

ALLERGYWATCH®

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

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Treatment by Specialists Improves Outcomes for Patients With Asthma

WITH the increased use of managed care, patients face restrictions on access to medical specialists. There is some evidence that specialist care leads to improved outcomes for patients with chronic health problems, such as hypertension or diabetes. This survey study examined the effects of physician specialty on treatment provided and outcomes for patients with asthma.

The study used survey data from 1,954 adult asthma patients enrolled in 12 managed care organizations. All patients had had at least two medical care encounters for asthma within the previous 2 years. A further survey was performed to gather information from 1,078 physicians involved in the patients' care. Various treatment indicators and patient outcomes were compared for 378 patients treated by a generalist vs 204 treated by an "experienced generalist," ie, an internist or family practitioner specializing in asthma care; 292 treated by a pulmonologist; and 382 treated by an allergist.

Treatment by an asthma specialist was associated with significant differences in several aspects of care, including consistency of care; knowledge of flare-ups, medications, or triggers; having an inhaled corticosteroid; and undergoing an allergy evaluation. Peak flowmeters were used by 52% to 54% of patients treated by a specialist or experienced generalist, compared with 42% of those treated by generalists. Treatment by an allergist was associated with lower rates of canceled activities, hospitalizations and ED visits for asthma. Allergist treatment was also linked to better ratings for quality of care and physical functioning, while pulmonologist treatment improved the chances of very good to excellent improvement in symptoms.

Specialist treatment appears to improve measures of care and outcome among managed care patients with asthma. Improvements are noted in some of the outcomes most important to patients, employers, and managed care organizations alike. The precise factors leading to the improved outcomes remain to be determined.



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- Annals of Allergy, Asthma and Immunology
- Journal of Allergy and Clinical Immunology
- 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 Pediatrics
- Thorax
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- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal

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COMMENT: This report adds to the information data base showing improved outcomes of adults with asthma seen by respiratory specialists (allergists and pulmonologists) compared to generalists (internists and family practitioners) in a managed care setting. Patients who had seen a specialist had the best outcomes, likely because of both patient education about nonpharmacologic control measures and asthma action plans, as well as implementation of better treatment paradigms such as home peak flow monitors, allergy evaluations, and regular inhaled corticosteroids. The study is somewhat limited by the fact that the patient population was largely Caucasian. This study offers additional evidence to support the contention that asthma specialists (particularly allergists) as well as generalists highly experienced in asthma care provide superior clinical care in a cost-effective manner, at least in a managed care population.

G. D. M.

Wu AW, Young Y, Skinner EA, et al: Quality of care and outcomes of adults with asthma treated by specialists and generalists in managed care.

Arch Intern Med 161:2554-2560, 2001. ♦♦

Early Exposure to Dogs Lowers Risk of Childhood Wheezing

STUDIES of factors associated with childhood asthma have sometimes given surprising results. Several studies have suggested that keeping pets in the house is actually associated with a lower risk of asthma or atopy, although these studies have been limited to high-risk populations or cross-sectional in nature. Long-term follow-up data from a prospective birth cohort were used to assess the relationship between early pet exposure and later risk of frequent wheezing or allergic sensitization.

The birth cohort included 1,246 healthy babies born between 1980 and 1984. With prospective follow-up to the age of 13 years, 22% of the children developed frequent wheezing. The cumulative incidence of this outcome was 17.1% for homes with dogs when the child was an infant, compared to 24.6% for homes without dogs. The relationship was apparent mainly among children whose parents did not have asthma. Cat exposure during infancy was not significantly related to frequent wheezing. However, the inverse relationship with dog exposure remained significant even after adjustment for confounders, hazard ratio 0.53.

Although information on changes in pet ownership were incomplete, removing dogs from the home between the ages of 3 and 6 years was associated with an increased risk of frequent wheezing. Pet exposure during infancy was unrelated to the results of skin prick testing.

Exposure to dogs during infancy may actually reduce the risk of frequent wheezing later in childhood. The risk of allergic sensitization appears unaffected by pet ownership. Pet avoidance during infancy and early childhood does not appear to be useful for primary prevention of asthma and allergy.

COMMENT: The effect of pet ownership in infancy on the subsequent risk of atopy and asthma has been further investigated in this cohort study from Dr. Martinez's group. Using prospective data from the 1,200 children in the Tucson Children's Respiratory Study, which began in the early 1980s, they reported that pet (specifically, dog) ownership in the homes of infants had a protective effect for the development of wheezing. When the dogs were removed from the homes, as the children grew, there was an increasing incidence of wheezing. Interestingly, this was not shown for homes with cats. Should we change our recommendations about avoidance of pets in the homes of our patients? In the editorial that accompanies this article, Dr. Marks recommends that we should probably not be recommending pet ownership as prophylaxis against asthma.

S. M. F.



Remes ST, Castro-Rodriguez JA, Holberg CJ, et al: Dog exposure in infancy decreases the subsequent risk of frequent wheeze but not of atopy. *J Allergy Clin Immunol* 108:509-515, 2001. ♦♦

Study Looks at Allergen Levels in Day Care Centers

THE number of American children attending day care continues to increase. Day care centers are a potentially important site of allergen exposure, which is a risk factor for allergic sensitization and asthma in young children. Levels of common aeroallergens were measured in a sample of day care centers.

Dust and air samples were collected from 20 day care centers in Tampa, Fla. Immunochemical techniques were used to measure concentrations of mite, cat, and cockroach allergens. Just four of the centers had linoleum floors; the rest were carpeted.

Mite allergens were detected at 10 centers. The most prevalent was Der p 1, found at 8 centers in concentrations of 1.0 to 21.8 µg/g of dust. Three centers had detectable levels of Der f 1. All centers had low concentrations of cockroach and cat allergens: from 8 to 1,806 ng/g for Per a 1 and from 0.2 to 120 U/g of dust for Fel d 1. Eighteen centers had detectable airborne mite allergens, in levels ranging from 0.01 to 2.7 AU/m³ during the daytime and from 0.01 to 0.12 AU/m³ at night.

In this study, day care centers in an American city with a warm, humid climate show significant concentrations of mites and indoor allergens. Some of the measured levels are associated with a significant risk of sensitization. Indoor air quality likely has an important impact on respiratory symptoms in preschool children.

COMMENT: The authors provide us with very useful and relevant bioaerosol data from day care centers. Since the exposed children are at an age when allergic disease may develop, allergen avoidance measures may be extremely important. This is valuable information since allergen levels were sufficient for sensitization or triggering of symptoms in many at-risk children.

A. M.

Fernández-Caldas E, Codina R, Ledford D, et al: House dust mite, cat, and cockroach allergen concentrations in daycare centers in Tampa, Florida. *Ann Allergy Asthma Immunol* 87:196-200, 2001. ♦♦

Influenza Vaccination Doesn't Increase Exacerbation Rate in Asthma Patients

INFLUENZA predisposes to exacerbations in patients with asthma, therefore influenza vaccination has the potential to reduce asthma-related morbidity. However, asthma patients have low rates of influenza vaccination, reflecting fear that vaccination may cause exacerbations. The safety of influenza vaccination in asthma patients was investigated.

Two thousand thirty-two patients with asthma, children and adults, received influenza vaccine or placebo in randomized, double-blind fashion. The injections were given a median of 22 days apart. For 2 weeks after each injection, the patients made daily peak expiratory flow and symptom recordings. The main outcome measure was the rate of asthma exacerbations after influenza vs placebo vaccination.

The rate of asthma exacerbations was similar after the two injections: 28.8% for influenza vaccine and 27.7% after placebo injection. Patients were somewhat more likely to report body aches after influenza vaccination; otherwise, symptoms were similar with influenza vaccine and placebo.

This randomized trial supports the safety of influenza vaccination in children and adults with asthma. In this study, the frequency of exacerbations is similar after influenza vaccination vs placebo injection, even in patients with severe asthma.

COMMENT: Naturally occurring influenza infection can seriously complicate the control of asthma, yet only about 10% of asthma patients are being vaccinated each year. Perhaps this relates to the young age of many asthma patients, or to fears among asthmatics that the vaccine may not be safe. This placebo-controlled study of over 2,000 patients with stable asthma aged 3 to 64 years provides reassurance that various asthma outcome measures were no different in the vaccinated group than in the placebo group in the 2 weeks following vaccination.

R. J. M.

The American Lung Association Asthma Clinical Research Centers: The safety of inactivated influenza vaccine in adults and children with asthma.

N Engl J Med 345:1529-1536, 2001. ♦♦

Early Farm Exposures Protect Against Childhood Asthma

CHILDREN who grow up on farms have lower rates of allergic diseases and sensitization. Certain immune system processes are regulated by microbial compounds such as endotoxin, suggesting that early-life microbial exposure could play an important role in the development of a nonatopic immune response. Children in rural areas were studied to determine the link between early exposure to microbial compounds and subsequent risk of allergic diseases.

The cross-sectional survey included children, aged 6 to 13 years, living in rural areas of Austria, Germany, and Switzerland. Parents provided information on the children's symptoms of asthma, hay fever, and atopic dermatitis. Blood samples were obtained for measurement of specific serum IgE to common allergens. To avoid confounding by ethnicity, the final analysis included 812 native-born children whose parents were nationals of the countries in which they lived. Allergic disease outcomes were compared for farmers' children vs non-farmers' children, including analysis of age at the time of certain farming-related exposures. ➤➤

The asthma rate was just 1% for children who were exposed to stables and consumed farm milk before 1 year of age, compared to 11% for those exposed at age 1 to 5 years. Early farm-related exposures were also associated with lower rates of hay fever, 3% vs 13%; and atopic sensitization, 12% vs 29%. The protective effect against asthma was independent from that against atopic sensitization. For children with continual exposure to stables to age 5, the rates of asthma and hay fever were only 0.8%, while the sensitization rate was 8.2%.

Farming-related exposures during early childhood have a substantial protective effect against the development of asthma and other allergic diseases. The mechanism of this effect is unknown but may involve exposure to bacterial compounds such as endotoxin.

COMMENT: *These authors report a significantly lower frequency of asthma, hay fever, and atopic sensitization in children growing up on a farm. The timing and duration of exposure to stables and farm milk in the first 5 years of life is critical to the protection derived. The precise mechanism of the protective effect remains to be elucidated, but it's believed to be related to an efficient T-helper-1 response to allergen.*

E. J. B.

Riedler J, Braun-Fahrlander C, Eder W, et al: *Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey.* *Lancet* 358:1129-1133, 2001. ♦♦

Patients Who React to NSAIDs May Also React to COX-2 Inhibitors

THE new selective cyclo-oxygenase (COX)-1 and COX-2 inhibitors cause fewer GI and hematopoietic adverse effects than the nonselective COX inhibitors. However, there are few data on the safety of the new medications in patients who have angioedema or urticaria in response to the conventional COX inhibitors. Tolerance to COX-2 inhibitors was evaluated in patients with cutaneous reactions to classic nonsteroidal anti-inflammatory drugs (NSAIDs).

The study included 110 patients with a history of urticaria or angioedema in response to NSAIDs. Single-blind, placebo-controlled oral provocation tests were performed to assess cross-reactivity to COX-2 inhibitors. A total of 184 challenges were performed using nimesulide, meloxicam, celecoxib, and rofecoxib.

Reaction rates varied significantly between drugs, from 3% for rofecoxib to 33% for celecoxib. Seventy-five percent of patients were cross-reactors, while 25% were single reactors.

The findings demonstrate the relative safety of some selective COX-2 inhibitors—particularly rofecoxib—in patients with a history of cutaneous reactions to NSAIDs. Celecoxib may be more likely to cause reactions, though the difference was not significant in this trial. The results strengthen the theory that COX-1 inhibition is the major mechanism of cutaneous reactions to NSAIDs, although other factors appear to be operative as well.

COMMENT: *The use of COX-2 inhibitors for chronic and acute pain and inflammation has increased dramatically. Although they appear to be safe drugs in most patients, these agents do have variable degrees of COX-1 inhibition. Clinicians must be aware of the significant degrees of cross-reactivity among COX-1 and COX-2 agents. (Also see AllergyWatch Nov./Dec. 2001, p. 4.)*

A. M.

Borges MS, Capriles-Hulett A, Caballero-Fonseca F, Pérez C: *Tolerability to new COX-2 inhibitors in NSAID-sensitive patients with cutaneous reactions.* *Ann Allergy Asthma Immunol* 87:201-204, 2001. ♦♦

African Study Links Kerosene Heat to Increased Allergy Risk

VARIABLES associated with a more affluent or urban lifestyle appear to increase the risk of allergic disease. One such factor may be the use of cleaner fuels in the home, such as kerosene or gas, instead of biomass fuels. The population of an African town with a rising rate of asthma was studied to assess the relationship between type of heating fuel and risk of allergy.

The cross-sectional survey study included 9,844 residents of the town of Jimma, Ethiopia, as well as from rural communities in the Jimma district. All respondents provided information on allergy symptoms, domestic fuel use, and lifestyle factors. In addition, skin tests for allergic sensitization were performed in 2,372 subjects.

Ten percent of respondents used non-biomass fuels, although nearly all used some biomass fuels as well. The allergic sensitization rate was significantly elevated for respondents using non-biomass fuels: odds ratio 1.98, 95% confidence interval 1.21 to 3.22. Most of the effect was attributable to kerosene use, which was significantly associated with all outcomes studied.

In an urbanizing part of the developing world, allergic symptoms and sensitization are significantly associated with the use of modern, non-biomass fuels. Kerosene use is significantly associated with skin sensitization and allergic symptoms; gas use is associated with sensitization only. The mechanisms of these associations await further study.

COMMENT: *It has been suggested that petrochemical pollutants may predispose some to developing atopy. The authors studied factors associated with developing allergic sensitivity in an Ethiopian city that has become more urban over the past 20 years. Interestingly, the incidence of asthma has significantly increased during the same time. This study surveyed over 2,300 adults and children using both questionnaires and allergy skin testing. It found a significant association between allergic sensitization, upper and lower airway symptoms, and use of kerosene or gas in homes. These findings provide further evidence supporting the association between petrochemical pollutant exposure and development of atopy.*

G. D. M.



Venn AJ, Yemaneberhan H, Bekele Z, et al: Increased risk of allergy associated with the use of kerosene fuel in the home. *Am J Respir Crit Care Med* 164:1660-1664, 2001. ♦♦

Flunisolide Causes Less HPA-Axis Suppression Than Fluticasone

INHALED corticosteroids are effective in reducing underlying airway inflammation in asthma, but physicians are concerned about the potential for endocrine and other systemic effects. Hypothalamic-pituitary-adrenal (HPA) axis suppression, measured in terms of adrenal cortisol output, is a useful marker of the systemic bioavailability of steroids. Studies of healthy volunteers have shown significant suppression of cortisol by the inhaled corticosteroid fluticasone propionate. This study compared the HPA effects of two commonly used corticosteroids--flunisolide and fluticasone--in patients with mild to moderate asthma.

The randomized, placebo-controlled, open-label study included 153 adult patients with persistent, mild to moderate asthma who had not received corticosteroids in any form for the preceding 6 months. They were randomized to receive 21 days of flunisolide, 500 or 1,000 µg twice daily; fluticasone, 110, 220, 330, or 440 µg twice daily; or prednisone, 7.5 mg daily. High-performance liquid chromatography was performed to assess serum and urinary cortisol levels. The study was funded by the manufacturer of flunisolide.

One hundred twenty-five patients completed the study and were at least 80% compliant with their assigned treatment. The cortisol measurements showed dose-dependent HPA suppression by both fluticasone and flunisolide. However, this effect was substantially greater with fluticasone: serum cortisol suppression per 1 µg increase in corticosteroid dose was 4.4-fold higher with fluticasone than flunisolide.

At clinically used doses in patients with mild to moderate asthma, inhaled fluticasone causes significantly greater HPA-axis suppression than flunisolide. The difference seems to result from the episodic nature of flunisolide's cortisol-suppressing effect. The results suggest that systemic corticosteroid exposure is significantly lower with flunisolide than fluticasone.

COMMENT: *The safety of inhaled steroid preparations remains a significant concern to patients and physicians. In this report the authors show a dose-dependent suppression of HPA function for both flunisolide and fluticasone. Although fluticasone showed a greater degree of suppression, the differences are likely explained by the greater molecular potency of this drug. The results highlight the importance of using the lowest effective dose of any inhaled steroid.* A. M.

Casale TB, Nelson HS, Stricker WE, et al: Suppression of hypothalamic-pituitary-adrenal axis activity with inhaled flunisolide and fluticasone propionate in adult asthma patients. *Ann Allergy Asthma Immunol* 87:379-385, 2001. ♦♦

Flotation Method Can't Tell How Much Drug Is Left in MDI Canisters

TO ensure continuity of anti-inflammatory therapy for asthma, some reliable method of assessing the amount of medication remaining in metered-dose inhalers (MDIs) is needed. One suggested approach is the flotation method, in which the way the canister floats in a container of water is taken as an indicator of how much medication is left. The reliability of this technique was tested.

Three different types of MDIs were studied, containing albuterol sulfate, with hydrofluoroalkane propellant; triamcinolone acetate; and fluticasone propionate. At baseline, before any actuations, each canister was floated in a container of water. At 2-minute intervals, the devices were actuated. After 25%, 50%, 75%, and 100% of prescribed actuations, the canisters were floated again. The positions in which the canisters floated did not accurately reflect the amount of medication left in the canisters. Before and after actuations, each of the three devices had its own unique floating pattern.

The flotation method is not a reliable indicator of how much medication is left in MDIs. Each of the devices tested has its own different floating characteristics, independent of the amount of medication remaining. Better methods of assessing the contents of inhaler devices are needed.

COMMENT: *The inability to easily quantify medication in MDI canisters has long frustrated patients, treating physicians, and clinical trial investigators. The simple notion that the buoyancy of an MDI canister reflects the quantity of contained drug is appealing. Unfortunately, this report indicates that the idea has sunk. Fortunately, newer delivery systems have incorporated indicators of remaining medication.*

D. K. L.

Cain WT, Oppenheimer JJ: The misconception of using floating patterns as an accurate means of measuring the contents of metered-dose inhaler devices. *Ann Allergy Asthma Immunol* 87:417-419, 2001. ♦♦

Immunotherapy Reduces Rate of New Sensitizations in Monosensitized Children

SPECIFIC immunotherapy (SIT) is now established as an effective treatment for IgE-mediated respiratory tract diseases. Among asthma patients, SIT may produce a greater effect in children than adults. The ability of SIT to prevent further sensitization in monosensitized children with asthma was investigated.

The 6-year, longitudinal study included 134 children, aged 5 to 8 years, with intermittent asthma, with or without rhinitis. All children were monosensitized to house dust mite (HDM), as demonstrated by skin prick testing and specific IgE measurements. All children were offered SIT, and 75 accepted. The remaining 63 children, who received medication only, served as controls. The SIT group received 3 >>>

years of immunotherapy using a biologically standardized mite mix. Throughout this period and for 3 years afterward, children in both groups were followed by skin prick testing and serum-specific IgE measurements.

The two groups had similar characteristics at baseline; 123 children completed the study. At enrollment, 62.3% of children in the SIT group had asthma only and 37.7% had asthma and rhinitis. In the control group, 57.4% of children had asthma only while 42.6% had asthma and rhinitis.

At follow-up, 75.4% of children receiving SIT had no new sensitization, compared with 33.3% of children in the control group. The most common type of new sensitization was to local pollens.

Specific immunotherapy may reduce the rate of new sensitizations among monosensitized, asthmatic children. The rate of new sensitizations is reduced from about two-thirds to about one-fourth, although protection is not complete. The mechanism of the protective effect is unclear but may involve a shift in the Th1:Th2 ratio.

COMMENT: This Italian study focused on children with mild asthma who were monosensitized to dust mite. After 6 years of follow-up, those treated with immunotherapy for 3 years were much less likely to have developed new sensitizations than those who did not undergo immunotherapy. There was no difference in the proportion of subjects in each group who still had asthma. The capacity for conventional immunotherapy in monosensitized subjects to prevent subsequent sensitization to other allergens is a fascinating concept. The practical application of the immunotherapeutic strategy will require further study, especially given the tendency in the United States for allergists to reserve immunotherapy almost exclusively for polysensitized patients.

S. A. T.

Pajno GB, Barberio G, de Luca Fr, et al: Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy. A six-year follow-up study.

Clin Exp Allergy 31:1392-1397, 2001. ♦♦

Inhaled Budesonide Doesn't Alter BHR for Adolescent Asthma Patients in Remission

FOR children with asthma, adolescence can be a time of long-term clinical remission. It might be assumed that these remissions would be accompanied by normalization of bronchial hyperresponsiveness (BHR), yet adolescent patients who are symptom free commonly show continued evidence of BHR. The effects of inhaled corticosteroid therapy on BHR in adolescent asthma patients in remission were evaluated.

The randomized, double-blind trial included 37 adolescent asthma patients in long-term remission; all patients had been free of symptoms and medications for the previous 2 years. The treatment group received inhaled budesonide, two 200 µg puffs twice daily for 9 months, while the control group received a placebo inhaler. A group of 19 symptomatic patients

receiving the same budesonide regimen were studied as well.

The three groups had a similar methacholine PC₂₀ at the start of treatment. Neither of the two remission groups had a significant change in PC₂₀ during treatment. In contrast, the symptomatic patients had a significant increase in PC₂₀ during budesonide treatment.

Prolonged treatment with inhaled budesonide does not improve BHR in adolescent asthma patients in long-term clinical remission. The mechanism of BHR in this group of patients may differ from that of patients with continued asthma symptoms. The results suggest that symptomatic remission should be the goal of treatment for adolescent asthma patients.

COMMENT: Bronchial hyperresponsiveness is a significant measure of airway severity and underlying airway inflammation. This study addresses the perplexing question, Do inhaled corticosteroids decrease BHR in adolescent asthmatics in long-term remission? The answer appears to be no. Is the situation different in adolescent asthmatics in long-term remission? Nasal symptoms often precede lower respiratory symptoms. It might be worthwhile to investigate the beneficial effects of inhaled corticosteroid therapy in adults who again develop allergic rhinitis, although their childhood asthma is in remission.

A. L. L.

Koh YY, Sun YH, Lim HS, et al: Effect of inhaled budesonide on bronchial hyperresponsiveness in adolescents with clinical remission of asthma.

Chest 120:1140-1146, 2001. ♦♦

Egg and Milk Reactions in Children: Parental Perceptions and Dietary Restrictions

PARENTS tend to overestimate the extent to which children's symptoms are caused by foods. Milk and eggs are nutritionally important foods for children, and commonly perceived as causing adverse reactions. This population-based study examined the frequency of milk- and egg-restricted diets in children perceived by their parents as reacting to these foods.

From a consecutive birth cohort, 2,979 families responded to a questionnaire when the child was 2 years old. The parents were asked whether the child had had any reactions to foods, and whether any foods had been eliminated from the child's diet. The relationship between dietary restrictions and the eventual diagnosis of food allergy was evaluated.

The parents perceived a reaction to egg or milk by age 2 in 206 children. Seventy-three of these children had been placed on a strict diet to eliminate the suspected food; in 17 children, both egg and milk were restricted. Fifty-four percent of parents perceiving a food reaction had consulted a physician regarding the problem. In at least 20% of children who had been placed on strict elimination diets, allergy to the restricted food was eventually disproved. In contrast, in nearly half of children with a confirmed or possible reaction, no dietary restrictions >>

were observed. High maternal education was a risk factor for unnecessary dietary restriction.

Many parents perceive that their children have had reactions to egg or milk and limit the child's intake of these foods, often unnecessarily. Especially for milk, these dietary restrictions raise nutritional concerns. Parents should be encouraged to seek medical confirmation of suspected food reactions to ensure that dietary restrictions are implemented only when necessary.

COMMENT: *This is a carefully documented 2-year prospective study of Norwegian infants whose mothers perceived a food reaction. The results show that there were some infants who were placed on a strict diet of egg and/or milk elimination but were later found to be not allergic, while other infants were not placed on a strict diet but were allergic. As the authors point out, the child should be evaluated by a physician at the time of the possible food reaction to ensure proper advice on diet.*

J. A. A.

Eggesbø M, Botten G, Stigum H: Restricted diets in children with reactions to milk and egg perceived by their parents.

J Pediatr 139:583-587, 2001. ♦♦

Postmarketing Data Show Low Rate of Side Effects with SLIT

RESearch supports the use of sublingual immunotherapy (SLIT) as an alternative to subcutaneous immunotherapy. Although SLIT appears reasonably safe, there are safety concerns related to self-administration by the patient. This postmarketing surveillance study examines the occurrence of side effects among patients taking SLIT.

The patients were 115 women and 83 men, mean age 24 years, who were taking SLIT in the form of monomeric allergoid tablets. Patients received SLIT for a single seasonal or perennial allergen only; treatment was given before or during allergy season for pollen and continuously for mites. Patients received regular follow-up for side effects, which were rated for type and severity. At 3 years' follow-up, effectiveness was assessed by questionnaire.

There were just 17 adverse events, 3 of which were local. The frequency of adverse events was 7.5% of patients or 0.52 per 1,000 doses. There were 7 episodes of rhinitis, 3 of mild lip edema, and 1 of mild abdominal pain; all were self-limiting, requiring no treatment modifications. Temporary dose adjustments were needed for 2 cases of urticaria and 2 of abdominal pain or nausea. Oral antihistamines were given for 1 episode of urticaria and conjunctivitis.

The results support the safety of SLIT in clinical practice. Side effects are infrequent and usually require no treatment. Mild somnolence may be related to the use of oral antihistamines.

COMMENT: Since SLIT was approved in a recent consensus statement of the World Health Organization, it has been used with increasing frequency in Europe. This approach has not been similarly embraced in the United States. This study

addresses one of the most important concerns about SLIT, ie, self-administration in the absence of physician supervision. The study found the incidence of side effects was 7.5% of patients (approximately 1 per 1,000 doses administered). About two-thirds of the reported side effects were mild and required no medical treatment.

E. J. B.

Lombardi C, Gargioni S, Melchiorre, A. et al: Safety of sublingual immunotherapy with monomeric allergoid in adults: multicenter post-marketing surveillance study.

Allergy 56:989-992, 2001. ♦♦

First- and Second-Line Antibiotics Have Similar Outcomes in Acute Sinusitis

SINUSITIS carries significant morbidity and costs. Antibiotic therapy for initial management of acute sinusitis is highly variable, and is the topic of ongoing debate. This study compared the effectiveness and costs of treatment with first-line vs second-line antibiotics for acute, uncomplicated sinusitis.

The analysis used the comprehensive Express Scripts Patient Treatment Episode registry, which includes more than 2 million covered lives from several large HMOs. The investigators collected demographic, clinical, treatment, and charge information on 29,102 adult patients receiving initial antibiotic therapy for acute sinusitis during 1996-97. Patients who received no antibiotic prescription after their index office visit were excluded.

The patients were prescribed a total of 17 different antibiotics, with 59.5% receiving a first-line antibiotic. Primary care physicians were somewhat more likely than specialists to prescribe a first-line antibiotic. Treatment success rates were 90.4% overall, 90.1% for patients receiving first-line antibiotics, and 90.8% for those receiving second-line antibiotics. One patient in each group developed periorbital cellulitis. Rates of treatment success or failure and relapse were similar for patients receiving first- vs second-line antibiotics. Direct charges were \$66 higher with second-line antibiotics.

For patients with acute, uncomplicated sinusitis, outcomes are similar for those treated with a first-line vs a more expensive second-line antibiotic. The results support recent recommendations suggesting that antibiotics should be reserved for patients with more severe symptoms of sinusitis. The authors acknowledge the limitations of their study methods, including the lack of a widely accepted way of assessing the success of treatment for acute sinusitis.

COMMENT: *Sinusitis is the fifth most common diagnosis for which antibiotics are prescribed. In addition to efficacy data, the development of bacterial resistance in the individual and community and the cost of care must be considered when choosing an antibiotic therapy, particularly since the majority of untreated, acute bacterial sinusitis resolves without complication. The rub is that allergists/immunologists do not often see, or think they see, uncomplicated, acute sinusitis. To prescribe or not to prescribe, to prescribe new antibiotics or not to prescribe* ►►

new antibiotics--these remain the questions. This paper suggests an answer.

D. K. L.

Piccirillo JF, Mager DE, Frisse ME, et al: Impact of first-line vs second-line antibiotics for the treatment of acute uncomplicated sinusitis.

JAMA 286:1849-1856, 2001. ♦♦

Snoring in Children: Frequency and Risk Factors

SNORING may be a sign of sleep apnea or other forms of sleep-disordered breathing. Previous studies have suggested that snoring in children resolves spontaneously in about half of cases. However, children who continue to snore have problems such as sleepiness, hyperactivity, and poor sleep. The frequency of snoring in children and associated anthropometric and clinical findings were investigated.

The study included 2,209 Italian school children, aged 10 to 15 years, who were studied by questionnaire and clinical examination. Overall, 5.6% of children were classified as habitual snorers, while another 10.4% reportedly snored occasionally in the absence of colds. Snoring was more frequent among boys aged 15 years or older who were above the 90th percentile for body weight. Clinical factors associated with snoring included asthma, rhinitis, and otitis. Certain airway findings were also related to an increased rate of snoring, including decreased nasal patency, septal deviation, nasal obstruction, and enlarged tonsils or a history of adenoidectomy.

Snoring in children appears to be related to body weight, decreased nasal patency, and conditions associated with narrowing of the pharyngeal airway. Some children who snore have increased hemoglobin levels, suggesting possible hypoxia during sleep. Obesity and parental smoking are also risk factors for snoring in children.

COMMENT: Habitual snoring was identified in 5.6% of 2,209 Italian schoolchildren. Risk factors include boys over the age of 15 with body mass greater than 90%, as well as decreased nasal patency for any reason. Tonsil enlargement was strongly correlated with snoring. Interestingly, adenoidectomy (without tonsillectomy) was also an independent risk for snoring.

J. A. A.

Corbo GM, Forastiere F, Agabiti N, et al: Snoring in 9- to 15-year-old children: risk factors and clinical relevance.

Pediatrics 108:1149-1154, 2001. ♦♦

Longer Duration of Breast-Feeding Leads to Lower Asthma Risk

EARLY-life factors appear to influence susceptibility to childhood asthma. Breast-feeding is a possible protective factor, acting to reduce allergic sensitization or through immune system effects. Population-

based data were used to assess the influence of breast-feeding on asthma risk in young children.

The analysis included data 2,184 children, aged 12 to 24 months, from the National Longitudinal Survey of Children and Youth. Duration of breast-feeding was compared with physician-diagnosed asthma and wheezing within the previous year, with adjustment for potential confounders.

Asthma was reported in 6.3% of children and wheezing in 23.9%. Forty-four percent of children were breast-fed for less than 2 months or not at all. On unadjusted analysis, asthma was related to duration of breast-feeding, male sex, parents' history of asthma, prenatal and postnatal smoking, prematurity, and low birth weight. All of these factors were somewhat less strongly associated with wheezing. In an adjusted sensitivity analysis, infants breast-fed for less than 9 months were significantly more likely to develop asthma, odds ratio 2.39. The odds ratio for wheezing was 1.54. The longer the duration of breast-feeding, the greater the protective effect.

Breast-feeding appears to lower the risk of asthma in dose-response fashion--infants who breast-feed for a longer time are less likely to develop asthma. The authors urge targeted efforts to increase the rates and duration of breast-feeding in the population.

COMMENT: This large Canadian population-based study shows that breast-feeding confers a protective effect against asthma and wheeze in the first 2 years of life. The association appears to be dose dependent, since those infants nursed for at least 9 months had a reduced risk of developing wheezing or asthma compared to those nursed for 2 or 6 months. The researchers were unable to control for breast-feeding exclusivity, which may be a limitation of the study. Earlier studies did show that exclusive breast-feeding for at least 15 weeks can reduce respiratory illness (BMJ 316:21-25, 1986). Either way, the importance of promoting breast-feeding to help reduce disease has, once again, been demonstrated. Breast is best!

S. M. F.

Dell S, To T, Breastfeeding and asthma in young children: findings from a population-based study.

Arch Pediatr Adolesc Med 155:1261-1265, 2001. ♦♦

Effects of LTE₄ vs LTD₄ on Airway Inflammatory Cells

THE cysteinyl leukotrienes LTC₄, LTD₄, and LTE₄ cause airway bronchoconstriction and play a pathogenetic role in asthma. Relatively little is known about their role in allergen-induced airway hyperresponsiveness and inflammation, however. This study compared the effects of inhaled LTD₄, LTE₄, and allergen on the airways of patients with allergic asthma.

The study included 21 patients with mild, clinically stable atopic asthma. In randomized, crossover fashion, each patient inhaled diluent, LTD₄, LTE₄, and allergen. The effects on lung function and sputum inflammatory cells were analyzed. ►►

The early reduction in FEV₁ was 23.6% with LTD₄, 21.6% with LTE₄, and 29.3% with allergen, compared to 4.0% with diluent. Sputum eosinophil count was increased 7 and 24 hours after inhalation of LTE₄ and allergen, but not LTD₄. Sputum basophil count was also increased 7 hours after inhaled LTE₄ as well as allergen. Examination of airway biopsy specimens showed a higher eosinophil count in the lamina propria after LTE₄ than after LTD₄ or diluent.

In subjects with mild allergic asthma, LTE₄ inhalation is associated with evidence of prolonged airway inflammation. Inhaled LTE₄ attracts eosinophils into the airway, whereas LTD₄ does not. In addition to their role in allergen-induced bronchoconstriction, the cysteinyl leukotrienes may also be involved in airway eosinophil accumulation.

COMMENT: *The association of the cysteinyl leukotrienes and asthma is well established. Many have considered LTD₄ the most important in asthma pathophysiology while LTE₄ is considered a metabolite with little clinical relevance. This study compared the effects of inhaled LTD₄ vs LTE₄ in mild atopic asthmatics and found that LTE₄ was most potent in recruiting eosinophils to airways. These data suggest that LTE₄ is not an irrelevant metabolite but rather may be an important mediator of late-phase allergic inflammation.*

G. D. M.

Gauvreau GM, Parameswaran KN, Watson RM, O'Byrne PM: *Inhaled leukotriene E₄, but not leukotriene D₄, increased airway inflammatory cells in subjects with atopic asthma.*

Am J Respir Crit Care Med 164:1495-1500, 2001.♦♦

Montelukast Is Highly Effective in Chronic Urticaria Associated with ASA or Food Additives

CHRONIC urticaria is associated with frequent IgE-independent reactions, which may not be adequately controlled by antihistamines. This suggests that other mediators—such as leukotrienes—may be involved. The leukotriene-receptor antagonist montelukast was compared with the antihistamine cetirizine for the treatment of chronic urticaria in patients with intolerance to acetylsalicylic acid (ASA) or food additives.

The 51 patients all had clinical evidence of chronic urticaria, along with a positive food challenge to ASA, food additives, or both. Patients were randomized to receive montelukast 10 mg once daily, cetirizine 10 mg once daily, or placebo. Treatment continued for 4 weeks.

Patients taking montelukast had a significantly higher percentage of days free from hives and itching, compared with cetirizine. Montelukast was also associated with less interference with sleep. Patients in the montelukast group had a median of 24 days without rescue medication, compared with 18 in the cetirizine and placebo groups. The rate of adverse events was low.

Montelukast is a highly effective treatment for patients with chronic urticaria associated with

intolerance to ASA and/or food additives. The findings suggest that leukotrienes may play an important pathogenetic role in this difficult-to-treat condition.

COMMENT: *Although the proportion of chronic urticaria that is caused by ASA or food additives is small, this study reports remarkable clinical efficacy of a leukotriene antagonist in such patients. Further studies are necessary to shed light on the mechanisms involved. Perhaps a trial of leukotriene antagonist will help identify those patients for whom dietary elimination may be worthwhile.*

S. A. T.

Pacor ML, Di Lorenzo G, Corrocher R: *Efficacy of leukotriene receptor antagonist in chronic urticaria. A double-blind, placebo-controlled comparison of treatment with montelukast and cetirizine in patients with chronic urticaria with intolerance to food additive and/or acetylsalicylic acid.*

Clin Exp Allergy 31:1607-1614, 2001. ♦♦

Ethiopian Study Links Increase in Wheezing to Decrease in Hookworm Infection

IN developing countries, asthma rates rise with increasing urbanization and affluence in the population. Among the proposed explanations is an increase in exposure to house dust mite associated with changes in housing and bedding. This study assessed the influence of mite exposure and other factors on the risk of asthma in an Ethiopian population.

From a previous study of nearly 13,000 residents living in urban and rural areas of Ethiopia, the authors identified 205 subjects who reported wheezing within the past year and 399 controls. Sensitization to *Dermatophagoides pteronyssinus* was assessed, along with Der p 1 levels in bedding. Other factors analyzed included parasites in fecal samples; hepatitis A antibodies; serum cholinesterase, as an indicator of organophosphorus exposure; and total and specific IgE.

Hookworm infection was a significant and independent protective factor against wheezing: odds ratio 0.48. Der p 1 level was associated with an increased risk of wheezing: odds ratio 1.26 per quartile of exposure. Hepatitis A antibody status and cholinesterase concentration were not significant factors.

The association between mite sensitization and wheezing was stronger in urban residents than rural residents: odds ratios 9.45 vs 1.95, respectively. Where parasite infection was common, mite sensitization was not significantly related to wheezing.

In the African population studied, a reduced rate of hookworm infection appears to be a factor in the rising rate of asthma. The increase in asthma is also associated with an increase in dust mite exposure, as are other, unidentified factors. The findings are consistent with the theory that parasitic infection has a protective effect against allergic disorders, as well as the growing body of evidence that mite allergen is an asthma risk factor.

COMMENT: *This large cross-sectional study suggests that the increased occurrence of asthma associated with urbanization of an Ethiopian population was partly caused by loss of a protective effect from hookworm infection and partly by increased dust mite exposure. It adds to the increasing body of evidence implicating Der p 1 as a risk factor for asthma.* E. J. B.

Scrivener S, Yemaneberhan H, Zebeignus M, et al: *Independent effects of intestinal parasite infection and domestic allergen exposure on risk of wheeze in Ethiopia: a nested case-control study.* Lancet 358:1493-1499, 2001. ♦♦

HFA vs CFC Flunisolide for Mild to Moderate Asthma

NEW inhaled flunisolide formulations use hydrofluoroalkane (HFA) propellant, rather than the previously used chlorofluorocarbon (CFC). With HFA, the mass median aerodynamic diameter of the aerosol droplets is significantly smaller than with CFC--1.2 vs 3.8 μm --which may improve corticosteroid deposition in the small airways. This placebo-controlled trial compared the safety and efficacy of flunisolide with HFA vs CFC propellant.

Six hundred sixty-nine patients, 12 years or older, with mild to moderate asthma participated in a 2-week, open-label run-in period with CFC flunisolide, 500 μg twice daily. They were then randomized in double-blind fashion to 12 weeks of treatment with HFA flunisolide, 85, 170, or 340 μg twice daily; CFC flunisolide, 250, 500, or 1,000 μg twice daily; or placebo.

Five hundred forty-eight patients completed the study. The mean percentage increase in FEV_1 was 12.22% in patients taking the 170 μg dose of HFA flunisolide and 14.69% in those taking the 340 μg dose, compared with 5.35% for those taking placebo. The effects of HFA flunisolide on pulmonary function were comparable to those of CFC flunisolide, at substantially lower doses. Other efficacy measures were nonsignificantly superior with HFA flunisolide; both formulations had good safety characteristics.

Flunisolide with HFA propellant offers similar safety and efficacy to CFC flunisolide, at one-third the dose. The advantages of HFA flunisolide result from increased lung drug deposition. Both formulations show a clear dose-response relationship for change in FEV_1 .

COMMENT: *An inhaled therapy must be evaluated as a unit--the delivery system and the medication. Comparisons among the various inhaled therapies for asthma are complicated by the variables introduced by both the drug and the delivery system. This study confirms that flunisolide--as is true for albuterol, beclomethasone, and fluticasone--behaves very differently with hydrofluoroalkane (HFA) compared to chlorofluorocarbon (CFC) propellant. The percentage of flunisolide delivered to the airway and the amount deposited in the smaller airways is increased with HFA. Based upon available studies, HFA-drug is a different medication compared to*

CFC-drug, with the differences varying with each drug. Comparisons between metered-dose inhaler and dry power devices also show significant differences. Choice is good, but the plot thickens.

D. K. L.

Corren J, Nelson H, Greos LS, et al: *Effective control of asthma with hydrofluoroalkane flunisolide delivered as an extrafine aerosol in asthma patients.* Ann Allergy Asthma Immunol 87:405-411, 2001. ♦♦

β_2 -Adrenoreceptor Alleles Linked to Asthma Risk in Sedentary Women

PREVIOUS studies have linked the Gly 16 polymorphism of the β_2 -adrenoreceptor gene to asthma severity and downregulation of the β_2 -adrenoreceptor, though not to asthma diagnosis per se. Downregulation of the β_2 -adrenoreceptor may be limited by the Glu27 polymorphism. The Glu27 polymorphism may also be a predictor of body mass index, particularly in sedentary individuals. Data from the prospective Nurses' Health Study were used to evaluate these β_2 -adrenoreceptor polymorphisms as predictors of adult-onset asthma in sedentary women.

The analysis included two groups of women who were lifelong nonsmokers: 171 who had adult-onset asthma requiring medication and 137 age-matched controls. The women provided information on physical activity and BMI in response to questionnaires. The β_2 -adrenoreceptor polymorphisms were assessed using genomic DNA from buccal brushings.

Two hundred thirty-two women were classified as active and 76 as sedentary. Among the sedentary women, the Gly16 allele was significantly associated with asthma. Adjusted odds ratios were 7.4 for asthma overall and 13.8 for asthma requiring steroid treatment. Among active women, the Gly16 allele was unrelated to asthma status. For sedentary women, the presence of both the Gly16 and Glu27 alleles conferred a lesser elevation in asthma risk. There was a significant association between BMI, asthma, and the Glu27 allele among sedentary women.

The Gly16 polymorphism of the β_2 -adrenoreceptor gene appears to be associated with an increased risk of asthma among sedentary, but not active, women. The results are consistent with a possible interaction between genetics and environment in asthma. Additional study is needed to assess the possibility that a sedentary lifestyle "unmasks" a genetic predisposition to asthma.

COMMENT: *The genetics of asthma is a mystery, which is further clouded by environmental factors. This study explores an intriguing connection between β_2 -adrenoreceptor polymorphism, exercise, and onset of adult asthma in women. β_2 -Adrenoreceptor polymorphism has been associated with asthma severity and down-regulation of β_2 -receptors. This study suggests also that the substitution of glycine for arginine at codon 16 of the β_2 -adrenoreceptor gene is linked to the onset of adult asthma in sedentary women, but not in women who exercise on a >>>*

regular basis. This is further evidence that we should encourage our patients to be physically active.

A. L. L.

Barr RG, Cooper DM, Speizer FE, et al: β_2 -Adrenoreceptor polymorphism and body mass index are associated with adult-onset asthma in sedentary but not active women.

Chest 120:1474-1479, 2001. ◆◆

Eastern and Western European Children Differ in Asthma Symptoms, but Not Sensitization Rates

PREVIOUS results from the International Study of Asthma and Allergies in Childhood (ISAAC) have found significant global variation in the reported prevalence of asthma. For reported rate of wheezing in the past year in children aged 13-14 years, the United Kingdom is on the high end of the range, 32%; while Albania is on the low end, 3%. Further comparisons of allergic sensitization and pulmonary function between these two countries were conducted.

The study included about 1,000 children, aged 9 to 11 years, from each country. Assessments included examination of the skin for evidence of flexural dermatitis and skin prick testing for house dust mite, cat, and pollens. Peak expiratory flow was measured as well.

Responses to a parental questionnaire confirmed the variation in symptoms of asthma and allergy. Visible evidence of flexural dermatitis was 3.3-fold more frequent in the U.K. children. However, there were few differences in the prevalence of allergic sensitization between countries. Children in Albania had higher rates of sensitization to *Dermatophagoides pteronyssinus* and *Alternaria* than British children, although the U.K. group was more likely to be sensitized to grass and tree pollens. The British children showed a significant association between exercise-induced bronchospasm and the results of skin prick testing, which the Albanian children did not. The finding of atopy was associated with the presence of rhinoconjunctivitis and flexural dermatitis only in the U.K. group.

Rates of asthma symptoms among children vary significantly between European countries. These differences are not accounted for by differences in the prevalence of allergic sensitization. Further investigation of these differences between Eastern and Western Europe could provide new insights into the prevention of respiratory morbidity.

COMMENT: At age 13 to 14 years, wheezing in the previous 12 months was reported by 3% of Albanian children compared to 32% of children in the United Kingdom. However, the prevalence of allergic sensitization differed very little between these populations of children. These observations confirm the significant differences in asthma prevalence across Europe, but clearly eliminate allergic sensitization as the explanation. One wonders whether lifestyle differences may provide insight into these variations.

E. J. B.

Priftanji A, Strachan D, Burr M, et al: Asthma and allergy in Albania and the UK.

Lancet 358:1426-1427, 2001. ◆◆

Pet Allergen Is Found on Hard Surfaces in Homes

ALTHOUGH carpets are a major reservoir for pet allergens, the particles can also drift and settle on surfaces, including walls, furniture, and smooth floor. The presence and removal of allergens from these surfaces has not been studied in detail. The distribution of dog, cat, and mite allergens on hard surfaces in the home was investigated, including assessment of a new dusting product removing allergen from these surfaces.

The study included 24 homes in which the floors, furniture and walls had not been cleaned for at least 1 week. Dust samples were taken from smooth wood or vinyl floors, hard-surfaced furniture, and walls for allergen measurement. Twenty-three of the homes had Can f 1 allergen on at least one of the sampled surfaces, including homes with no dog. Cat and dog allergen was found on all three types of hard surfaces of homes with and without pets. Allergens were found mainly in the carpets of homes with pets, but were more uniformly distributed in homes without pets. Very low levels of mite allergen were found on hard surfaces.

The study also assessed the allergen-removing effects of dry-dusting with a Pledge Grab-it dust cloth, followed by brush-vacuuming. The Grab-it cloths were highly effective in removing allergen.

Pet allergens are found in significant levels on hard surfaces, even in homes without pets. These surfaces should be addressed, along with carpets, in efforts to reduce exposure to indoor allergens. Dry dusting with Grab-it cloths is an effective means of removing allergen from hard surfaces.

COMMENT: Allergen avoidance measures may be the most important treatment modality we can offer patients with allergic diseases. This interesting article highlights the importance of "dry dusting" hard surfaces in homes with and without pets. Perhaps we need to "expand our horizons" with regard to the environmental control measures we recommend to our patients.

A. M.

Arlian LG, Neal JS, Morgan MS, et al: Distribution and removal of cat, dog and mite allergens on smooth surfaces in homes with and without pets.

Ann Allergy Asthma Immunol 87:296-302, 2001. ◆◆

REVIEWS OF NOTE

Nzeako UC, Frigas E, Tremaine WJ: Hereditary angioedema: a broad review for clinicians. Arch Intern Med 161:2417-2429, 2001.

COMMENT: This represents an up-to-date, comprehensive review of an uncommon condition that presents with rather common symptoms, and may be misdiagnosed in certain circumstances. This is especially true in acquired types of C1 esterase inhibitor deficiency.

E. J. B.



Salpeter S, Ormiston T, Salpeter E: Review: single-dose and longer-duration cardioselective β -blockers do not increase respiratory symptoms in reversible airway disease.

Cochrane Database Syst Rev 2001;(3):CD002992 (latest version 26 May 2001).

COMMENT: This important review suggests that patients with mild to moderate obstructive lung disease with significant reversibility may tolerate cardioselective β -blockers, and these drugs should not be withheld from patients who could clinically benefit from them.

E. J. B.

Ada G: Vaccines and vaccination.
N Engl J Med 345:1042-1053, 2001.

COMMENT: Vaccination-induced immunity against the scourges of infectious diseases such as smallpox, polio, measles, and diphtheria is perhaps the greatest medical success story of all time. In 1966 there were 20 million cases of smallpox worldwide; by 1980, the disease was "eradicated." In this review the author addresses relevant new immunization concepts, such as regional immunity, transcutaneous immunization, peptide subunit antigens, DNA vaccines, and potential immunizations against autoimmune diseases, cancer, HIV, and Alzheimer's disease.

R. J. M.

Naureckas ET, Solway J: Mild asthma.
N Engl J Med 345:1257-1262, 2001.

COMMENT: Since the publication of the 1997 NIH Guidelines for asthma, of the four categories of severity, the greatest controversy over treatment has been in the "mild persistent" group. The Guidelines left considerable discretion to the treating physician in the choice of medications, including β -agonists, inhaled corticosteroids, cromolones, leukotriene antagonists, and theophyllines. This clinical vignette highlights the treatment options and makes specific recommendations. This is a wonderful article to send to your primary care colleagues along with your consultation report.

R. J. M.

von Mutius E: Infection: friend or foe in the development of atopy and asthma? The epidemiological evidence.

Eur Respir J 18:872-881, 2001.

COMMENT: The questions relating the relative contributions of genetics vs environment on development of allergic and asthmatic conditions have been focused by a paradigm from the hygiene hypothesis. This paradigm has come under criticism in that exceptions and inconsistencies exist in multiple setting. Yet the principle elucidated remains viable. This report reviews the role of various infection (and their products) on the incidence of atopy and asthma in various settings with epidemiologic studies. Such studies repeatedly (although not invariably) show a relationship between infection with Th1-inducing organisms and a reduced incidence of atopy or asthma when the exposure is during the time of susceptibility when a predominant Th2-balanced immune system can be tipped toward an anti-allergic Th1-predominant system. This excellent review provides the reader with a comprehensive, up-to-date summary of the pro and con evidence for an important paradigm.

G. D. M.

American Academy of Pediatrics, Subcommittee on Management of Sinusitis and Committee on Quality Improvement: Clinical practice guideline: management of sinusitis.
Pediatrics 108:798-808, 2001.

COMMENT: This AAP clinical practice guideline focuses on the management of sinusitis in children. The most important recommendations are as follows: (a) The diagnosis of acute bacterial sinusitis should be based on clinical criteria, (b) Imaging studies are not necessary to confirm the diagnosis in children 6 years or younger, (c) Sinus CT scan should be reserved for children in whom surgery is being considered, (d) Antibiotics should be used for sinusitis children. I endorse these recommendations.

J. A. A.

Tangsinmankong N, Bahna, SL, Good RA: The immunologic workup of the child suspected of immunodeficiency.

Ann Allergy Asthma Immunol 87:362-370, 2001.

COMMENT: An outstanding review by noted experts in the field.

A. M.

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