

ALLERGYWATCH®

*A Synopsis of Allergy and
Asthma Literature,
Resulting from an Unbiased,
Comprehensive Review of
Sixteen Major Medical Journals.*

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Inhaled Corticosteroids Reduce Subepithelial Collagen Deposition in Asthma

THE airway wall remodeling caused by bronchial asthma involves thickening of the subepithelial basement membrane and hypertrophy and hyperplasia of the airway smooth muscle. Inhaled corticosteroids can prevent remodeling of the airways. However, their effects on matrix metalloproteinases (MMPs) and on tissue inhibitors of metalloproteinases (TIMPs)—which contribute to tissue remodeling—are unknown. The effects of inhaled corticosteroid therapy on MMP and TIMP expression were evaluated in a randomized trial including 230 patients with asthma.

The patients were assigned to receive 6 months of treatment with inhaled beclomethasone dipropionate, 800 µg/d, or placebo. Immunohistochemical analysis of bronchial biopsy specimens showed significantly decreased collagen type III deposition in the subepithelial basement membrane of patients receiving

beclomethasone. Expression of submucosal MMP-9 was significantly decreased in the beclomethasone group, while submucosal TIMP-1 expression was significantly increased. Epithelial and submucosal MMP-9 expression were significantly correlated with submucosal collagen type III deposition. Beclomethasone also reduced inflammatory cell numbers in the bronchial mucosa.

In patients with asthma, inhaled beclomethasone therapy reduces subepithelial collagen thickness and submucosal MMP-9 expression and increases submucosal TIMP-1 expression. The findings help in understanding the mechanisms of inhaled corticosteroids in preventing airway remodeling. The clinical improvement after 6 months of therapy is accompanied by significant reductions in subepithelial collagen deposition and airway inflammatory cells.

COMMENT: *Inflammatory airways remodeling with deposition of collagen beneath the subepithelial basement membrane is a consequence of asthma. This >>>*

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- American Journal of Respiratory and Critical Care Medicine
- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
- Journal of Occupational and Environmental Medicine
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine

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Japanese study found that one important benefit of inhaled corticosteroids in asthma is decreasing MMPs, which are involved in airways remodeling, and increasing TIMPs, thus decreasing subepithelial basement thickening. These results reinforce the important role of inhaled corticosteroids as anti-inflammatory therapy for asthma.

M. S. B.

Hoshino M, Takahashi M, Takai Y, Sim JJ: Inhaled corticosteroids decrease subepithelial collagen deposition by modulation of the balance between matrix metalloproteinase-9 and tissue inhibitor of metalloproteinase-1 expression in asthma. *J Allergy Clin Immunol* 104:356-363, 1999. ◆◆

Systemic Reactions to Skin Tests Are Rare

A 5-year, retrospective study was performed to assess the rate of systemic reactions to diagnostic skin testing. The review included a total of 497,656 tests performed in 18,311 patients, for an average of approximately 27 tests per patient. Sixteen thousand five hundred five patients underwent skin puncture testing, while 1,806 had skin puncture and intradermal skin testing. Information on systemic reactions and treatment was recorded by physicians and nurses.

Six systemic reactions occurred in 6 patients, all of whom had asthma. The overall rate of systemic reactions was 33 per 100,000 skin tests. Five of the 6 reactions were to skin puncture tests. Rates of systemic reactions to specific tests were 152 or 220 reactions per 100,000 latex skin tests, depending on whether 1 particular patient had a reaction to latex; 72 reactions per 100,000 penicillin and antibiotic skin tests; and 15 or 23 reactions per 100,000 aeroallergen skin tests, again depending on the reaction of a particular patient. The systemic reaction rate was 30 reactions per 100,000 skin puncture tests and 55 reactions per 100,000 skin puncture and intradermal skin tests. Most of the reactions occurred within 25 minutes. All of the reactions responded to subcutaneous epinephrine and oral antihistamines; all of the patients were discharged within 1 hour after the start of treatment.

This large study suggests that the rate of systemic reactions to skin testing is very low. Even when they do occur, such reactions are mild and respond promptly to treatment. The results support the safety of skin testing for allergic patients.

COMMENT: This important study reviews the clinical experience with almost a half-million skin tests at the Mayo Clinic over a 5-year period. This article points out that, when done appropriately, skin testing is safe. Only 6 patients had systemic reactions, all of which were treated easily. As opposed to previous series, no deaths were reported. These findings are reassuring but should not change our level of caution.

A. M.

Valyasevi AM, Maddox DE, Li JTC: Systemic reactions to allergy skin tests. *Ann Allergy Asthma Immunol* 83:132-136, 1999. ◆◆

Study Casts Doubt on Monosodium Glutamate Sensitivity

It has been suggested that the common food additive monosodium glutamate (MSG) may provoke asthma. One hundred asthma patients underwent a single-blind, placebo-controlled oral MSG challenge, 2.5 mg. Thirty of the patients had a history of asthmatic attacks occurring in Oriental restaurants. Seventy-eight proved to have aspirin sensitivity.

In none of the patients—including those with an MSG-positive history—did FEV₁ decrease or asthma symptoms develop. Estimates of the exact 1-sided 95% confidence interval for the probability of MSG sensitivity were extremely low, even when data from previous studies that failed to ►►

detect MSG-provoked asthma were included.

This and previous studies question the existence of MSG sensitivity among patients with asthma. Even patients with a history of asthmatic reactions in Oriental restaurants show no reaction to oral MSG challenge. Many asthma patients have significant fear and anxiety regarding the possibility of MSG-induced attacks, and are relieved to find they are not MSG-sensitive.

COMMENT: Allergists are frequently asked about MSG sensitivity, and there are many ardent believers in it. These well-respected researchers orally challenged 100 asthmatics, 30 of whom believed MSG had induced their asthma and 78 of whom were aspirin sensitive, and reviewed the previously published studies. No challenged subject reacted to MSG. The authors recommend "a healthy skepticism about the existence of MSG sensitivity in individuals with asthma."

R. J. M.

Woessner KM, Simon RA, Stevenson DD: Monosodium glutamate sensitivity in asthma. *J Allergy Clin Immunol* 104:305-310, 1999. ◆◆

Population-Based Study Examines Epidemiology of Anaphylaxis

PREVIOUS epidemiologic studies of anaphylaxis have focused on selected groups of subjects, rather than the general population. Prevention of recurrent anaphylaxis requires information on its clinical features and causes. A unique general population data base was used to describe the epidemiology of anaphylaxis in a general population, including the incidence and occurrence rate of anaphylaxis, the rate of recurrent anaphylaxis, the rate of atopic anaphylaxis, and the percentage of episodes leading to hospitalization and death.

Review of the medical records of 1,255 residents of Olmsted County, Minn., for a 5-year period identified 133 residents with a total of 154 episodes of anaphylaxis. Most episodes occurred in the summer. The average annual incidence was 21 per 100,000 person-years, with an occurrence rate of 30 per 100,000 person-years. Overall, 53% of the residents with anaphylaxis were atopic, including 33% with bronchial asthma. Fifty-two percent received an allergy consultation. Seven percent were hospitalized. One patient died in the hospital, for a case-fatality rate of 0.91%. A suspected causative allergen was identified in 68% of patients. The most commonly implicated allergens were foods, medications, and insect stings.

This general population-based study suggests that the incidence of anaphylaxis is less than 1%. Few episodes lead to hospitalization, and even fewer are fatal. The rate of anaphylaxis is significantly higher for patients who are atopic. Anaphylactic episodes frequently go unrecognized by patients and physicians alike. Whenever anaphylaxis occurs, the patient should receive allergy referral to identify the cause and prevent recurrent episodes.

COMMENT: Olmsted County, Minnesota, is home to the Mayo Clinic. The county has a unique computer-

linked medical diagnostic data base for all residents, which allows for interesting epidemiologic investigation. These investigators determined retrospectively the incidence of anaphylaxis in a defined population over a 5-year period. Interesting findings included the percentage of cases of anaphylaxis that were idiopathic (32%), that were "atopic" (53%), that were fatal (0.65%), and that were not referred for allergy consultation (48%).

R. J. M.

Yocum MW, Butterfield JH, Klein JS, et al: Epidemiology of anaphylaxis in Olmsted County: a population-based study. *J Allergy Clin Immunol* 104:452-456, 1999. ◆◆

Home Air Cleaners Are Beneficial for Asthmatic Children with Pets

AIR cleaners have been shown to have little effect on exposure to house dust mite allergen. However, pet allergens bind to smaller particles, which can remain airborne for prolonged periods. In a double-blind, crossover trial, Philips model HR 4330 and HR 4320 air cleaners were placed in the living rooms and bedrooms of 20 asthmatic children who were sensitized to cat or dog allergen. The air cleaners' effects on selected clinical variables were assessed, including lung function, airway hyperresponsiveness, medication use, and asthma symptoms. Floor dust samples were taken for measurement of animal allergen levels.

The air cleaner filters captured significant levels of cat and dog allergen, whereas sham air cleaners captured little allergen. Three months after air cleaners were placed, the children showed a significant reduction in airway hyperresponsiveness, with a 1.2 doubling dose increase of PC₂₀adenosine. Air cleaner use was also associated with a reduction in peak flow amplitude. Floor dust allergen levels were unchanged.

Placing air cleaners in the home may reduce airway responsiveness and peak flow amplitude in asthmatic children sensitized to pet allergen. Air cleaners can reduce levels of airborne pet allergen, and may therefore be of benefit to asthmatic patients who are allergic to animals but want to keep their pets. Air cleaners do not affect dust and allergen reservoirs, such as carpets and furniture.

COMMENT: It is very difficult for physicians to convince patients with pet allergy to remove their pets from their homes. The use of air cleaners has been controversial as an effective measure in decreasing symptoms in patients with pet allergy. This 3-month study demonstrated the benefit of air cleaners in decreasing bronchial reactivity in children with pet allergy when the devices were placed in the bedroom and living room.

M. S. B.

van der Heide S, van Aalderen WMC, Kauffman HF, et al: Clinical effects of air cleaners in homes of asthmatic children sensitized to pet allergens. *J Allergy Clin Immunol* 104:447-451, 1999. ◆◆

Rhinitis Is an Asthma Risk Factor Even in Nonatopic Subjects

THE finding that perennial rhinitis and asthma commonly appear together has been ascribed to differing manifestations of underlying atopy. Few studies have evaluated rhinitis as a possible asthma risk factor. This study evaluated rhinitis as a risk factor for asthma in subjects without atopy and elevated total IgE levels.

The European Community Respiratory Health Survey included 1,412 young adults with rhinitis and 5,918 community controls. All had complete data on asthma, bronchial hyperresponsiveness, atopy, and family history of asthma. Asthma was strongly associated with rhinitis. After adjustment for confounding variables, odds ratios were 8.1 (95% confidence interval [CI] 5.4 to 12.1) for atopic subjects with rhinitis and 11.6 (95% CI 6.2 to 21.9) for nonatopic subjects with rhinitis. The association of asthma with nonatopic rhinitis remained strong even among subjects with normal IgE levels. Subjects who had rhinitis in the absence of asthma also had a significantly elevated rate of bronchial hyperresponsiveness.

This large, population-based study finds that the association between perennial rhinitis and asthma is present even in nonatopic subjects with normal IgE levels. This association does not appear to be explained by defects in immunologic function, and supports the theory that upper respiratory tract disease may affect the lower airways. Rhinitis appears to be an independent risk factor for asthma.

COMMENT: *The relationship between allergic rhinitis and the development of asthma is well documented, but is nonallergic rhinitis also a risk factor for asthma? This multicenter European study found a clear association between patients with nonallergic rhinitis and normal IgE levels and risk for asthma. Now, patients with nonallergic rhinitis should be counseled regarding their increased chance of developing asthma, just like their allergic counterparts.*

M. S. B.

Leynaert B, Bousquet J, Neukirch C, et al: Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects. Results from the European Community Respiratory Health Survey. J Allergy Clin Immunol 104:301-304, 1999. ◆◆

Early RSV Infection Is a Risk Factor for Wheezing in Later Childhood

IN children up to 3 years old, most cases of lower respiratory tract disease with wheezing are caused by respiratory syncytial virus (RSV) infection. Previous studies have shown that children with early RSV lower respiratory illness have reduced lung function later in life, but the cause of these lung function deficits is unclear. This prospective follow-up study included 472 children who developed at least one lower respiratory tract illness before 3 years of age. Tests for viral and other causes revealed RSV illness in 44% of children, para-influenza illness in 14%, other causes of lower res-

piratory illness in 14%, and negative test results in 27%. The children were followed up for wheezing, pulmonary function measures, and atopic status up to 13 years of age.

Throughout follow-up, the point prevalence of infrequent wheezing remained stable at 17% to 19%. The prevalence of frequent wheezing ranged from 8% to 10%. Both outcomes were significantly more frequent in children with early RSV lower respiratory illness. At age 6, odds ratios in the RSV group were 3.2 (95% confidence interval [CI] 2.0 to 5.0) for infrequent wheezing and 4.3 (95% CI 2.2 to 8.7) for frequent wheezing. These risks decreased rapidly with time, becoming non-significant by age 13. Early RSV lower respiratory illness was unrelated to later atopic status.

Children with RSV lower respiratory illness during the first 3 years of life are at increased risk of wheezing through age 10 years. However, this association is no longer present by age 13. The factors responsible for the association between RSV illness and wheezing are unknown, but there is no increase in allergic sensitization.

COMMENT: *Respiratory syncytial virus lung infection before the age of 3 years is a risk factor for the subsequent development of wheezing up to age 11. Children with persistent wheezing episodes during childhood were also more likely to be atopic than those who were not wheezy by age 11. However, RSV infection in early life was not associated with subsequent allergic sensitization.*

Another recent article from The Lancet (Simoes AF: Respiratory syncytial virus [RSV] infection. Lancet 354:847-852, 1999) provides an excellent, succinct review of RSV and its role as a significant pathogen in the lower respiratory tract of infants and adults—especially the elderly. The lack of effectiveness of corticosteroids and bronchodilators in the treatment of wheezing associated with bronchiolitis is discussed. As well, the relative merits of humanized monoclonal antibody (palivizumab) vs monthly infusions with RSV immune globulin are considered.

E. J. B.

Stein RT, Sherrill D, Morgan WJ, et al: Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. Lancet 354:541-545, 1999. ◆◆

High-Dose Inhaled Steroids Differ in Their Systemic Effects

VARIOUS inhaled steroids were compared in terms of plasma cortisol suppression in healthy male volunteers. The drugs investigated were beclomethasone dipropionate, budesonide, flunisolide, fluticasone propionate, and triamcinolone acetonide. All were given at doses of approximately 1,000 µg twice daily.

All study drugs significantly reduced 24 hour plasma cortisol (cortisol-AUC₂₄) after a single dose. Mean reductions in cortisol-AUC₂₄, compared with placebo, were 7% with flunisolide, 16% with budesonide, 18% with beclomethasone, 19% with triamcinolone, and 35% with fluticasone. In response to >>>

seven consecutive doses, the values were 5% with flunisolide (not significantly different than placebo), 18% with budesonide, 25% with triamcinolone, 28% with beclomethasone, and 79% with fluticasone. Fluticasone had a significantly greater suppressive effect than the other corticosteroids, which did not differ significantly from each other.

Different inhaled corticosteroids vary significantly in their systemic effects when given in high doses. Inhaled corticosteroids should be used in the lowest dose that will control asthma symptoms. The authors call for studies to compare the various agents for efficacy and systemic effects across a wide dose range.

COMMENT: *This study compares the hypothalamic-pituitary-adrenal axis effects of all inhaled steroids available in the United States. However, the doses examined, while similar in micrograms (880 to 1,000 µg/d) are actually quite different in potency. According to estimates of comparative doses for inhaled steroids in the 1997 National Heart, Lung and Blood Institute Practical Guide for the Diagnosis and Management of Asthma, the respective drug doses in this study and their estimated potency would be "low to moderate" for flunisolide and triamcinolone, "high" for beclomethasone, and very "high" for budesonide (threshold for "high" being >600 µg) and fluticasone (threshold for "high" being >660 µg). The results of the study must be considered in that context.*

M. S. D.

Brus R: Effects of high-dose inhaled corticosteroids on plasma cortisol concentrations in healthy adults. Arch Intern Med 159:1903-1908, 1999. ♦♦

Fatal Fire Ant Attacks in Nursing Homes Reported

FIRE ants were introduced into the United States from South America in 1930. They now infest large areas of the southeastern United States, with major effects of agriculture and wildlife. One study found that more than half of people in endemic areas are stung by fire ants, with 16% developing specific IgE antibodies. Fire ant stings cause an immediate sensation of severe burning and itching, followed by the development of a localized hive, and later a sterile pustule. Death may result from an anaphylactic reaction; other major complications have been reported as well.

The authors report 2 cases in which elderly residents of two separate nursing homes died after being stung by fire ants. Although neither patient developed any symptoms of anaphylaxis, both died of medical complications, including worsening congestive heart failure. Death occurred 5 days and 13 months, respectively, after the fire ant attacks.

A total of 10 indoor attacks by fire ants have been reported since 1989. These include 2 earlier reports of fire ant attacks on nursing home residents previously reported. All of these patients have been immobile and neurologically compromised. In none of the nursing home attacks was any food present in the victims' rooms to attract the ants. Most attacks in med-

ical facilities have resulted in lawsuits. The mechanism of nonanaphylactic reactions to fire ant stings remains unclear. Physicians in endemic areas should be aware of the medical consequences of fire ant stings. If fire ants are detected, efforts should be made to eradicate active colonies, especially where immobile people are present.

COMMENT: *Since the unfortunate introduction of the fire ant into the southeastern United States, the extent of infestation and its medical consequences have increased. In this troubling report of two nursing home attacks, the authors present a review of the literature that reminds us that fire ant stings can occur both indoors and outdoors. While these cases were apparently nonanaphylactic in nature, the effects were devastating. Eradication efforts must be stressed by allergists to their patients at risk.*

A. M.

deShazo RD, Williams DF, Moak ES: Fire ant attacks on residents in health care facilities: a report of two cases. Ann Intern Med 131:424-429, 1999. ♦♦

Childhood Asthma Severity Increases as Hospitalization Rates Remain Stable

DESPITE the increasing morbidity and mortality of asthma, there is evidence that the rate of hospitalization for childhood asthma has stabilized. Using objective measures of asthma severity, this study examined recent trends in childhood asthma hospitalization rates and the severity of acute asthma episodes. The analysis included all 29,329 hospitalizations of pediatric patients in one New York County from 1991 through 1995. Of these, 2,028 hospitalizations were for asthma. A 22% random sample of asthma hospitalizations were reviewed for severity, defined primarily as the worst oxygen saturation (SaO₂) recorded during the first 24 hours in the hospital: mild, SaO₂ 95% or greater; moderate, 90% to 94%; severe, less than 90%. Changes in the annual asthma hospitalization rate were compared with changes in severity.

The annual asthma hospitalization rate was 2.04 hospitalizations per 1,000 child-years, and remained relatively stable throughout the study period. At the same time, the rate of hospitalization for severe asthma rose sharply (from 0.57 to 1.55 per 1,000 child-years) while the rate of hospitalization for mild asthma decreased (from 0.26 to 0.12 per 1,000 child-years). Severe asthma accounted for 32% of asthma hospitalizations in 1991, compared to 60% in 1995. The percentage of hospitalizations for mild asthma decreased from 14% to 5%. All of the increase in asthma severity occurred in children less than 12 years old.

This study documents an increase in the severity of childhood asthma in one geographic area during the first half of the 1990s. However, because of changes in the threshold for hospitalization, the overall rate of hospitalization for childhood asthma remained stable. Improvements in asthma therapy may allow physicians to provide better care for acute episodes, thus reducing the need for hospitalization in mild to moderate cases. Physicians appear to be treating a more severely ➤➤

ill population without increasing the use of inpatient care. The study is limited by its reliance on SaO₂ as a measure of asthma severity.

COMMENT: *This study showed that severity increased substantially during a 5-year period among children hospitalized for asthma in Rochester, N.Y. The increase was attributable entirely to changes among children under the age of 12. Because of an increase in admission threshold, the overall rate remained unchanged despite an increase in the severity of episodes.*

J. B.-M.

Russo MJ, McConnochie KM, McBride JT, et al: Increase in admission threshold explains stable asthma hospitalization rates. *Pediatrics* 104:454-462, 1999. ♦♦

Steroid-Insensitive Asthma Carries Poor Quality of Life

SOME cases of severe, chronic asthma are insensitive to steroid therapy. These patients would be expected to have worse outcomes than those with other forms of chronic asthma. Thirty-four pediatric patients with steroid-insensitive asthma were followed up for 2 years to assess their clinical outcomes. The mean age was 15 years; 53% of the patients were boys. The follow-up evaluation included information on current and past asthma treatment, asthma functional severity, and impact of asthma on quality of life. A group of 22 patients with steroid sensitive asthma were studied for comparison.

Both patient- and parent-completed questionnaires suggested that patients with steroid-insensitive asthma had a lower quality of life than patients with steroid-sensitive asthma. The two groups were similar in other measures of clinical outcome, including oral glucocorticoid dose, number of glucocorticoid bursts, emergency room visits and hospitalizations, and functional impact of asthma.

Steroid-insensitive asthma has a significantly greater impact on quality of life than steroid-sensitive asthma. However, other clinical outcomes appear comparable. A longer follow-up period may be needed to demonstrate significant differences in outcome. The findings suggest that steroid-insensitive asthma may be a worse form of disease because it has a more indolent, chronic course with a more fixed pattern of lung obstruction. The long-term clinical and cellular outcomes of this form of asthma remain to be determined.

COMMENT: *These investigators from the National Jewish Center have further reported on a unique group of asthmatics. Clearly, these patients have a poorer quality of life with worse lung function, which may be reversible. Although these patients represent a small proportion of asthmatics, the morbidity associated with their condition is substantial.*

A. M.

Wamboldt FS, Spahn JD, Klinnert MD, et al: Clinical outcomes of steroid-insensitive asthma. *Ann Allergy Asthma Immunol* 83:55-60, 1999. ♦♦

Tree Pollen Plays a Key Role in Springtime Allergic Rhinitis

PREVIOUS studies have suggested that grass pollen is a more important cause of allergic rhinitis occurring in the spring than tree pollen. The contribution of fungal spores is unclear. Allergy patients in Indiana were studied to compare the relative importance of these three causes of spring allergic rhinitis. In 189 patients, clinical sensitivity to tree or grass pollens was studied retrospectively. Another 51 patients participated in a springtime prospective study, in which their symptom and medication scores were correlated with daily pollen and spore counts.

In the retrospective study, 69% of patients were allergic to tree pollen and 71% to grass pollen, with 57% being allergic to both grass and tree pollen. Symptoms occurred during May and June in 71% of patients, decreasing steadily after grass pollination peaked. In the prospective study, symptoms increased along with tree pollen counts, from mid-March to early May. Use of medications peaked during the highest period of grass pollination, in early June. Both symptoms and medication use decreased after this time, even as fungal spore counts continued to increase.

At least in Indiana, tree pollen appears to be an important cause of springtime allergic rhinitis than suggested in the literature. Together, tree and grass pollens are much more important than fungal spores. Symptom scores rise and fall with pollen counts. The rigid outer wall of fungal spores may inhibit protein release, making spores less allergenic than pollens.

COMMENT: *This is a very interesting and relevant study from a private practice in Indiana. The physicians prospectively studied 51 patients and retrospectively reviewed 189 patients with spring and early summer seasonal allergic rhinitis. Although mold spore counts were significantly elevated throughout the spring and summer, no correlation between spore counts and symptom scores or medication use could be established. These are important findings in the difficult area of clinical mold allergy and emphasize the more important role of tree and grass pollen in patients who suffer from pollen and mold allergy.*

A. M.

Wu LYF, Steidle GM, Meador MA, et al: Effect of tree and grass pollens and fungal spores on spring allergic rhinitis: a comparative study. *Ann Allergy Asthma Immunol* 83:137-143, 1999. ♦♦

Serum sICAM-1: a Serologic Marker of Asthma Severity?

SYMPTOMS and lung function measurements are the current standards for evaluation of asthma severity. There is evidence that intercellular adhesion molecule-1 (ICAM-1) could play a pathogenetic role in asthma. The soluble form of ICAM-1 (sICAM-1) is present in high levels in the serum of patients with various inflammatory, immune, or malignant conditions. Serum sICAM-1 was evaluated as a potential marker of asthma >>>

severity by measuring serum concentrations in 45 children with exacerbations of bronchial asthma and 20 healthy controls. Based on clinical and physiologic variables, the exacerbations were classified as mild, moderate, and severe in 15 patients each. Serum sICAM-1 measurements were made using an immunoenzymatic assay.

Mean level of serum sICAM-1 was 390 ng/mL in the asthmatic children vs 193 ng/mL in controls. Within the asthmatic group, serum sICAM-1 levels were significantly correlated with the severity of the attacks: 300 ng/mL in the mild group, 367 ng/mL in the moderate group, and 502 ng/mL in the severe group. There were no significant differences by sex or age.

Children with acute exacerbations of bronchial asthma have elevated serum levels of sICAM-1, with mean levels nearly double those of healthy children. The increase could reflect extensive airway inflammation occurring in the airways during acute exacerbation. Serum sICAM-1 could become a useful marker of asthma severity, enhancing early diagnosis and therapy and providing a means of monitoring the effects of treatment.

COMMENT: *A serologic marker of asthma severity would be a very useful clinical tool. In this study, the serum levels of sICAM-1 in children during asthma exacerbations was elevated and correlated with the severity of the exacerbation. There are still unanswered questions regarding the utility of sICAM as a diagnostic tool, as the study does not address baseline sICAM levels, or the effects of infection and/or other inflammatory diseases on sICAM levels.*

S. A. T.

El-Sawy I, Badr-El-Din OM, El-Azzouni OE, Motawae HA: Soluble intercellular adhesion molecule-1 in sera of children with bronchial asthma exacerbation. Int Arch Allergy Immunol 119:126-132, 1999. ♦♦

Gas Cooking Doesn't Affect Respiratory Health

PREVIOUS studies have found that the use of natural gas for cooking is associated with reduced lung function and increased respiratory symptoms. However, other studies have found no such relationship or a variable association between countries. This question was further addressed in a study of 1,449 subjects from the British National Child Development Study. At age 34 to 35 years, the subjects were interviewed about exposure to gas cooking during childhood and about current asthma or chest symptoms. Ventilatory function and skin prick tests were performed as well. Data on the incidence and age of onset of childhood asthma or wheezing was determined prospectively from previous follow-up reports.

Exposure to gas cooking--either in childhood or adulthood--was unrelated to asthma or other respiratory problems. The study found no association with asthma incidence or prognosis,

allergic sensitization, or current severity of asthma symptoms.

This study--using prospective data on childhood asthma and objective measures of allergic sensitization and ventilatory function in adulthood--finds no effect of exposure to gas cooking on lung function and respiratory symptoms. Gas cooking appears to have no major effect on respiratory illness in young adults.

COMMENT: *There has been increasing attention to the influence of indoor air quality on respiratory and allergic diseases. This study concludes that ongoing or prior exposure to environments with gas cooking is unlikely to be a major influence on respiratory disease in young adults. This disputes observations of some prior studies.*

M. S. D.

Moran SE, Strachan DP, Johnston DA, Anderson HR: Effects of exposure to gas cooking in childhood and adulthood on respiratory symptoms, allergic sensitization and lung function in young British adults. Clin Exp Allergy 29:1033-1041, 1999. ♦♦

Fruit Peels Have Higher Allergenicity Than Pulp

SOME patients who have allergic reactions after ingesting whole apples, pears, or peaches have no reaction when eating just the pulp of the fruit. Thirty-three patients with allergy to apples, pears, and peaches were studied to compare the allergenicity of the peels and pulps of these fruits, all members of the family Rosaceae. The study assessed clinical reactions as well as skin-prick responses to peel and pulp, separately and together. Total IgE measurements and radioallergosorbent tests (RAST) were performed, and cross-reactivity between apple and peach was assessed by RAST inhibition.

Ninety-seven percent of the patients reported adverse reactions to peach, 76% to apple, and 48% to pear. Adverse reactions were more common and more severe when peel and pulp were ingested together vs pulp alone. Whereas 15 of 21 patients had a reaction to apple peel and pulp, only 8 of 21 reacted to the pulp alone. The in vitro tests showed much stronger responses to peels than pulps. The RAST inhibition studies showed significant cross-allergenicity between apple and peach, with the peel containing a larger amount of shared epitopes than the pulp.

Patients allergic to fruits of the Rosaceae family have stronger and more frequent responses when they eat the peel of the fruit along with the pulp. There appears to be significant cross-reactivity between apple and peach peels and pulps, although the amount of shared allergenic epitopes seems to be higher in peels. The findings have important implications for clinical evaluation and diagnostic testing of patients with fruit allergy, and should prompt further study of the allergenic composition of Rosaceae peels and pulps.

COMMENT: *When patients have IgE-mediated food allergy, one typically expects that there will be a consistent history of reactions whenever the food is* ►►

ingested. However, some patients are known to develop allergic reactions to an uncooked food, yet tolerate the cooked food. This apparently results from heat denaturing the food's allergenic protein, rendering it nonallergenic. This study demonstrates that there is another explanation of why patients may have inconsistent allergic reactions to certain fruits.

M. S. D.

Fernández-Rivas M, Cuevas M: Peels of Rosaceae fruits have a higher allergenicity than pulps. *Clin Exp Allergy* 29:1239-1247, 1999. ♦♦

Pets Increase Asthma Symptoms and Inflammatory Markers in Sensitized Patients

EFFORTS to reduce allergen exposure are the mainstay of treatment for allergic patients. However, few studies have documented the effects of reducing allergen exposure. The authors assessed the impact of owning a cat or dog on various markers of asthma severity in patients sensitized to these animals.

The study included 129 patients with adult-onset asthma who were sensitized to cats and/or dogs. Thirty-nine of the patients had pets at home and 90 did not; of the latter group, 39 had pets when they developed asthma but removed them because of allergy. Of the group with pets, 22 had cats, 15 had dogs, and 2 had both. All patients underwent clinical interviews, skin prick testing, measurement of specific IgE and eosinophil counts, and methacholine challenge testing.

The two groups had a similar duration of asthma, although the patients with pets were somewhat older and had a lower rate of childhood asthma or bronchitis. Patients with pets were more likely to be lifelong non-smokers. The groups were similar in their levels of sensitization to other allergens. The patients with pets had significantly more daytime and nighttime asthma symptoms than those without pets. They also used more oral and inhaled steroids. The differences were significant after adjustment for age, sex, smoking, and childhood asthma or bronchitis. Although patients with pets were more likely to report that something in the home environment was causing their symptoms, they were less likely to ascribe the symptoms to contact with cats or dogs. Patients with pets also had a higher rate of abnormal peak-flow recordings, greater variation in peak flow, higher eosinophil counts, and greater bronchial responsiveness.

The results strongly suggest that living with a cat or dog increases symptoms and airway inflammation among asthmatic patients sensitized to these animals. If the pet owners in this study were to get rid of their animals, the prevalence of inhaled steroid use would decrease from about 50% to 25%, the investigators estimate. Many sensitized patients underestimate the contribution of pet allergy to their symptoms. The findings support the removal of pets from the home as a form of allergen avoidance.

COMMENT: Reduction of exposure to allergens is the obvious keystone to the treatment of allergic asthma

and rhinitis. This study verifies that having a cat or dog aggravates symptoms and markers of airway inflammation in sensitized asthmatics.

E. J. B.

Plaschke P, Janson C, Balder C, et al: Adult asthmatics sensitized to cats and dogs: symptoms, severity, and bronchial hyperresponsiveness in patients with furred animals at home and patients without these animals. *Allergy* 54:843-850, 1999. ♦♦

Profilin May Account for Cross-Reactivity Between Diverse Allergen

PREVIOUS studies have demonstrated patients with allergies to plant-derived foods are commonly sensitized to pollen, and that many patients with latex hypersensitivity are also allergic to fruits. The recombinant Bet v 1 and Bet v 2 (birch profilin) antigens have recently been isolated. Patients with fruit or vegetable allergy who lived in an area free of birch trees were studied to assess IgE reactivity to recombinant Bet v 1 and Bet v 2, as well as cross-reactivity to other allergens. The Spanish study included 29 patients with fruit or vegetable allergy. All underwent skin prick testing with a wide range of fruits and vegetables and with common inhalant allergens, including environmentally relevant pollens. IgE reactivity to recombinant Bet v 1 and Bet v 2 was assessed, as well as to various pollens, natural latex, papain, and bromelain. Cross-reactivity between Bet v 2 and pollen were assessed using CAP inhibition assays.

Seventy-nine percent of patients had allergy to grass pollen, while 2 had clinical latex allergy. Despite the absence of birch trees in the study area, 65% of patients had serum IgE to birch pollen, 52% to Bet v 2, 3% to Bet v 1, 59% to latex, 52% to bromelain, and 17% to papain. Patients with positive IgE to Bet v 2 also reacted to latex, grass, and other pollens; those without pollen allergy did not have IgE reactivity to latex, Bet v 1, or Bet v 2. Reactivity to latex was significantly correlated with Bet v 2, birch, and ryegrass. Immunoblotting studies in patients with a positive CAP to birch pollen revealed IgE binding to a 156 kDa band recognized by a monoclonal antibody against profilin.

The findings implicate profilin as the antigen responsible for cross-reactivity among pollens, fruits, vegetables, and natural latex. In these patients, the presence of IgE reactivity to birch profilin may result from primary sensitization to profilins from grass or weed pollen. Thus a serologic finding of sensitization to birch may actually reflect the influence of other allergen sources. The authors propose IgE reactivity to Bet v 2 as a marker of broad sensitization.

COMMENT: The observations from this study suggest that profilin may well be the antigen causing cross-reactions between pollens, fruits, vegetables, and natural rubber latex. A large number of subjects sensitized to grass, weed, and tree pollens as well as some plant-derived foods may have anti-profilin IgE antibodies

that are responsible for the positive CAP results to latex.

E. J. B.

Díez-Gómez ML, Quirce S, Cuevas M, et al: Fruit-pollen-latex cross-reactivity: implication of profilin (Bet v 2). *Allergy* 54:951-961, 1999. ◆◆

Is Cockroach Allergy a Major Cause of Infantile Asthma?

BECAUSE allergy is not regarded as a major cause of infantile asthma, affected children do not usually undergo skin testing. Cockroach allergy is a major cause of asthma in inner-city children, but traditionally regarded as unusual in rural areas. A group of children with infantile asthma were studied for skin test reactivity to cockroach and other inhalant allergens. The children, all less than 3 years old, were seen at a West Virginia pediatric allergy clinic. Ninety percent were white, and 55% were on Medicaid or had no insurance. The children underwent allergy skin testing to alternaria, cat, dog, cockroach, and house dust mite allergy.

One or more skin tests was positive in 45% of patients tested. The most common allergy was to cockroach (26%), followed by house dust mite (17%) and cat (14%). The incidence of cockroach sensitivity did not vary significantly by insurance status.

This rural population of children with infantile asthma has a higher-than-expected frequency of allergy to cockroach. This and other indoor allergens may play an important role in causing infantile asthma. Skin testing to indoor allergens may be indicated in infants and young children with asthma, allowing appropriate environmental control measures for patients sensitized to these allergens.

COMMENT: *Asthma due to cockroach allergy is a known risk factor in inner-city populations. Children with asthma less than 3 years of age in a rural area of West Virginia were skin tested to a small battery of inhalant allergens. Twenty-six percent of the predominantly Caucasian group of children were skin-test-positive to cockroach—more than to dust mite and cat. Children of all socioeconomic groups were included. Moreover, this area is not thought to have high levels of cockroach infestation. Since cockroach cross-reacts with other inhalant insect allergens, such as moths and crickets, which insect was the primary sensitizer?*

S. R. W.

Wilson NW, Robinson NP, Hogan MB: *Cockroach and other inhalant allergies in infantile asthma.* *Ann Allergy Asthma Immunol* 83:27-30, 1999. ◆◆

Thimerosal-Containing Vaccines Should Not Be Withheld from Children

THIMEROSAL has long been used as an additive to vaccines because of its antibacterial actions. Concerns have arisen about the potential for mercury toxicity from thimerosal, which contains nearly 50% mercury by weight. Many commonly used vaccines have

thimerosal concentrations of 0.01%, providing a mercury dose of up to 25 µg/0.5 mL. Fish ingestion is the major source of environmental exposure to mercury; it can also be absorbed via inhalation and through the skin. Efforts are ongoing to reduce mercury exposure through these routes, as well as in vaccines.

The American Academy of Pediatrics presents its recommendations regarding thimerosal-containing vaccines. All children should be vaccinated according to current guidelines. The use of thimerosal-containing vaccines should be reduced or eliminated. However these vaccines should be given as indicated to prevent diseases that pose an immediate threat to young infants, such as pertussis and *Haemophilus influenzae* infection. Detailed recommendations are given for the prevention of hepatitis B infection. No blood, urine, or hair testing is necessary in children who have received thimerosal-containing vaccines. As with all vaccines, the risks and benefits of thimerosal-containing vaccines should be discussed with parents.

COMMENT: *Thimerosal has been used as an additive to biologics and vaccines since the 1930s. It is very effective in killing bacteria used in several vaccines and in preventing bacterial contamination. The American Academy of Pediatrics urges government agencies to work rapidly toward reducing children's exposure to mercury from all sources. Further, the Academy believes that physicians should minimize children's exposure to thimerosal. However, they should not compromise the health of children by withholding routinely recommended immunizations.*

J. B.-M.

American Academy of Pediatrics Committee on Infectious Diseases and Committee on Environmental Health: Thimerosal in vaccines—an interim report to clinicians. *Pediatrics* 104:570-574, 1999. ◆◆

Large-Particle Allergens Can Be Spread from Surfaces

THE relationship between airborne dust mite allergen and respiratory uptake, which leads to sensitization, is unclear. Sensitization is likely to rely on direct nose or hand-to-nose contact with surfaces, especially bedding and carpeting. This study used ^{99m}technetium-labeled ragweed pollen—similar in its aerodynamic properties to dust mite allergen—to assess the spread of allergen through contact with surfaces. The radiolabeled pollen was embedded into pillows and a section of linoleum, which was subsequently touched with the hand. Both simulated and actual human exposure studies were carried out. In the human studies, a gamma camera was used to measure the percentage of respiratory uptake of particles and the location of their deposition.

The simulation studies suggested respiratory pollen uptake of 20.0% by hand-to-nose transfer and 1.4% from pillows directly to the nose. In human studies, uptake was 6.6% by hand-to-nose transfer and 1.5% directly from pillows. Most of the radioactivity was detected in the nasal vestibule, with 13% to 39% localized to the pharyngeal region. ➤➤

These experiments demonstrate the transfer of aerodynamically large allergen particles from surfaces. Transfer from surfaces to the nose can occur directly or via the hand, resulting in deposition of particles into the anterior nose and the pharyngeal area. This type of exposure to dust-mite allergen from bedding, carpeting, and floors could lead to sensitization and asthma.

COMMENT: *While this is a somewhat technical article, the authors address the extremely relevant issue of surface dust mite allergen exposure. Most clinicians assume that airborne distribution is the most important mode of allergen exposure. However, these authors have clearly demonstrated surface-to-nose and hand-to-nose transmission of dust mite-sized allergen. They have given new meaning to the term "fomite."*

A. M.

Lewis RD, Sterling DA, King B, et al: Evidence of large particle allergen inhalation from contact with surfaces. *Ann Allergy Asthma Immunol* 83:41-48, 1999. ♦♦

Heliox Relieves Airflow Obstruction and Dyspnea in Severe Asthma Attacks

HELIUM-oxygen mixtures (heliox) have been shown to improve ventilation in both intubated and non-intubated acidotic patients with acute severe asthma, and to reduce airway pressures in intubated patients. Heliox reduces subjective dyspnea in patients with acute asthma. Thirty-three patients with acute severe asthma were randomized in the emergency department to receive 70%/30% heliox or 30% oxygen. In addition to the subjective response, peak expiratory flow (PEF) was measured to assess the effect of heliox on airflow obstruction. The effects of heliox were monitored up to 8 hours after administration.

By 20 minutes, 82% of the heliox group had a greater than 25% increase in percent predicted PEF (%PEF), compared with 17% of the oxygen group. The heliox group had another significant improvement in %PEF at 8 hours. By comparison, the oxygen group had no significant improvement until 6 hours. At the end of the study, discontinuation of heliox had no significant effect on PEF. The heliox group had significant reductions in dyspnea score and respiratory rate within the first 20 minutes, but no significant improvements thereafter.

For patients with acute severe asthma, heliox administration rapidly increases PEF while decreasing dyspnea. These improvements are maintained for at least 8 hours after heliox administration; however, there is no further improvement after the initial effect, despite heliox-driven nebulized β -agonist treatment. Heliox may be a useful treatment for patients with acute severe asthma while waiting for corticosteroids to take effect.

COMMENT: *This prospective, controlled study suggests that 70%/30% heliox may have an advantage over 30% oxygen in the early management of acute asthma exacerbations. However, there were no significant differences shown for rates of hospitalization, intubation, or mortality. Larger studies showing an improvement*

in one of these outcomes are necessary before heliox will become standard practice for acute asthma management.

S. A. T.

Kass JE, Terregino CA: The effect of heliox in acute severe asthma: a randomized controlled trial. *Chest* 116:296-300, 1999. ♦♦

Quality of Spirometry Testing in Primary Care Questioned

PRI-MARY care practices are increasingly using spirometry for screening, diagnosis, and monitoring of respiratory disease. Spirometry is widely regarded as a simple screening test for chronic obstructive pulmonary disease and airflow obstruction. However, there have been no formal quality assurance studies of spirometry in primary care practice. A 16-week study analyzed a total of 1,012 spirometry tests performed at 30 randomly selected primary care practices. Uploaded spirometry data were analyzed for acceptability and reproducibility using American Thoracic Society (ATS) criteria. A physician and nurse from one-half of the practices received training in spirometry, including an initial workshop at the beginning of the study and a "maintenance of standards" workshop at 12 weeks.

Only 19% of spirometry tests at trained practices and 5% at untrained practices consisted of three acceptable "blows." The proportion of tests meeting full ATS criteria for acceptability and reproducibility were 14% and 3%, respectively. Nevertheless, at least two acceptable blows were achieved in 33% of tests at trained 13% at untrained practices. The major reason for unacceptable tests was failure to meet end-of-test criteria, ie, a blow of at least 6 seconds. Less than 15% of these blows reached a plateau on the volume-time curve. Analysis of a subset of tests suggested that the primary care physician's interpretation was correct on 53% of patients, with no difference between the trained and untrained groups.

Most spirometry tests performed in the primary care physician's office do not meet standard criteria for acceptability and reproducibility, the results suggest. Performance is better, but still suboptimal, in practices receiving formal training. Most test failures are related to end-of-test criteria, suggesting that the findings may still be clinically valid and usable. Spirometry should be available in primary care settings; training and quality assurance are needed to ensure that it is performed correctly.

COMMENT: *This study underscores a serious potential problem in asthma management. With the recent emphasis placed on objective documentation of lung function, primary care practices are performing screening spirometry with increasing frequency. In this study, fewer than one-third of the 1,012 spirometry tests analyzed met minimum ATS requirements for acceptability. Only about one-half were interpreted correctly. It would be of interest to repeat this study for spirometry tests performed in asthma specialists' offices.*

S. A. T.



Eaton T, Withy S, Garrett JE, et al: Spirometry in primary care practice: the importance of quality assurance and the impact on spirometry workshops. *Chest* 116:416-423, 1999. ♦♦

Idiopathic Rhinitis Linked to Abnormal Sympathetic Responses

SOME studies of idiopathic rhinitis--also known as vasomotor rhinitis--have described a vasomotor response of the nasal mucosa in response to cold stimulation of the skin. This study examined the pathophysiologic characteristics of the nasal mucosa in patients with idiopathic rhinitis. Of 866 patients seen at a nasal allergy clinic, 28 (3.2%) were diagnosed as having idiopathic rhinitis. A subset were studied to determine their threshold of nasal reaction to histamine, the characteristics of inflammatory cells in nasal lavage fluid and scraped from the nasal mucosal epithelium, and the vasomotor response of the nasal mucosa to cold stimulation of the feet and of the nasal mucosa. Patients with allergic rhinitis and normal controls were studied for comparison.

There was no increase in inflammatory cells among patients with idiopathic rhinitis. These patients did have increased nasal reactivity to histamine compared to normal controls, although not as great as in patients with allergic rhinitis. Cold stimulation of the feet produced swelling of the nasal mucosa in patients with idiopathic rhinitis. In normal controls, cold stimulation caused mucosal contraction as a result of sympathetic excitation. However, in patients with idiopathic rhinitis, the sympathetic nasal vasomotor response was inhibited, leading to swelling and increased secretions. Cold stimulation of the nasal mucosa caused a reduction in nasal volume, greatest in patients with idiopathic rhinitis.

Idiopathic rhinitis appears to be associated with inhibition of sympathetic reactions and enhancement of the parasympathetic vasomotor response. The pathogenesis of this condition remains unclear, but appears to involve abnormal neurologic responses to cold and other stimuli. Cold may directly cause degranulation of nasal mucosa mast cells, as in cold urticaria.

COMMENT: *Despite the widespread prevalence of vasomotor rhinitis, our understanding of its pathophysiology has lagged behind what we know about allergic rhinitis. This study confirms the lack of an inflammatory cell infiltrate in symptomatic patients with vasomotor rhinitis. It also describes a unique pattern of nasal obstruction and secretion in response to submerging subjects' feet in cold water. Additional neurophysiologic studies should shed more light on the pathophysiology of this disease.*

S. A. T.

Numata T, Konno A, Hasegawa S, et al: Pathophysiological features of the nasal mucosa in patients with idiopathic rhinitis compared to allergic rhinitis. *Int Arch Allergy Immunol* 119:304-313, 1999. ♦♦

Intervention Improves Outcomes for Inner-City Asthma Patients

MINORITY patients living in the inner city experience disproportionately high morbidity and mortality from asthma. Although effective treatments are available, patient education and cooperation are essential to good compliance. An inpatient education program (IEP) for inner-city patients with acute asthma is described and evaluated. The program targeted patients hospitalized with asthma attacks for intensive education, using the principle of functional redundancy to reinforce critical information and concepts. The IEP also included identification and, if possible, removal of barriers to care; a telephone call 24 hours after discharge; and outpatient follow-up in an allergy-pulmonary asthma clinic 1 week after discharge.

Seventy-seven patients, aged 18 to 45 years, with a primary admission diagnosis of asthma were randomized to either the IEP or routine care. All were admitted from the emergency department. The two groups had similar rates of successful discharge from the hospital. Sixty percent of patients in the IEP group attended their initial follow-up visit, compared with 27% in the routine care group. Three-fourths of IEP patients who returned for their initial visit were still in the outpatient program 1 year later. Patients assigned to the IEP also had reduced rates of emergency department visits and hospital admissions for asthma over the subsequent 6 months.

This intensive, inpatient asthma education program significantly improves follow-up for inner-city adult patients with asthma. Significant cost savings result from reduced emergency department and hospital utilization. Key aspects of the IEP include the use of metered-dose inhalers, a focus on symptom recognition and response, simple adherence-promoting techniques, and removal of obstacles to care. The study is limited by its lack of generalizability--it excluded critically ill patients and those with significant morbidity--and by the possibility of a placebo effect.

COMMENT: *Treatment of inner-city asthma is highly problematic, in part because of social and educational factors that contribute to poor patient compliance and understanding of disease management. This study describes a program that has apparently been able to address some of these issues, and thereby serves as a model for developing asthma management programs for inner-city populations.*

M. S. D.

George MR, O'Dowd LC, Martin I, et al: A comprehensive educational program improves clinical outcome measures in inner-city patients with asthma. *Arch Intern Med* 159:1710-1716, 1999. ♦♦

Umbilical Cord IgE Predicts Atopy in Early Childhood

EFFECTIVE prevention of atopy in young children requires information on accurate predictors of early-life atopy. It has been suggested that the ►►

level of IgE in the umbilical cord at birth is a reliable predictor of atopy during childhood. This hypothesis was evaluated in a study of 1,546 consecutive children in whom umbilical cord serum total IgE was measured at birth. Clinical data on signs and symptoms of allergic disease at 4 years of age were available in 1,218 children. Nine hundred eighty-one underwent skin testing to common food allergens and aeroallergens.

Eighteen percent of the children with clinical follow-up had symptoms of allergic disease, and 20% of those undergoing skin testing had positive responses. Forty-four percent of the children who had symptoms of respiratory allergy at 4 years of age had a positive skin test to aeroallergens. Fifty-eight percent of the subjects had undetectable cord IgE levels at birth (less than 0.2 kU/L), while 13% had elevated cord IgE levels (0.5 kU/L or greater). The rate of elevated cord IgE was 15% in infants with a family history of atopy and 10% for those with no such history. Thirty-five percent of infants with elevated cord IgE at birth became sensitized to aeroallergens, compared with 17% of those without elevated cord IgE. The combination of paternal atopy and elevated cord IgE had a positive predictive value of 78% for development of aeroallergen sensitivity. However, cord IgE did not predict the development of clinical asthma or rhinitis by age 4. The risk of respiratory allergic disease was actually lowest for children with elevated cord IgE and a negative family history of atopy.

Newborns with elevated umbilical cord serum total IgE are at increased risk of becoming sensitized to aeroallergens by age 4. However, cord IgE is unrelated to the risk of respiratory allergic disorders by this time. Cord IgE is a better predictor of early-childhood atopy than family history.

COMMENT: *This large, prospective epidemiologic study helps settle the debate about whether the umbilical cord IgE level is a predictor of atopy. Since clinical allergy often begins after age 4, follow-up study of these subjects in several years will be needed to establish whether umbilical cord IgE also predicts allergic symptoms.*

S. A. T.

Tariq SM, Arshad SH, Matthews SM, Hakin EA: Elevated cord serum IgE increases the risk of aeroallergen sensitization without increasing respiratory allergic symptoms in early childhood. *Clin Exp Allergy* 29:1042-1048, 1999. ♦♦

Adenoidectomy of Little Help in Children with Recurrent Otitis Media

A DENOIDECTOMY and adenotonsillectomy are the most commonly performed pediatric surgical procedures in the United States. Many of these patients are operated on because of otitis media, although the efficacy of adenoidectomy and adenotonsillectomy for this indication remains doubtful. Two randomized trials were performed to assess the efficacy of adenoidectomy and adenotonsillectomy for children with persistent or recurrent otitis media. The trials included a total of 461 children undergoing one of the two operations, without previous tympanostomy tube placement, over a 14-year period. One study compared the effects of adenoidectomy alone vs adenotonsillectomy.

Both studies found only a modest effect of surgery, with most of the benefit limited to the first year of follow-up. In one trial, adenotonsillectomy was slightly more efficacious than adenoidectomy. Failure to comply with assigned treatment was more common in the surgery groups.

In children with recurrent acute otitis media, adenoidectomy and adenotonsillectomy appear to be of limited value. The results suggest that neither operation is the best choice for initial surgery in children whose only indication is recurrent acute otitis media. Adenotonsillectomy may be somewhat more efficacious than adenoidectomy alone. This raises the questions of whether otitis media might be related to infection in the oropharynx as well as the nasopharynx, and whether children with continued otitis media after tube extrusion might have better results with adenotonsillectomy.

COMMENT: *This 14-year study of children aged 3 to 15 with recurrent otitis media showed little advantage of performing adenoidectomy or adenotonsillectomy as a first surgical intervention. Between 10% and 20% of the subjects had "definite or probable" allergy as defined by an unspecified algorithm, and about 80% had "possible or unlikely" allergy. These findings suggest that a significant atopic population may have been involved. Were the allergic children less likely to respond to surgical intervention? Were the older children more likely to have allergic disease? Unfortunately, the study doesn't answer these important questions, but we hope it will discourage unnecessary referrals for surgery in children with recurrent otitis media.*

S. R. W.

Paradise JL, Bluestone CD, Colborn DK, et al: Adenoidectomy and adenotonsillectomy for recurrent acute otitis media: parallel randomized clinical trials in children not previously treated with tympanostomy tubes.

JAMA 282:945-953, 1999. ♦♦

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