified by skin prick testing. This group was composed of patients sensitized only to HDMs (n = 715) and patients sensitized to HDMs and other allergen(s) (n = 927). The birth month distributions of the group of HDM-sensitive asthmatics or its subgroups were compared with that of a reference population (total live births in the same years as the studied subjects). The risk ratio of a given birth month in relation to all the other months was calculated as an odds ratio (OR) with the corresponding 95% confidence interval (CI). RESULTS: A significant difference in birth month distribution was observed for HDM-sensitive asthmatics ($\chi^2 = 23.6$, $P = 0.015$), with higher rates of birth in August (OR: 1.23, 95% CI: 1.04-1.46) and September (1.24, 1.04-1.46). When the two subgroups were analyzed separately, significantly more births were noted in August (1.34, 1.06-1.71) and September (1.34, 1.05-1.70) for those sensitized only to HDMs, whereas no such birth month preference was observed for those sensitized to HDMs and other allergen(s). CONCLUSIONS: The HDM-positive asthmatics showed a greater proportion of births in August and September, which correspond to high HDM exposure. However, this birth month pattern was evident in asthmatic-sensitive only to HDMs, but was not observed in those sensitive to HDMs and other allergen(s).
- Yoos H.L. et al.** *Barriers to anti-inflammatory medication use in childhood asthma.* Ambul Pediatr. 2003; 3(4) : 181-90.p Abstract: OBJECTIVES: To identify parental barriers to anti-inflammatory medication use and to develop an instrument for use in research and health care settings to identify at-risk populations. METHODS: Instrument development consisted of 4 phases: 1) gaining the professional perspective (N = 8 experts in asthma management), 2) gaining the perspective of parents of children with asthma (qualitative interviews with 21 parents), 3) instrument pretesting and refinement (N = 133 parents), and 4) determining the instrument's psychometric properties. Study participants were diverse in race, socioeconomic status, and the child's illness severity. The final instrument consisted of 51 questions in 5 domains (nature of disease, cause, ideas about medications, treatment expectations, and health care provider relationship). RESULTS: The final instrument exhibited strong reliability (Cronbach alpha =.87) and validity. Significant barriers to appropriate anti-inflammatory medication use were parents' diminished treatment expectations and fears about anti-inflammatory medications. Minority families were more likely than white families to view asthma as unpredictable and uncontrollable ($P = .01$) and to have negative attitudes toward anti-inflammatory medications ($P = .004$). Eight questions were significantly correlated with a suboptimal medication regimen and may serve as a "quick

screen" for potential nonadherence in clinical settings. CONCLUSIONS: Diminished treatment expectations and negative attitudes toward anti-inflammatories may be powerful predictors of nonadherence to medications.

- Yorke J. et al.** *Family therapy for chronic asthma in children.* Cochrane Database Syst Rev. 2005; (2) : CD000089.p Abstract: BACKGROUND: Psychosocial and emotional factors are important in childhood asthma. Nevertheless, drug therapy alone continues to be the main treatment. Treatment programmes that include behavioural or psychological interventions have been developed to improve disturbed family relations in the families of children with severe asthma. These approaches have been extended to examine the efficacy of family therapy to treat childhood asthma in a wider group of patients. This review systematically examines these studies. OBJECTIVES: Recognition that asthma can be associated with emotional disturbances has led to the investigation of the role of family therapy in reducing the symptoms and impact of asthma in children. The objective of this review was to assess the effects of family therapy as an adjunct to medication for the treatment of asthma in children. SEARCH STRATEGY: We searched the Cochrane Airways Group trials register, PsycInfo and PsycInfo. Searches are current as of January 2005. SELECTION CRITERIA: Randomised trials comparing children undergoing systematic therapy focusing on the family in conjunction with asthma medication, with children taking asthma medication only. DATA COLLECTION AND ANALYSIS: Two reviewers assessed the studies for inclusion in the review. MAIN RESULTS: Two trials with a total of 55 children were included. It was not possible to combine the findings of these two studies because of differences in outcome measures used. In one study, gas volume, peak expiratory flow rate and daytime wheeze showed improvement in family therapy patients compared to controls. In the other study, there was an improvement in overall clinical assessment and number of functionally impaired days in the patients receiving family therapy. There was no difference in forced expiratory volume or medication use in both studies. AUTHORS' CONCLUSIONS: There is some indication that family therapy may be a useful adjunct to medication for children with asthma. This conclusion is limited by small study sizes and lack of standardisation in the choice of outcome measures.
- Yoshihara S. et al.** *Association of epithelial damage and signs of neutrophil mobilization in the airways during acute exacerbations of paediatric asthma.* Clin Exp Immunol. 2006; 144(2) : 212-6.p Abstract: We examined whether epithelial damage is associated with mobilization of neutrophils or eosinophils in the airway lumen during acute exacerbations of paediatric asthma. Aspirated sputum samples were harvested from 65 paediatric patients (mean age 3.4 +/- 0.4 years) during acute exacerbations of asthma. Patients with signs of infection (i.e. "Creola bodies") in the aspirated sputum was utilized as a marker of epithelial damage. Among the paediatric asthma patients, 60% displayed Creola bodies (CrB+: n = 39) in their sputum samples whereas the remaining patients did not (CrB-: n = 26). CrB+ patients displayed more than a 20-fold increase in the concentration of the neutrophil-mobilizing cytokine interleukin (IL)-8 (pg/ml) and of the neutrophil product neutrophil elastase (NE, g/l), respectively, compared with CrB- patients (IL-8: 7468.2 +/- 1953.6 versus 347.9 +/- 72.6, $P < 0.01$; NE: 2072.4 +/- 419.0 versus 438.5 +/- 125.7, $P < 0.01$). Even though not statistically significant, a corresponding trend was observed for the relative number of sputum neutrophils. In contrast, the concentration of the eosinophil-mobilizing cytokine IL-5 and the eosinophil product ECP tended to be lower in CrB+ than in CrB- patients ($P > 0.05$). In conclusion, as indicated by the analysis of aspirated sputum, epithelial damage is associated with a locally enhanced chemotactic signal for and activity of neutrophils, but not eosinophils, during acute exacerbations of paediatric asthma. It remains to be determined whether these indirect signs of neutrophil

mobilization in the airway lumen mirror an increased number of neutrophils in the surrounding airway tissue.

Yoshikawa K. et al. *A novel single-nucleotide substitution, Glu 4 Lys, in the leukotriene C4 synthase gene associated with allergic diseases.* Int J Mol Med. 2005; 16(5) : 827-31.p **Abstract:** Cysteinyl leukotrienes (cysLTs) play important roles in bronchial asthma, and can mediate bronchial smooth muscle constriction and increase mucous secretion, vascular permeability and cellular infiltration. We identified a novel heterozygous single-nucleotide substitution 10G>A (Glu 4 Lys) in the first exon of the leukotriene C4 synthase gene (LTC4S). This substitution was detected in 5 of 141 allergic patients, but not in 110 nonallergic subjects. There was a difference in the Glu 4 Lys frequency between the allergic patients and nonallergic subjects (Fisher's exact test, $p=0.0460$). The five patients with Glu 4 Lys had allergic diseases such as bronchial asthma and/or allergic dermatitis. Furthermore, a familial analysis of Glu 4 Lys revealed a link with allergic diseases. Thus, our results suggest that Glu 4 Lys in the LTC4S might be associated with allergic diseases.

Young B. et al. *Parents' accounts of wheeze and asthma related symptoms: a qualitative study.* Arch Dis Child. 2002; 87(2) : 131-4.p **Abstract:** AIMS: To examine parents' accounts of how they recognise and judge respiratory symptoms in children, and to investigate their interpretations of respiratory survey questions about wheeze, shortness of breath, and cough. METHODS: Qualitative study using semistructured interviews. Data were analysed using the constant comparative method. Nineteen parents of children aged under 6 years were recruited from a cohort of parents who had responded to an earlier respiratory symptom survey and from one general practice. RESULTS: Parents judged respiratory symptoms using a range of cues, including changes in the sound of breathing and changes in appearance and behaviour. Experiential resources and contextual factors played an important role in parents' judgements. Interpretations of questions about respiratory symptoms were varied, particularly in relation to the terms "attacks of wheeze" and "shortness of breath". Parents' descriptions of wheeze differed from descriptions of the sound of wheeze used in some survey questionnaires. Parents drew fine distinctions between different "types" of cough and identified a distinct "asthma" cough. CONCLUSIONS: Attention needs to be given to the complexity of reporting respiratory symptoms in children and to the importance of contextual factors in parents' judgements. We suggest that questions which require parents to report on children's internal feelings or states be avoided. Consideration should be given to providing parents with explicit direction on what cues to attend to or ignore in reporting symptoms, and to clarifying some questions that are currently used in clinical practice and in surveys.

Yu J. et al. *Bronchial responsiveness and serum eosinophil cationic protein levels in preschool children with recurrent wheezing.* Ann Allergy Asthma Immunol. 2005; 94(6) : 686-92.p **Abstract:** BACKGROUND: Bronchial hyperresponsiveness is a universally recognized phenomenon of asthma, and increased levels of eosinophil cationic protein (ECP) have been identified in the serum of patients with asthma. OBJECTIVES: To investigate whether enhanced bronchial responsiveness and elevated serum ECP levels are associated with recurrent wheezing in preschool children and to examine the possible relationship between these 2 variables. METHODS: We recruited 130 children aged 4 to 6 years: 59 with at least 3 episodes of wheezing in the previous year (current wheezers), 38 with a documented history of wheezing before 3 years of age but no subsequent wheezing episodes (past wheezers), and 33 who had never experienced wheezing (nonwheezers). The children underwent methacholine bronchial provocation tests using a modified auscultation method and blood sampling for the measurement of ECP levels. RESULTS: Current wheezers showed greater bronchial responsiveness than past wheezers and nonwheezers, as

demonstrated by lower provocation concentrations that caused audible wheeze and lower provocation concentrations that caused a decline in oxygen saturation of at least 5% from baseline. Likewise, current wheezers had higher serum ECP levels than the other 2 groups. Among current wheezers, ECP levels showed a significant negative correlation with provocation concentrations that caused oxygen desaturation and a marginally significant correlation with provocation concentrations that caused audible wheeze. CONCLUSIONS: Enhanced bronchial responsiveness and elevated serum ECP levels are associated with recurrent wheezing in 4- to 6-year-old children. These results suggest that wheezing during preschool years may be phenotypically similar to wheezing in older children.

Yu J. et al. *The relationship between delta-forced vital capacity (percent fall in forced vital capacity at the PC20 dose of methacholine) and the maximal airway response in patients who have mild asthma.* Allergy Asthma Proc. 2005; 26(5) : 366-72.p **Abstract:** Airway hypersensitivity is routinely evaluated by measuring the concentration (PC20) of inhaled methacholine or histamine that causes a 20% fall in forced expiratory volume in 1 second (FEV1). It has been suggested that a percentage fall in forced vital capacity (FVC) measured at the PC20 dose of inhaled agonist (deltaFVC) is a potentially useful clinical measure in patients who have asthma because it provides indirect information about gas trapping and therefore the maximal airway response. The relationships between serum eosinophil cationic protein (ECP) levels and the maximal airway response or deltaFVC are largely unknown. The aims of this study were to determine whether deltaFVC is correlated with the degree of maximal airway response and to examine the relationships between serum ECP and deltaFVC or maximal airway response in patients who have mild asthma. Fifty-eight patients with mild asthma underwent high-dose methacholine challenge testing. The PC20, maximal airway response, and deltaFVC were measured on the methacholine dose-response curves. Serum ECP levels also were determined. Subjects without a maximal response plateau ($n = 33$) had a significantly higher level of deltaFVC ($17.9 \pm 4.1\%$) than subjects with a plateau ($n = 25$; $14.9 \pm 4.8\%$). A significant correlation was found between deltaFVC and the level of maximal response plateau ($r = 0.446$; $p = 0.026$). Not only methacholine PC20 but also maximal airway response or deltaFVC had no relationships with serum ECP levels. Our results suggest that deltaFVC can be used as a surrogate marker of maximal airway response in patients who have mild asthma and that neither maximal airway response nor deltaFVC reflects blood eosinophil activation any more than methacholine PC20.

Yuksel H. et al. *Lower arrhythmogenic risk of low dose albuterol plus ipratropium.* Indian J Pediatr. 2001; 68(10) : 945-9.p **Abstract:** OBJECTIVE: Wheezy infants are in need of urgent bronchodilatation owing to their intermittent bronchoconstriction. beta 2 agonists are frequently used in emergencies and have previously shown to increase the QT dispersion (QTd), which may be associated with high risk of cardiac arrhythmia, in asthmatics. However, effect of low dose beta 2 agonist therapy in combination with the anticholinergic agents on QTd in wheezy infants is not known. This study aimed to assess the effect of standard dose of nebulized albuterol (NAB) and low doses of NAB combined with ipratropium-bromide (NIB) on QTd in wheezy infants. METHODS: Twenty-nine children, under 2 years old, with the diagnosis of wheezy infant with acute exacerbation were enrolled in the study. Thirteen were treated by standard dose of NA therapy (0.15 mg/kg) and low doses of NAB (0.075 mg/kg) plus NIB (250 micrograms/dose) therapy was given to the remaining subjects. Respiratory distress score, O2 saturation and side effects were studied and QTd were measured from the standard electrocardiograms at baseline and after treatment. Significant improvement was achieved in clinical score and oxygenation of both groups. RESULT: The evaluation of the corrected QTd (QTcd)

showed that there was no significant difference between pretreatment values of both groups ($p > 0.05$). However, while there was no statistically significant difference in the pre and post-treatment values of QTcd of infants treated with combination therapy, QTcd was found to be significantly increased in NAB group after treatment ($p < 0.05$). CONCLUSION: Our results suggest that, while clinical improvement is same, the increase of the QT dispersion is more prominent with the use of standard dose of NAB compared to low dose NAB plus NIB therapy. So, low dose of beta 2 agonist in combination with anticholinergic agents may be much safer than the use of standard dose of beta 2 agonists alone in regard to preventing the possibility of arrhythmogenic effects in wheezy infants with acute exacerbation.

Yusoff N.A. et al. *The effects of exclusion of dietary egg and milk in the management of asthmatic children: a pilot study.* J R Soc Health. 2004; 124(2) : 74-80.p **Abstract:** Current understanding of the use of exclusion diets in the management of asthma in children is limited and controversial. The aim of this study was to examine the effects of excluding eggs and milk on the occurrence of symptoms in children with asthma and involved 22 children aged between three and 14 years clinically diagnosed as having mild to moderate disease. The investigation was single blind and prospective, and parents were given the option of volunteering to join the 'experiment' group, avoiding eggs, milk and their products for eight weeks, or the 'control' group, who consumed their customary food. Thirteen children were recruited to the experimental group and nine to the control group. A trained paediatrician at the beginning and end of the study period assessed the children. A seven-day assessment of food intake was made before, during and immediately after the period of dietary intervention in both groups. A blood sample was taken from each child for determination of food specific antibodies and in those children who could do so, the peak expiratory flow rate (PEFR) was measured. Based on the recommended nutrient intake (RNI), the mean percentage energy intake of the children in the experimental group was significantly lower ($p < 0.05$) in the experimental group. After the eight-week study period and compared with baseline values, the mean serum anti-ovalbumin IgG and anti-beta lactoglobulin IgG concentrations were statistically significantly reduced ($p < 0.05$) for both in the experimental group. In contrast, the values for anti-ovalbumin IgG in the control group were significantly increased and those for anti-beta lactoglobulin IgG were practically unchanged. The total IgE values were unchanged in both groups. Over the study period, the PEFR in those children in the experimental group able to perform the test was significantly increased, but no such change was noted in the children in the control group who could do the test. These results suggest that even over the short time period of eight weeks, an egg- and milk-free diet can reduce atopic symptoms and improve lung function in asthmatic children.

Zacharasiewicz A. et al. *Repeatability of sodium and chloride in exhaled breath condensates.* Pediatr Pulmonol. 2004; 37(3) : 273-5.p **Abstract:** Exhaled breath condensate (EBC) has been proposed as a noninvasive tool to study airway inflammation. The reproducibility of breath condensates was recently questioned. We therefore measured sodium and chloride concentrations in EBC and assessed the repeatability of these measurements in healthy adults and children with airway disease. We investigated technical repeatability and within-day repeatability in five healthy adults, and compared these results with those of 10 asthmatic children and 9 children with cystic fibrosis (CF). We also assessed within-period repeatability in the healthy controls. We report that the variability of measurements was similar for within sample, within day, and between visits, for both normals and children with asthma and CF, and that the major source of variability of sodium and chloride measurements is restricted by the reproducibility of the measurement assay method used. The wide use of EBC is more likely to depend on the

development of highly sensitive and reproducible assays, rather than further refinements of the collection technique.

Zajac L.M. et al. *Costs of environmentally attributable diseases in the Arab-American community in the Detroit area.* Ethn Dis. 2005; 15(1 Suppl 1) : S1-47-8.p

Zanconato S. et al. *Office spirometry in primary care pediatrics: a pilot study.* Pediatrics. 2005; 116(6) : e792-7.p **Abstract:** OBJECTIVE: The aim of this study was to investigate the validity of office spirometry in primary care pediatric practices. METHODS: Ten primary care pediatricians undertook a spirometry training program that was led by 2 pediatric pulmonologists from the Pediatric Department of the University of Padova. After the pediatricians' training, children with asthma or persistent cough underwent a spirometric test in the pediatrician's office and at a pulmonary function (PF) laboratory, in the same day in random order. Both spirometric tests were performed with a portable turbine flow sensor spirometer. We assessed the quality of the spirometric tests and compared a range of PF parameters obtained in the pediatricians' offices and in the PF laboratory according to the Bland and Altman method. RESULTS: A total of 109 children (mean age: 10.4 years; range: 6-15) were included in the study. Eighty-five (78%) of the spirometric tests that were performed in the pediatricians' offices met all of the acceptability and reproducibility criteria. The 24 unacceptable test results were attributable largely to a slow start and failure to satisfy end-of-test criteria. Only the 85 acceptable spirometric tests were considered for analysis. The agreement between the spirometric tests that were performed in the pediatrician's office and in the PF laboratory was good for the key parameters (forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow between 25% and 75%). The repeatability coefficient was 0.26 L for forced expiratory volume in 1 second (83 of 85 values fall within this range), 0.30 L for forced vital capacity (81 values fall within this range), and 0.58 L/s for forced expiratory flow between 25% and 75% (82 values fall within this range). In 79% of cases, the primary care pediatricians interpreted the spirometric tests correctly. CONCLUSIONS: It seems justifiable to perform spirometry in pediatric primary care, but an integrated approach involving both the primary care pediatrician and certified pediatric respiratory medicine centers is recommended because effective training and quality assurance are vital prerequisites for successful spirometry.

Zanoni L.Z. et al. *Myocardial ischemia induced by nebulized fenoterol for severe childhood asthma.* Indian Pediatr. 2005; 42(10) : 1013-8.p **Abstract:** We examined for myocardial ischemia induced by continuous inhalation of fenoterol in children with severe acute asthma. Thirty children with severe acute asthma were evaluated for signs of myocardial ischemia when treated with 0.5 mg/kg dose (maximum 15 mg) of inhaled fenoterol for one hour. The heart rate was measured before and after inhalation. Cardiac enzymes (creatinase kinase, creatine kinase MB fraction and troponin levels) were measured at admission and 12 hours later. An EKG was recorded before inhalation was started and immediately after its completion to detect the presence of any evidence of myocardial ischemia. All patients developed significant increase in heart rate. Six patients showed EKG changes compatible with myocardial ischemia, despite normal enzyme levels. Patients with severe acute asthma show tachycardia and may show EKG changes of myocardial ischemia.

Zar H.J. et al. *A 500-ml plastic bottle: an effective spacer for children with asthma.* Pediatr Allergy Immunol. 2002; 13(3) : 217-22.p **Abstract:** Inhaled therapy using a metered-dose inhaler (MDI) with attached spacer has been increasingly recognized as the optimal method for delivering asthma medication for acute attacks and chronic prophylaxis. However, in developing countries the cost and

availability of commercially produced spacers limit the use of MDI-spacer delivery systems. A 500-ml plastic bottle has been recently adapted to function as a spacer. This article reviews the current data on the efficacy of this bottle-spacer and discusses its advantages and limitations. It is concluded that a modified 500-ml plastic bottle is an effective spacer; modification and use of this device should be incorporated into international guidelines for the management of children with asthma.

Zar H.J. et al. *Treatment of acute asthma--a metered dose inhaler with spacer is an optimal delivery system.* S Afr Med J. 2001; 91(8) : 653-5.p

Zebrack M. et al. *The pediatric hybrid observation unit: an analysis of 6477 consecutive patient encounters.* Pediatrics. 2005; 115(5) : e535-42.p **Abstract:** OBJECTIVES: Pediatric observation units (OUs) are becoming more common in hospitals throughout the United States, providing physicians with a new disposition option for children who are judged to be too ill for home management. Some OUs function as "hybrid" units, serving both acutely ill and injured observation patients as well as scheduled elective procedure patients. How best to utilize this new resource is not yet defined. We studied the utilization of our pediatric hybrid OU during the first 2 years of operation to determine (1) the spectrum and frequency of diagnoses treated, (2) diagnoses and procedures most (and least) likely to attain discharge successfully within 24 hours, and (3) whether age was associated with inability to be discharged from the OU within 24 hours. METHODS: The study setting was a 20-bed hybrid OU located in a pediatric tertiary care hospital in Salt Lake City, Utah. The records of all patients admitted during the first 2 years of OU operation, from August 1999 through July 2001, were examined retrospectively. RESULTS: There were 6477 OU admissions: 4189 (65%) for acutely ill and injured observation patients and 2288 (35%) for scheduled elective procedure patients. For the observation patients, median age was 2.5 years and median length of stay was 15.5 hours. Common admission diagnoses in these patients included enteritis/dehydration (n = 722), orthopedic injuries (n = 362), asthma (n = 327), closed head injury (n = 289), urgent transfusion/infusion (n = 221), bronchiolitis (n = 212), croup (n = 207), abdominal pain (n = 199), cellulitis (n = 177), and nonfebrile seizure (n = 98). Overall, 15% of observation patients required subsequent inpatient admission for >24-hour stay. Observation diagnoses that were most likely to require inpatient admission were hematochezia (60%), viral pneumonia (46%), and bronchiolitis (43%). We demonstrated successful OU discharge rates (>85%) for several diagnoses not commonly reported: neonatal hyperbilirubinemia, aseptic meningitis, and diabetic ketoacidosis in the patient with known diabetes. Among the scheduled elective procedure patients, median age was 5.0 years and median length of stay was 3.0 hours. Only 1% of these patients required subsequent inpatient admission. In both populations, age < or =30 days was associated with increased need for inpatient admission, with a relative risk of 1.9 (95% confidence interval: 1.4-2.6) among the observation patients and 13.9 (95% confidence interval: 3.0-65.0) among scheduled procedure patients. CONCLUSION: Our pediatric hybrid OU played an important role in the treatment of children who were admitted for observation as a result of acute illness or injury, as well as children who required scheduled procedures. For both patient types, we identified diagnoses that are most and least likely to attain successful discharge within 24 hours. The majority (85%) of observation patients were discharged successfully within 24 hours. Successful discharge rates for diagnoses that are not commonly managed in other pediatric OUs were reported. We identified certain age groups within selected diagnoses that may not have been appropriate for the OU.

Zeder S.L. et al. *Paediatric problems in a paediatric surgical department.* Pediatr Surg Int. 2004; 20(5) : 329-33.p **Abstract:** It is not unusual for paediatric surgical patients to suffer from paediatric diseases in addition to their surgical problems. These diseases demand further

diagnostic procedures and pre- or postoperative therapy. The aim of this study was to discover how many and what kinds of additional paediatric diseases are seen in our paediatric surgical inpatients. We retrospectively evaluated the hospital charts of all inpatients for 1 year. The following data were collected: cause of admission, therapeutic procedure (conservative/operative), surgical discharge diagnosis, additional paediatric diagnoses, and transfer to other departments. A total number of 5,026 hospital stays for 5,840 operations in 4,300 children was evaluated. In 38% of all hospital stays, the children had one or more paediatric diseases. These could be divided into two groups: acute diseases and chronic conditions. In the acute group, 638 children suffered from acute infectious diseases such as respiratory infections and enteritis/gastroenteritis. The most common chronic conditions were allergy, asthma, epilepsy, anaemia, and mental retardation. A special group of patients consists of 21% of the children admitted because of suspected appendicitis. These children not only had a significantly higher incidence of additional paediatric diseases (mostly acute infectious diseases), but also a higher incidence of atopic diseases compared with the patients admitted for other reasons. The early diagnosis and treatment of additional paediatric diseases is essential for the success of paediatric surgery. The paediatrician has a significant role in caring for surgical patients and assisting in the perioperative management, but the paediatric surgeon should also be aware of the spectrum of medical diseases.

Zeiger R.S. et al. *Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma.* J Allergy Clin Immunol. 2006; 117(1) : 45-52.p **Abstract:** BACKGROUND: Outcome data are needed to base recommendations for controller asthma medication use in school-aged children. OBJECTIVE: We sought to determine intraindividual and interindividual response profiles and predictors of response to an inhaled corticosteroid (ICS) and a leukotriene receptor antagonist (LTRA). METHODS: An ICS, fluticasone propionate (100 mcg twice daily), and an LTRA, montelukast (5-10 mg nightly, age dependent), were administered to children ages 6 to 17 years with mild-to-moderate persistent asthma using only as-needed bronchodilators in a multicenter, double-masked, 2-sequence, 16-week crossover trial. Clinical, pulmonary, and inflammatory responses to these controllers were evaluated. RESULTS: Improvements in most clinical asthma control measures occurred with both controllers. However, clinical outcomes (asthma control days [ACDs], the validated Asthma Control Questionnaire, and albuterol use), pulmonary responses (FEV₁/forced vital capacity, peak expiratory flow variability, morning peak expiratory flow, and measures of impedance), and inflammatory biomarkers (exhaled nitric oxide [eNO]) improved significantly more with fluticasone than with montelukast treatment. eNO was both a predictor of ACDs (P = .011) and a response indicator (P = .003) in discriminating the difference in ACD response between fluticasone and montelukast. CONCLUSIONS: The more favorable clinical, pulmonary, and inflammatory responses to an ICS than to an LTRA provide pediatric-based group evidence to support ICSs as the preferred first-line therapy for mild-to-moderate persistent asthma in children. eNO, as a predictor of response, might help to identify individual children not receiving controller medication who achieve a greater improvement in ACDs with an ICS compared with an LTRA.

Zhang L. et al. *Accuracy of parental and child's reports of changes in symptoms of childhood asthma.* Indian Pediatr. 2006; 43(1) : 48-54.p **Abstract:** This cohort study was conducted to evaluate the accuracy of parental and child's reports of changes in asthma symptoms. Fifty three asthmatic children and their parents were interviewed at enrollment and after 4 and 8 weeks. The outcomes were parental and child's reports of changes in asthma symptoms, changes in mean daily symptom scores and changes in pulmonary function. Among patients 6 to 10 years old, parental reports were more strongly than child's reports to correlate with changes in mean daily symptom scores (r: 0.54 vs 0.23). In patients aged 11 yr or

older, parental and child's reports were equally correlated with changes in mean daily symptom scores (r : 0.63 vs 0.57). In both age groups, neither parental nor child's reports were significantly correlated with changes in pulmonary function. Conclusion Parental reports of changes in asthma symptoms are more reliable than child's reports in patients under 11 yr. Among patients aged 11 yr or older, child's reports are so valid as their parents reports for clinical judgment of asthma control.

Zhang L. et al. *Accuracy of parental and child's report of changes in symptoms of childhood asthma.* Indian Pediatr. 2005; 42(12) : 1220-5.p **Abstract:** This cohort study was conducted to evaluate the accuracy of parental and child's reports of changes in asthma symptoms. Fifty three asthmatic children and their parents were interviewed at enrollment and after 4 and 8 weeks. The outcomes were parental and child's reports of changes in asthma symptoms, changes in mean daily symptom scores and changes in pulmonary function. Among patients 6 to 10 years old, parental reports correlated more strongly than child's reports with changes in mean daily symptom scores (r : 0.54 vs 0.23). In patients aged 11 years or older, parental and child's reports correlated comparably with changes in mean daily symptom scores (r 0.63 vs 0.57). In both age groups, neither parental nor child's reports correlated significantly with changes in pulmonary function. The relatively low coefficient of correlation between parental,child report with symptom score suggests that these may not be very accurate reflections of change in asthma status. Nevertheless, for the age group 6 to 10 year, parental reports are more reliable than child reports, while both are comparable in the age group 11-18 years.

Zhang Y. et al. *Positional cloning of a quantitative trait locus on chromosome 13q14 that influences immunoglobulin E levels and asthma.* Nat Genet. 2003; 34(2) : 181-6.p **Abstract:** Atopic or immunoglobulin E (IgE)-mediated diseases include the common disorders of asthma, atopic dermatitis and allergic rhinitis. Chromosome 13q14 shows consistent linkage to atopy and the total serum IgE concentration. We previously identified association between total serum IgE levels and a novel 13q14 microsatellite (USAT24G1; ref. 7) and have now localized the underlying quantitative-trait locus (QTL) in a comprehensive single-nucleotide polymorphism (SNP) map. We found replicated association to IgE levels that was attributed to several alleles in a single gene, PHF11. We also found association with these variants to severe clinical asthma. The gene product (PHF11) contains two PHD zinc fingers and probably regulates transcription. Distinctive splice variants were expressed in immune tissues and cells.

Zhou Y. et al. *Cloning and polymorphism analysis of IL-4 proximal promoter in asthmatic children.* Chin Med J (Engl). 2002; 115(11) : 1624-7.p **Abstract:** **OBJECTIVE:** To clone and study the polymorphism within interleukin-4 (IL-4) proximal promoter of asthmatic children. **METHODS:** The IL-4 proximal promoter segments were amplified and selected by polymerase chain reaction (PCR) and single strand conformation polymorphism (SSCP) with genomic DNA from ten healthy children and forty patients with dominantly allergic familial histories as templates. The selected PCR segments were cloned into recombinant plasmids pIL-4-Jx2. The PCR inserts were sequenced by dideoxy chain termination method. **RESULTS:** Seven aberrant bands were found in SSCP analysis from forty asthmatic patients. The sequencing results showed that four variant sites were found within or adjacent to the known IL-4 regulatory element. A C to A transversion located at -229 position was just within the positive regulatory element-I (PRE-I) in one patient. A C to T transition adjacent to the negative regulatory element-II (NRE-II) and an extra G adjacent to TATA box were found in two patients. A five base nucleotide deletion was found near signal transducers and activators of transcription-6 responsive element (STAT-6 RE) in one patient. **CONCLUSION:** There were

polymorphisms within the IL-4 proximal promoter of allergic asthmatic patients and these polymorphisms might result in aberrant expression of IL-4 gene and asthma.

Zielen S. et al. *Effectiveness of budesonide nebulising suspension compared to disodium cromoglycate in early childhood asthma.* Curr Med Res Opin. 2006; 22(2) : 367-73.p **Abstract:** **OBJECTIVE:** The optimal treatment for early childhood asthma remains controversial. Budesonide (BUD) has shown superiority over placebo in infants, and over disodium cromoglycate (DSCG) in children aged > 2 years. The aim of this double-blind, randomised, parallel-group study was to compare the effectiveness of nebulised BUD and DSCG in asthmatic children aged < 36 months. **Research design and methods:** 82 infants (mean age 18.0 months [range, 11.6-31.2 months]) with suspected asthma (three exacerbations of dyspnoea and wheezing during the past 12 months, with one or more exacerbations in the past 3 months) were treated for 3 months with nebulised BUD (Pulmicort Respules) 0.5 mg/2 mL bid or DSCG 20 mg/2 mL tid. Follow-up was at 6 months. **Main outcome measures and results:** Patients treated with BUD had a lower exacerbation rate than DSCG-treated patients after 3 months of treatment (5.4% vs. 31.7%; p = 0.003) and towards the end of follow-up (30% vs. 49%; p = 0.062). During treatment, days without cough were 80% and 65% for BUD and DSCG, respectively (p = 0.014), and nights without cough were 89% and 78%, respectively (p = 0.016). Side-effects were mild and of similar frequency in both groups. **CONCLUSIONS:** Inhaled nebulised BUD was well tolerated and more effective than nebulised DSCG in reducing the incidence of asthma exacerbations and days with symptoms. These beneficial effects of BUD were maintained throughout the 6-month follow-up.

Zlotkowska R. et al. *Fetal and postnatal exposure to tobacco smoke and respiratory health in children.* Eur J Epidemiol. 2005; 20(8) : 719-27.p **Abstract:** The aim of this paper was to find out whether fetal exposure to environmental tobacco smoke (ETS), as compared to postnatal ETS exposure, is an independent risk factor for respiratory symptoms and diseases in younger schoolchildren. The cross-sectional epidemiological study comprised population of 1,561 Polish schoolchildren, aged 9-11 years. Information on the exposure to tobacco smoke and other sources of indoor air pollution at home, respiratory and allergic health status, and socio-economic status of the family was obtained by questionnaire survey. The respiratory health status was described by presence of wheezing, attacks of dyspnoea (noted during the last year or ever), bronchitis, wheezy bronchitis and asthma, ever diagnosed by a physician. Multivariate logistic regression analysis with adjustment for age, sex, area of residence, household density, damp and mould stains found at home, use of coal-fired stove, co-habitant pets, mother's education and paternal current and past smoking habit was used to assess the effect of fetal and postnatal exposures on respiratory health outcomes. The results of the multivariate analyses revealed statistically significant associations between fetal exposure to ETS and wheezing ever: log OR = 1.4 (95% CI: 1.0-2.0), attacks of dyspnoea ever: log OR = 1.8 (95% CI: 1.1-2.9), bronchitis: log OR = 2.1 (95% CI: 1.5-2.9), and wheezy bronchitis: log OR = 1.8 (95% CI: 1.1-2.9). The effect of postnatal ETS was statistically significant only for bronchitis: log OR = 1.4 (95% CI: 1.1-1.9). The results of our study showed that fetal exposure to tobacco smoke is an independent risk factor for symptoms of wheeze and wheezy bronchitis in schoolchildren when compared to postnatal ETS exposure.

Zollner E. et al. *Metered dose inhalers and spacers for childhood asthma-will increasing availability improve asthma care?* S Afr Med J. 2001; 91(8) : 665.p

Zubovic I. et al. *Manifold significance of serum eosinophil cationic protein in asthmatic children.* Acta Med Croatica. 2002; 56(2) : 53-

6.p Abstract: Asthma is the result of complex interaction between different cells, mediators and nervous system that leads to an inflammatory response accompanied by increased bronchial hyperactivity. Its clinical manifestations include recurrent cough, wheezing and difficult breathing. The purpose of this study was to establish the possibility of diagnosing inflammation in asthmatic patients based on the assessment of serum eosinophil cationic protein (ECP), and of following the efficacy of asthmatic treatment by the levels of inflammation mediators. In a prospective study, 134 children aged 1 to 18 (mean 8) years underwent serum ECP assessment. Experimental group included 87 patients with asthma, 56 boys and 31 girls, mean age 9.1 (range 2-17) years. Control group included patients with recurrent non-allergic disorders, 27 boys and

20 girls aged 1-16 (mean 6.1) years. Serum ECP was assessed using the Pharmacia CAP system ECP-FEIA method, i.e. fluoroimmunoassay test for quantitative assessment of serum ECP levels. Serum values of ECP were significantly higher in asthmatics than in controls ($p = 0.001$). Our results showed that increased levels of serum ECP to significantly correlate with increased eosinophil ($p = 0.018$) and immunoglobulin E ($p = 0.003$) levels. Increased ECP levels reflect the degree of inflammation and correlate with the clinical picture severity in asthmatic patients. Assessment of serum ECP levels can reveal eosinophilic activity, and indirectly detect immunologic inflammation in asthmatics. It is possible to follow the dynamics of immunologic inflammation during the course of treatment as well as treatment efficacy.