AllergyWatch®

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

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Avoidance Does Matter!

ENVIRONMENTAL control measures are a key part of asthma management guidelines. Previous studies have found it difficult to reduce allergen exposure in inner-city homes and to demonstrate clinical benefits of allergen avoidance measures. A multicomponent, individualized intervention to reduce allergen exposure for inner-city children with asthma was evaluated in a randomized, controlled trial.

The Inner-City Asthma Study included 937 children in seven U.S. cities. The children, aged 5 to 11 years, all had atopic asthma diagnosed by a research physician. One group received a 1-year intervention, including education for caregivers in environmental remediation, tailored to the child's specific sensitization and environmental risk profile. The main outcome of interest was maximal number of symptomatic days in the last 2 weeks.

During the study year, symptomatic days were significantly reduced for children in the intervention group: 3.39 days per 2-week period, compared with 4.20 days in the control group. The improvement persisted in the year after the study: 2.62 vs 3.21 days, respectively.

Home visits found significantly greater reductions in allergen levels in the intervention group, including levels of dust mite and cockroach allergen in the bed and on the bedroom floor. Reductions in allergen levels on the bedroom floor were associated with reduced asthma complications. Based on the symptomatic improvements, children in the intervention group had 34 fewer days of wheezing over the 2-year study period.

The multifaceted home-based intervention evaluated in this study can reduce allergen exposure and asthma-related morbidity for inner-city children with atopic asthma. In addition to reducing symptomatic days, the intervention seems likely to lead to reductions in unscheduled medical visits and missed school days. Benefits persist at 1-year follow-up.

COMMENT: *Environmental control of allergens is a bedrock principle of asthma management, because intuitively it makes sense. Now we have proof that* ➤➤

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The following journals have been selected as the primary focus of review in the preparation of materials within "AllergyWatch®".

- 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
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal

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inner-city children age 5 to 11 with allergic asthma have measurably and consistently improved asthma outcomes after education and remediation of allergens and tobacco smoke. Indoor air quality and allergies matter.
R. J. M.
Morgan WJ, Cram EF, Gruchalla RS, et al: Results of a home-based environmental intervention among urban children with asthma.
N Engl J Med. 2004;351:1068-1080. ♦♦

Venom Immunotherapy Works in Children

CONVENTIONAL wisdom holds that children usually "outgrow" allergen to insect stings. However, no studies have formally evaluated the truth of this assumption. The adult outcomes of children with a history of allergic reactions to insect stings were evaluated, with vs without venom immunotherapy.

The authors' center diagnosed allergic reactions to insect stings in a total of 1,033 children between 1978 and 1985. From 1997 to 2000, a follow-up survey was performed to assess the outcomes of subsequent stings. Contact was made with 512 patients, mean follow-up 18 years. For patients receiving venom immunotherapy, the mean duration of treatment was 3.5 years. Forty-three percent of patients had received subsequent insect stings.

Of 64 patients who had received immunotherapy, just 2 had a systemic reaction when stung again, a rate of 3%. In contrast, reactions to subsequent stings occurred in 19 of 111 untreated patients, a rate of 17%.
Among patients who had moderate to severe reactions in childhood, the reaction rate was 5% for treated patients vs 32% for untreated patients. In contrast, none of 21 patients who had only mild, cutaneous reactions in childhood had a systemic reaction to a subsequent sting.

Many children with allergic reactions to insect stings do not "outgrow" their allergy--they experience systemic reactions to subsequent stings at long-term follow-up. Giving venom immunotherapy in childhood reduces the risk of future reactions, especially in children with moderate to severe reactions. The benefits of venom immunotherapy in children persist at up to 20 years' follow-up, showing even greater prolonged benefit than in adults.

COMMENT: *This study confirms the clinical efficacy of venom immunotherapy in children, as determined 10 to 20 years after finishing treatment. It also finds that untreated children who were systemic reactors continued to react--ie, did not outgrow their allergy--at rates of 17% to 32%.*
R. J. M.
Golden BK, Kagey-Sobotka A, Norman PS, et al: Outcomes of allergy to insect stings in children, with and without venom immunotherapy.
N Engl J Med. 2004;351:668-674. ♦♦

Pollution Is Bad for the Lung

A growing number of studies have demonstrated that air pollution has harmful effects on lung development in children. Most studies have included relatively short follow-up periods. This study analyzed the long-term effects of exposure to ambient air pollution on growth in lung function between the ages of 10 and 18 years--a critical period of lung development.

The Children's Health Study included 1,759 fourth-graders from 12 communities in southern California, representing a wide range of ambient pollution levels. For each community, detailed information on ozone, nitrogen dioxide, and particulate air pollution was collected. Over 8 years' follow-up, the children underwent regular pulmonary function tests. The relationship between average air pollution levels and pulmonary function data was analyzed by a two-stage regression approach. ➤➤

Deficits in the expected increase in FEV_1 during adolescence were associated with levels of exposure to nitrogen dioxide, acid vapor, particulate matter of diameter less than 2.5 μm, and elemental carbon. These associations remained significant after adjustment for various confounding and modifying factors. Similar relationships were noted for other pulmonary function measures. The estimated rate of low FEV_1 was increased fivefold for subjects at the highest vs lowest level of exposure to particulate air pollution.

Exposure to high levels of air pollution during childhood is associated with adverse effects on lung development between the ages of 10 and 18 years. Children with long-term exposure to air pollution are more likely to have clinically significant deficits in FEV_1 as young adults. The specific harmful pollutants identified are products of primary fuel combustion, suggesting that the results may be generalized to other areas.

COMMENT: *Everyone "knows" that air pollution is bad for those with chronic lung diseases. Now we have the distressing evidence that air pollution (as measured in southern California over 8 years) is correlated with statistically and clinically significant deficits in normal children's FEV_1 attained by age 18. (So why are the housing prices so high in southern California?)*
R. J. M.
Gauderman WJ, Avol E, Gilliland F, et al: The effect of air pollution on lung development from 10 to 18 years of age.
N Engl J Med. 2004;351:1057-1067. ♦♦

Anti-IgE Reduces FcεRI in Mast Cells

IN patients with allergic rhinitis, omalizumab significantly reduces basophil mediator release in response to allergen stimulation, the result of rapid reductions in free IgE and in basophil high-affinity IgE receptors. Few studies have looked at the effects on FcεRI receptor density and function on tissue mast cells. Blood basophil and skin mast cell responses to omalizumab were compared.

The study included 3 patients with moderately severe allergic rhinitis who were treated with omalizumab in bimonthly IV infusions of 0.33 mg/kg/IU IgE/mL for 6 months. Responses to intradermal skin test titration with house dust mite antigen were analyzed at baseline and at day 7, 70, and 196 of treatment. Serum IgE and basophil FcεRI were measured, and skin biopsies were obtained for immunohistochemical studies of tryptase and FcεRIα. Five untreated subjects with allergic rhinitis were studied for comparison.

As expected, omalizumab reduced free IgE level and basophil FcεRIα expression within 7 days. Significant reductions in basophil FcεRIα immunoreactivity were apparent at both 70 and 196 days, occurring along with reductions in skin responsiveness to allergen. There were no accompanying changes in tryptase-positive mast cells.

Omalizumab treatment in allergic patients leads to rapid reductions in basophil FcεRI receptor expression. In contrast, reductions in FcεRI expression by skin mast cells occur more slowly, and in parallel with reductions in acute skin reactions to allergen. More study is needed to explain the phenotypic differences between mast cells and basophils in their response to anti-IgE therapy.

COMMENT: *The anti-IgE monoclonal antibody omalizumab is known to cause reductions in circulating free IgE levels as well as in basophil surface-bound IgE and IgE receptors. These Johns Hopkins researchers studied the effect of omalizumab on tissue mast cell IgE receptors using serial skin biopsy after intradermal skin testing with dust mite. Although there was an impressive fall in FcεRI receptor expression in the tissue mast cells, this change was found only after 70 days. In contrast, reductions of these receptor markers on basophils were seen after just 7 days of omalizumab infusion. Clearly, the mast cell doesn't respond to anti-IgE therapy as rapidly as the basophil, but the clinical implications have yet to be elucidated.*
S. M. F.
Beck LA, Marcotte GV, MacGlashan D Jr, et al: Omalizumab-induced reductions in mast cell FcεRI expression and function.
J Allergy Clin Immunol. 2004;114:527-530. ♦♦

More on Omalizumab!

THE mechanisms underlying the benefits of anti-IgE therapy with omalizumab in patients with allergic disease remain unclear. Along with inhibition of mast cell and basophil activation, a reduction in airway inflammation may play a role. The effects of omalizumab on airway inflammatory markers were studied.

The randomized trial included 45 patients with mild to moderate persistent asthma and sputum eosinophilia of 2% or higher. One group received anti-IgE therapy with omalizumab while the other received placebo. In addition to methacholine challenge testing to measure airway responsiveness, inflammatory markers were measured in induced sputum and bronchial biopsy specimens.

Mean sputum eosinophilia decreased from 6.6% to 1.7% in the omalizumab group compared with no significant change in the placebo group. This change was accompanied by a significant reduction in epithelial and submucosal eosinophil counts. Reductions in IgE-positive and FcεRI-positive cells in submucosal biopsy specimens were significantly correlated with each other, as well as with reductions in interleukin-4-positive cells. Eosinophil counts in submucosal biopsy specimens were not correlated with each other. These and other reductions in tissue inflammatory markers were not associated with reductions in airway hyperresponsiveness to methacholine.

In patients with allergic asthma, omalizumab treatment is associated with significant reductions in markers of airway inflammation. This anti-inflammatory mechanism could help explain the reduction in asthma exacerbations and other clinical benefits of anti-IgE therapy. However, there is no effect on methacholine ➤➤

responsiveness, indicating that IgE and eosinophils do not contribute to airway hyperresponsiveness in mild to moderate asthma.

COMMENT: *This paper is interesting from two perspectives. First, it adds to our knowledge that the immune effects of binding circulating IgE with a monoclonal antibody go beyond just removing allergen-specific IgE from the circulation of sensitive patients. The impact on airway inflammation is significant. Second, it again shows a disconnect between decreasing airway inflammatory cells (such as eosinophils and T cells) and airway hyperresponsiveness. This is similar to other studies with other monoclonal antibodies (ie, anti-interleukin-5) and supports a need to rethink the direct association of airway inflammatory cells and hyperresponsiveness.*
G. D. M.
Djukanović R, Wilson SJ, Kraft M: Effects of treatment with anti-immunoglobulin E antibody omalizumab on airway inflammation in allergic asthma.
Am J Respir Crit Care Med. 2004;170:583-593. ♦♦

Oral Steroid Has Benefits for Mild Croup

ORAL corticosteroids have demonstrated efficacy in children with moderate to severe croup. However, most children with croup have only mild symptoms--ie, typical barking cough, but without stridor at rest or retractions. The use of oral corticosteroids for children with mild croup was evaluated in a randomized, controlled trial.

The trial included 720 children with mild croup seen at four Canadian pediatric emergency departments. All had mild croup, based on the scoring system of Westley et al. In double-blind fashion, the children were randomized to receive a single dose of oral dexamethasone 0.6 mg/kg; or placebo. The main outcome measure was the need for medical attention for croup within 1 week.

The two groups had similar baseline characteristics; 61% were boys, with a mean age of 35 months. At 1 week's follow-up, 7.3% of children receiving dexamethasone required additional care for croup, compared with 15.3% of those receiving placebo. Secondary outcomes also favored the steroid group, including ongoing croup symptoms, lost sleep time, and parental stress. Small but significant economic benefits were apparent as well. Of children returning for care, those randomized to dexamethasone were more likely to require corticosteroids or epinephrine.

For children with mild croup, a single dose of oral dexamethasone has significant clinical benefits, including a lower rate of return treatment for croup. Economic and social benefits are demonstrated as well. While acknowledging that the long-term effects are unknown, the authors recommend oral dexamethasone for "essentially all children with croup."

COMMENT: *Have you ever had a call at night about a youngster with "noisy breathing" and been unable to determine over the phone whether it's asthma or croup? This study shows that mild croup (absent stridor and retractions) can be treated effectively with a single dose of oral dexamethasone. With a bronchodilator, the possibility of asthma would also be covered. This may be a good way to hedge your bet.*
R. J. M.
Bjornson CL, Klassen TP, Williamson J, et al: A randomized trial of a single dose of oral dexamethasone for mild croup.
N Engl J Med. 2004;351:1306-1313. ♦♦

Viruses Are the Main Cause of Wheezing in Younger, but Not Older Children

HOSPITALIZATION for wheezing is a common problem for children. Respiratory syncytial virus (RSV) is a major cause of wheezing in infants, particularly during the winter months. This study evaluated respiratory viruses in infants and children hospitalized for wheezing, including the effects of patient age and time of year.

The 1-year study included 133 children and adolescents, aged 2 months to 18 years, hospitalized for wheezing. Of these, 79 were less than 3 years old and 54 were 3 to 18 years old. The patients were matched to the same number of children hospitalized without wheezing. Nasal secretions were sampled for detection of common respiratory viruses. The viral pathogens were evaluated in relation to patient age, atopic characteristics, and time of year.

Most children under age 3 were admitted between December and March, whereas older children were more likely to be admitted from September through November. Respiratory viruses were detected in 84% of wheezing children under 3 years old, compared with 55% of controls. The major virus detected was RSV, especially during the winter months. Children under 6 months old were more likely to test positive for multiple viruses.

For children aged 3 to 18 years, viruses were detected in 68% of cases vs 50% of controls. The most commonly detected virus in this age group, and the only one significantly related to wheezing, was rhinovirus. Rates of rhinovirus positivity did not vary significantly by season. Total IgE levels were significantly higher for cases vs controls among older, but not younger children. In the older group, adjusted odds ratios for wheezing were 7.6 for children testing positive for respiratory viruses, 13.8 for those with allergic sensitization, and 104.1 for those with both findings.

For children under age 3, hospitalization for wheezing is strongly associated with the presence of respiratory viruses, especially RSV during the winter months. In contrast, for children over age 3, wheezing appears more strongly related to atopy. For these older children, atopy may be a key risk factor for hospital admission and adverse responses to infection with respiratory viruses, particularly rhinoviruses.

COMMENT: *In a well-designed case-control study, these University of Virginia researchers analyzed* ➤➤

children hospitalized for wheezing during a 1-year period. Although 84% of children younger than 3 years had detectable virus in their nasal secretions, this number fell to 68% in the 3- to 9-year-olds and down to 50% in the 10- to 18-year group. Respiratory syncytial virus predominated in the youngest children, with hospitalizations mainly in the winter months, whereas rhinovirus was prominent in the older group, who were mainly hospitalized in the fall. Serum IgE was elevated in the older children, compared to their case-controls or even the youngest group. The latter finding reconfirms that atopy plays a more important role in older children, while wheezing in infancy is predominantly viral.
S. M. F.
Heymann PW, Carper HT, Murphy DD, et al: Viral infections in relation to age, atopy, and season of admission among children hospitalized for wheezing.
J Allergy Clin Immunol. 2004;114:239-247. ♦♦

Endotoxin Reduces Risk of Allergy

SOME studies have suggested that home exposure to endotoxin promotes asthma, while others suggest a protective effect of endotoxin against allergic disease. The relationship between current exposure to house dust endotoxin in adults and the risk of allergic sensitization was assessed.

The study used data on 350 adult subjects, aged 25 to 50 years, from the European Community Respiratory Health Survey (ECRHS). Endotoxin was measured in samples of living room floor dust, while allergic sensitization was assessed by measurement of specific IgE against inhalant allergens, based on a cutoff IgE level of 3.5 kU/L.

On multiple logistic regression, exposure to house dust endotoxin was associated with a lower rate of severe allergic sensitization. With adjustment for residence, sex, age, and "caseness," the odds ratio for sensitization to one or more allergens among subjects with higher levels of endotoxin exposure was 0.80. For sensitization to two or more allergens, the odds ratio was 0.72. Endotoxin exposure had the strongest protective effect against sensitization to pollen, odds ratio 0.74.

In adults, current exposure to higher levels of house dust endotoxin is associated with a lower risk of allergic sensitization. More research is needed to clarify the role of childhood exposure to endotoxin in the development of allergy.

COMMENT: *Endotoxins are known to have strong immune-stimulatory and pro-inflammatory properties. They are ubiquitous constituents of house dust indoors, and are found in increased amounts where animals are kept as pets. These authors studied the association of house dust endotoxin and the presence of allergic sensitization in adults. Several studies have found an association between asthma severity and house dust endotoxin levels. This is a nested case-control study following a cross-sectional study in the ECRHS. The results show a negative association between exposure to house dust endotoxin and severe allergic sensitization. To fully understand the implications of this study, exposure during infancy and childhood has to be factored into the equation.*
E. J. B.
Gehring U, Bischoff W, Schlenvoigt G, et al: Exposure to house dust endotoxin and allergic sensitization in adults.
Allergy. 2004;59:946-952. ♦♦

PREVIOUS studies have suggested that young children exposed to endotoxin are less likely to develop allergies, asthma, and eczema. The association between exposure to endotoxin during early infancy and the later risk of eczema was evaluated in a prospective birth cohort study of infants at high genetic risk.

The Home Allergens and Asthma Study included 498 children with a parental history of asthma or allergies, born in the Boston area between 1994 and 1996. Data on endotoxin levels in living room dust were available for 401 families. Relationships between endotoxin exposure during the first months of life and the later development of allergic diseases were assessed, with adjustment for the sex of the child, family income, and season of birth.

Multivariate analysis suggested a lower risk of eczema for children exposed to higher levels of endotoxin in living room dust at age 2 to 3 months. For each quartile of exposure, the odds ratio for physician- or nurse-diagnosed eczema during the first year of life was 0.76. Being exposed to a dog in the first months of life was also a protective factor, although it lost significance when endotoxin exposure was added to the multivariate model. The presence of a dog was only modestly correlated with the level of endotoxin in the home.

For infants with a parental history of asthma or allergies, early exposure to endotoxin seems to affect the risk of developing eczema during the first year of life. The effects of dog exposure on endotoxin levels and on allergic disease outcomes remain unclear. Other risk factors for eczema in this cohort include paternal (not maternal) history of eczema and maternal sensitization to one or more allergens.

COMMENT: *There is a growing body of evidence demonstrating the protective value of early exposure to endotoxins, in the home, to children of allergic parents. Endotoxin exposure seems to decrease the risk of developing asthma or clinical manifestations of allergic diseases. In this large study of infants born in Boston from 1994 to 1996, the higher the home endotoxin level when the child was 2 to 3 months old, the less the diagnosis of eczema was made at 1 year of age. According to the authors, this association between endotoxin exposure and the subsequent development of atopic dermatitis has not been previously reported.*
J. A. A.
Phipatanakul W, Celedón JC, Raby BA, et al: Endotoxin exposure and eczema in the first year of life.
Pediatrics. 2004;114:13-17. ♦♦

Nasal Steroid Doesn't Improve Outcomes After Sinus Surgery

PATIENTS with nasal polyps and chronic rhinosinusitis are commonly treated with local corticosteroids, before and after surgery. However, the efficacy of nasal corticosteroids after functional endoscopic sinus surgery (FESS) remains unproven. The benefits of fluticasone propionate aqueous nasal spray (FPANS) after FESS were evaluated in a randomized, placebo-controlled trial.

The study included 162 adult patients undergoing FESS for chronic rhinosinusitis and nasal polyps. For the year after surgery, patients were randomized to receive FPANS, 400 or 800 µg bid; or placebo. The main study outcome was withdrawal from the trial because of recurrent or persistent nasal polyps and/or chronic sinusitis.

The patients had significant reduction in their symptoms after FESS. Median symptom score decreased from 78 preoperatively to 24 at 2 weeks postperatively in the placebo group, with similar changes in the FPANS groups. In the year after FESS, recurrence rates of nasal polyps and chronic rhinosinusitis were not significantly different among groups: 39% with placebo, 51% with FPANS 400 µg, and 55% with FPANS 800 µg. Recurrence rate ratios were also nonsignificant.

For patients with nasal polyps or chronic rhinosinusitis, nasal corticosteroid therapy does not seem beneficial after sinus surgery. Symptoms are significantly improved after FESS. However, 1-year recurrence rates are not significantly different with FPANS 400 or 800 µg bid, compared to placebo.

COMMENT: *Using topical corticosteroids to treat chronic rhinosinusitis tends not to have an impressive effect. This is frustrating, considering how well chronic rhinosinusitis responds to systemic steroids. This study suggests that topical steroids are ineffective even once the inflammation has been removed surgically.*
S. A. T.
Dijkstra MD, Ebbens FA, Poublon RML, Fokkens WJ: Fluticasone propionate aqueous nasal spray does not influence the recurrence rate of chronic rhinosinusitis and nasal polyps 1 year after functional endoscopic sinus surgery.
Clin Exp Allergy. 2004;34:1395-1400. ♦♦

Acute Asphyxial Asthma Occurs in Children Too, Review Finds

ADULT patients with acute asphyxial asthma (AAA), sometimes called rapid-onset or near-fatal asthma, have been well described. However, few studies have reported on this pattern of asthma attacks in children. A series of children with AAA are presented, focusing on differences in mechanical ventilation.

An 11-year chart review identified 32 children receiving mechanical ventilation for a primary diagnosis of status asthmaticus. They represented 11.4% of patients admitted to the pediatric ICU for severe asthma. The children were 20 boys and 12 girls, mean age 11.8 years; one patient required mechanical ventilation on two occasions. In 13 cases, the patient developed respiratory failure en route to the hospital or within 30 minutes after arrival in the emergency department (ED). In the remaining 20 cases, respiratory failure occurred either after 30 minutes in the ED or in the ICU.

Mean duration of mechanical ventilation was 29 hours for children with the rapid pattern of respiratory failure, compared to 88 hours for those with progressive respiratory failure. Intubation in the ED was also associated with a shorter duration of mechanical ventilation: 42 hours, compared with 118 hours for patients intubated in the pediatric ICU. Patients with rapid respiratory failure and/or ED intubation had greater improvement in ventilation and oxygenation.

Some children undergoing mechanical ventilation for status asthmaticus may be considered to have AAA. As in adults, this subgroup may be marked by a need for early intubation, which does not necessarily reflect failure of previous therapies. Pediatric AAA warrants further study as a subtype of life-threatening asthma in children.

COMMENT: *These investigators highlight a population of childhood asthmatics who have not received the attention they deserve. An 11-year chart review of children with status asthmaticus identified a group of childhood asthmatics (2 to 18 years) with rapid deterioration of lung function requiring intubation in the ED. These children recover quickly and are extubated on average in only 1 day, which is 3.5 days before children with progressive respiratory failure intubated in the pediatric ICU. Acute asphyxial asthma has been well described in adults, but not in children. This group of children should be identified when possible and closely followed.*
A. L. L.
Maffei FA, van der Jagt EW, Powers KS: Duration of mechanical ventilation in life-threatening pediatric asthma: description of an acute asphyxial subgroup.
Pediatrics. 2004;114:762- 767. ♦♦

Exhaled NO Rises in Response to ASA Challenge in Aspirin-Sensitive Asthma

PREVIOUS studies of asthma patients have suggested complex associations between nitric oxide and metabolites of arachidonic acid. Patients with asthma have increased fractional exhaled nitric oxide (FENO), likely related to airway inflammation. The effects of inhaled aspirin (ASA) on FENO were compared in aspirin-tolerant vs aspirin-intolerant asthma patients.

The study included two groups of asthma patients--10 aspirin-tolerant and 10 aspirin-intolerant--and 10 healthy controls. After baseline FENO measurement, the asthmatic patients underwent bronchial challenge with saline and with lysine-ASA. In addition to FENO, sputum eosinophil responses to the two challenges were compared.

Mean initial FENO values were 29.7 ppb for asthmatic patients vs 9.8 ppb for controls. The aspirin- ➤➤

tolerant and aspirin-sensitive groups were similar in terms of FENO as well as methacholine PD_{20}. In response to ASA challenge, FENO increased only in aspirin-sensitive patients: from 31.1 to 43.0 ppb, peaking 4 hours after bronchoconstriction. Likewise, sputum eosinophil percentage increased from 8.1% to 11.1% in the aspirin-sensitive patients, compared to no change in the aspirin-tolerant asthma patients or controls. In the aspirin-sensitive group, the FENO and sputum eosinophil changes were significantly correlated with each other.

Bronchial ASA challenge results in increased FENO and increased sputum eosinophilia in patients with aspirin-sensitive asthma. Thus exhaled NO may reflect eosinophilic airway inflammation after ASA exposure in aspirin-sensitive asthmatics. The increase in FENO remains significant even after spirometric changes have returned to baseline.

COMMENT: *These authors investigated FENO during inhaled ASA challenge in a group of ASA-tolerant and ASA-intolerant patients. Aspirin inhalation caused a significant increase in inhaled NO only in patients with ASA-intolerant asthma. The pattern of delayed increase in NO is similar to that observed after allergen challenge. It is hypothesized, but not proven, that eosinophil recruitment into the airway is the best explanation for the increase in exhaled NO. This suggests airway inflammation is present in patients with aspirin-intolerant asthma.*

E. J. B.

Rolla G, Di Emanuele A, Dutto L, et al: Effect of inhalation aspirin (ASA) challenge on exhaled nitric oxide in patients with aspirin-inducible asthma.

Allergy. 2004;59:827-832. ♦♦

Montelukast Isn't Effective for Moderate CIU

THE H_1-receptor antagonists are the mainstay of treatment for chronic idiopathic urticaria (CIU). This randomized trial evaluated an antileukotriene receptor as montherapy or add-on therapy for CIU.

The study included 160 patients with moderate CIU. In double-blind, double-dummy fashion, they were assigned to receive desloratadine 5 mg once daily, montelukast 10 mg once daily, desloratadine in the morning plus montelukast in the evening, or double placebo.

Most patients receiving montelukast only or placebo dropped out of the trial. Only the patients receiving desloratadine--alone or with montelukast--had significant improvements in total symptom score, hives, and pruritus. There was no apparent advantage of montelukast plus desloratadine over desloratadine alone.

The H_1-receptor antagonist desloratadine is a highly effective treatment for moderate CIU. Add-on therapy with montelukast does not improve symptom control, compared with desloratadine alone. Montelukast alone is not adequate treatment for CIU.

COMMENT: *Chronic idiopathic urticaria is often frustrating and difficult to manage. When antihistamines are ineffective for control of symptoms, additional medications are frequently given. These Italian researchers studied 160 patients with moderate CIU in a well-designed, carefully controlled protocol. The efficacy results were similar for the desloratadine alone and the desloratadine plus montelukast groups. Although montelukast alone was better than placebo, it was not as effective as either treatment including desloratadine. In fact, there was no additional benefit in symptom scores with the addition of montelukast. The strength of the study was the design, but the weaknesses included the small sample and the patient selection criteria, limited to those with moderate CIU. The search for the best addition to antihistamines for unrelenting CIU continues.*

S. M. F.

Di Lorenzo G, Pacor ML, Mansueto P, et al: Randomized placebo-controlled trial comparing desloratadine and montelukast in monotherapy and desloratadine plus montelukast in combined therapy for chronic idiopathic urticaria.

J Allergy Clin Immunol. 2004;114:619-625. ♦♦

Taking Vitamins in Infancy May Increase Allergic Disease Risks

VITAMINS have important effects on the immune system, including shifting T cells toward a Th1 or Th2 phenotype. Multivitamin supplements are widely used by U.S. infants and toddlers. Multivitamin use in infancy was evaluated as a risk factor for childhood asthma and allergic disease.

The study used data on 8,285 infants from the 1988 National Maternal-Infant Health Survey, as well as follow-up data from the 1991 Longitudinal Follow-up study of the same patients. African-Americans were intentionally overrepresented, accounting for 51% of the study population. Relationships between use of vitamin supplements during the first 6 months of life and the development of asthma or food allergy during follow-up were analyzed.

The follow-up data showed a 10.5% incidence of asthma and a 4.9% incidence of food allergy. On multivariate analysis, using vitamin supplements during the first 6 months of life was associated with an increased risk of asthma for African-American infants, odds ratio (OR) 1.27; but not for white infants. For infants who were exclusively formula-fed, early vitamin use was associated with an increased risk of food allergy, OR 1.63.

Vitamin use at age 3 was associated with an increased risk of food allergy in breast-fed (OR 1.62) as well as formula-fed infants (OR1.39). Asthma risk was unaffected.

Receiving multivitamins during the first months of life may increase the risk of asthma for African-American infants and increase the risk of food allergies for formula-fed infants. For all groups, taking vitamins at age 3 is associated with an increased risk of food allergies. The reasons for the observed racial difference is unknown; further study is needed to see if it reflects a true physiologic difference or some form of confounding or bias. ➤➤

COMMENT: *It seems, at one time or another, that all sorts of dietary factors have been blamed for some bad health effect! Only some have turned out to be serious threats in the long run. Now there appears to be an association between the use of multivitamin supplements in African-American infants and the subsequent development of asthma and/or food allergy. This study, using National Health Survey data, is based on over 8,000 babies born in 1988. The authors admit there are important limitations to their results and can only speculate on the reasons for the relationships. The study does not control for the possibility that children with known disease are more likely to receive supplemental therapy. We hope that further investigations will help clarify these issues.*
J. A. A.

Milner JD, Stein DM, McCarter R, Moon RY: Early infant multivitamin supplementation is associated with increased risk for food allergy and asthma.
Pediatrics. 2004;114: 27-32. ♦♦

Elevated LTE_4 Levels in Infants With Severe Bronchiolitis

NEW approaches to the treatment of infants with bronchiolitis are needed. Leukotrienes are known to influence the clinical manifestations of asthma, and may do so for viral bronchiolitis as well. Levels of leukotrienes and other eicanosoids were evaluated in the airways of infants with severe bronchiolitis caused by respiratory syncytial virus (RSV).

The prospective study included 14 infants undergoing intubation for respiratory compromise caused by bronchiolitis at one pediatric ICU. All had RSV infection, confirmed by testing of nasopharyngeal secretions. Eicanosoid levels in endotracheal aspirates were compared for the infants with bronchiolitis and a group of 14 control infants intubated for elective surgery.

The infants with bronchiolitis had a mean Respiratory Distress Assessment Instrument score of 8.2 before intubation, with a mean intubation time of 6.3 days. On testing of endotracheal aspirates, levels of various eicanosoids were significantly higher in bronchiolitis infants than controls, including leukotriene E_4 (LTE_4), leukotriene B_4, and prostaglandin E_2. Urinary LTE_4 levels were also higher in the bronchiolitis group. None of the eicanosoids measured were correlated with clinical severity or respiratory parameters.

Infants with severe RSV bronchiolitis show elevated levels of LTE_4 and other eicanosoids in the airway. Urinary LTE_4 is elevated as well. If elevated leukotrienes and prostaglandins are involved in the inflammatory process of RSV bronchiolitis, then leukotriene modifiers or cyclo-oxygenase-2 inhibitors might be useful treatments.

COMMENT: *Pediatricians are hungry for a new, effective and safe therapy for viral-induced bronchiolitis. This Canadian study involves 14 intubated infants with severe bronchiolitis and 14 controls undergoing elective surgery. Significant increases in the products of arachidonic acid metabolism, prostaglandins and leukotrienes (LTE_4 and LTB_4) were found in the endotracheal aspirates of RSV-positive patients. Will these preliminary results lead to large trials using combinations of leukotriene antagonists and cyclo-oxygenase-2 inhibitors in the treatment and prevention of bronchiolitis?*
J. A. A.

Sznajer Y, Westcott JY, Wenzel SE, at al: Airway eicosanoids in acute severe respiratory syncytial virus bronchiolitis.
J Pediatr. 2004;145:115-118. ♦♦

What Pulmonary Function Measure Best Reflects Asthma Severity in Children?

THE National Asthma Education and Prevention Program/Expert Panel Report 2 guidelines specify FEV_1% predicted values associated with mild, moderate, or severe asthma. This system is based on expert opinion; it has not been validated in either adults or children. The relationship of pulmonary function measures with other indicators of asthma severity--ie, symptom frequency and medication use--was evaluated in asthmatic children.

The prospective study included 219 children and adolescents with asthma, mean age 10.1 years, from two academic subspecialty clinics. Based on recent data on asthma symptom frequency and medication use, asthma was classified as mild intermittent in 6.9% of children, mild persistent in 27.9%, moderate persistent in 22.4%, and severe persistent in 42.9%. Across the four groups, there were no significant differences in mean FEV_1% predicted. Even the severe persistent asthma group had a mean FEV_1% predicted value much higher than 80%.

In contrast, children with more severe asthma based on symptoms and/or medications had lower FEV_1/FVC values. The proportion of patients with below-normal FEV_1/FVC was 33% overall: 17% for children with mild persistent asthma, 20% for those with moderate persistent asthma, and 51% for those with severe persistent asthma.

Asthma severity in children is more closely related to FEV_1/FVC than to FEV_1% predicted. The abnormal FEV_1/FVC may represent the exaggerated dysanapsis that is present in asthma, and is correlated with airway hyperresponsiveness. The role of the FEV_1/FVC in guiding asthma management remains to be determined.

COMMENT: *For many years, FEV_1 has been viewed as the gold standard for classifying asthma severity. Recent studies have questioned this objective measure in terms of sensitivity and specificity. This study attempted to correlate asthma symptoms and medication use with FEV_1 in the various stages of asthma in a pediatric population (ages 5 to 18) from two academic medical subspecialty practices. Although almost half of the subjects were classified as "severe persistent," FEV_1 did not correlate. However, FEV_1/FVC did decrease with increasing disease severity. This study further emphasizes the need to assess asthma severity in multiple dimensions--including subjective and objective--to* ➤➤

gain a truer picture of asthma severity in specific patients.
G. D. M.
Bacharier LB, Strunk RC, Mauger D, et al: Classifying asthma severity in children :mismatch between symptoms, medication use, and lung function.
Am J Respir Crit Care Med. 2004;170: 426-432. ♦♦

Biofeedback Has Benefits in Asthma

EFFECTIVE nondrug treatments would be a welcome addition or alternative to antiasthma medications. Some studies have shown promising results with biofeedback training to increase heart rate variability (HRV) in asthma. The benefits of HRV biofeedback for asthma patients were evaluated in a randomized, controlled trial.

After an initial stabilization on asthma controller drugs, 94 adult asthma patients were randomized into biofeedback and control groups. Two groups received HRV biofeedback, alone or as part of a "full protocol" including abdominal breathing through pursed lips with prolonged exhalation. One control group received placebo electroencephalographic feedback, while another was assigned to a waiting list. In blinded fashion, patients underwent regular, guideline-based titration of asthma medications.

Need for asthma medications was significantly reduced in both HRV biofeedback groups, with little difference between biofeedback only vs the full protocol. On average, HRV biofeedback was associated with one full level of improvement in asthma severity.

Biofeedback was also associated with gains in pulmonary function, based on regular measurements of oscillation resistance. There was evidence of a placebo effect in terms of the reduction in asthma symptoms, but not the improvement in pulmonary function. Rates of severe asthma exacerbations were similar across groups.

For patients with asthma, HRV biofeedback may be a useful form of complementary therapy. Potential improvements include reduced need for steroids, reduced symptoms, and improved pulmonary function. Further studies of biofeedback for asthma are needed.

COMMENT: *In this era of escalating health care costs and an asthma treatment literature dominated by pharmaceutical industry-sponsored clinical trials, nonpharmacologic treatments are often overshadowed. This study evaluated HRV biofeedback as an adjunctive treatment for asthma using both EEG biofeedback and non-adjunctive treatment as controls. The results were impressive, and suggest that HRV biofeedback may hold promise for the future. Of interest, one of the treatment groups included techniques that overlap with specialized speech therapy for vocal cord dysfunction. Additional, larger-scale studies are needed to validate these results.*
S. A. T.
Lehrer PM, Vaschillo E, Vaschillo B, et al: Biofeedback treatment for asthma.
Chest. 2004;126:352-361. ♦♦

Longer Protocol Is Effective for Carboplatin Desensitization

CARBOPLATIN is widely used in cancer chemotherapy. However, a key limiting factor is the high rate of systemic allergic reactions, occurring in up to 30% of patients. A successful approach to carboplatin desensitization is presented.

An experience with 8 consecutive patients with carboplatin allergy in during treatment for ovarian cancer is presented. All had a positive response to intradermal skin testing, performed by raising a 3 mm bleb by injection of undiluted carboplatin, 10 mg/mL. In the first 3 patients, a short desensitization regimen was attempted--ie, under 6 hours. In all 3 cases, desensitization failed after the first or second infusion.

Thereafter, the authors followed a gradual dose-escalation approach, giving a 4-log dose range over a 4-day period. At 3-week intervals thereafter, the patients received more rapid infusions, with the most dilute log dose omitted on each infusion day. All patients tolerated this gradual protocol, including the 3 in whom the short protocol failed. Seven of eight patients subsequently had evidence of tumor response to carboplatin.

A gradual, multiple-day approach to desensitization yields good results in cancer patients with allergic reactions to carboplatin. The longer infusion time is well tolerated with no further evidence of allergy, permitting a good oncologic response to carboplatin. This effective desensitization regimen can allow continued treatment of cancer patients for whom carboplatin-containing chemotherapy is the optimal treatment.

COMMENT: *Clinical allergists are frequently frustrated by the challenges of evaluating and treating nonantibiotic drug allergy. Since carboplatin remains a mainstay of many chemotherapeutic regimens and IgE-medicated reactions are so common in clinical practice, this report provides valuable insight and precedent for patient treatment.*
A. M.
Choi J, Harnett P, Fulcher DA: Carboplatin desensitization.
Ann Allergy Asthma Immunol. 2004;93:137-141. ♦♦

Study Supports IM Steroids for Asthma Patients Discharged from ED

PREVIOUS studies have suggested that depot corticosteroid preparations, administered by IM injection, might reduce the short-term relapse rate for asthmatic patients seen in the emergency department (ED). A single IM dose of depot methylprednisolone was compared with standard oral steroids in adult patients discharged from the ED after acute asthma exacerbations.

The randomized, controlled trial included 190 adult patients being discharged from the ED after standard treatment for an acute asthma exacerbation. One group received a single IM dose of 160 mg of depot methylprednisolone, while the other group received an 6- ➤➤

day tapering dose, also totaling 160 mg of methylprednisolone. Relapse was defined as the need for unscheduled medical care for persistent or worsening asthma at 10 days' follow-up.

Follow-up data were available on 180 patients. Relapse rates were almost identical between groups: 14.1% for those receiving IM depot methylprednisolone and 13.6% for those receiving oral methylprednisolone.

Intramuscular depot methylprednisolone is a reasonable alternative to oral methylprednisolone for adult patients being discharged from the ED after asthma exacerbations. No study to date has found any difference in clinical outcomes between the two routes of administration, though a much larger trial would be needed to prove equal efficacy.

COMMENT: *Compliance is often an issue in chronic diseases, especially asthma. This is most apparent in those asthmatics obtaining regular care through emergency services. In this ED study, adult asthmatics with an exacerbation were treated with either oral or 160 mg IM depot steroids (to ensure compliance). Pharmacokinetic studies of IM methylprednisolone demonstrate peak levels at 9 hours and a half life of 5.5 days. The endpoint in this study was relapse rates over 10 days in both groups, 14.1% in the IM group vs 13.6% in the oral group. Either option is a good choice for treatment of an exacerbation, but IM you know the medication has been administered. No ED visits for asthmatics, with good disease control, is the ticket! It would have been nice to have information on adrenal function at the end of the study.*
A. L. L.
Lahn M, Bijur P, Gallagher EJ: Randomized clinical trial of intramuscular vs oral methylprednisolone in the treatment of asthma exacerbations following discharge from an emergency department.
Chest. 2004;126:362-368. ♦♦

SLIT Reduces Bronchial Responsiveness in Children with Allergic Asthma

THERE is ongoing debate over the use of immunotherapy for pediatric asthma. Although sublingual immunotherapy (SLIT) offers favorable safety characteristics, few studies have examined its impact on pulmonary function and bronchial responsiveness. The effects of SLIT on these outcomes were investigated in asthmatic children with allergy to *Parietaria* pollen.

Thirty children with asthma induced by isolated *Parietaria* allergy were randomized to SLIT or placebo. Both groups underwent pulmonary function testing and methacholine challenge in the winter, before pollen season; and again during pollen season but before randomization. The measures were repeated during pollen season 2 years later, after SLIT or placebo.

In both groups, the mean methacholine PC_{20} decreased significantly from wintertime to pollen season: from 9.78 to 3.37 mg/mL for those assigned to SLIT and from 8.70 to 2.44 mg/mL in the placebo group. On retesting during pollen season after active treatment, methacholine PC_{20} was 9.10 mg/mL in the active-treatment group--not significantly different from the off-season baseline value. In contrast, patients in the placebo group still had significantly increased bronchial reactivity, with a PC_{20} of 2.46 mg/mL. Other pulmonary function measures-ie, FEV_1 and FEF_{25-75}-were similar between groups at all times.

In children with allergic asthma caused by allergy to *Parietaria* pollen, SLIT prevents the seasonal increase in bronchial responsiveness. Although further studies of the mechanisms of SLIT in asthma are needed, the results are consistent with a reduction in bronchial inflammation

COMMENT: *A large body of literature now supports specific immunotherapy in the pediatric population. It has been found to improve symptoms, reduce drug intake and variably improve bronchial hyperreactivity (BHR). Sublingual immunotherapy may represent an advance in this age group due to its safety profile. This double-blind, placebo-controlled study shows that SLIT with* Parietaria *abrogates the seasonal increase in BHR in children with seasonal asthma. Despite the latter, no significant improvement was noted in pulmonary function. Further studies are clearly needed.*
E. J. B.
Pajno GB, Passalacqua G, Vita D, et al: Sublingual immunotherapy abrogates seasonal bronchial hyperresponsiveness in children with Parietaria*-induced respiratory allergy: a randomized controlled trial.*
Allergy. 2004:59;883-887. ♦♦

Does HRCT Correlate with PFT in Children with CF?

HIGH-resolution CT (HRCT) scanning can demonstrate a wide variety of pulmonary abnormalities in patients with cystic fibrosis (CF). To provide a useful surrogate outcome measure for CF patients, the information provided by HRCT should complement that provided by the standard outcome measure of FEV_1. Associations between the results of HRCT and pulmonary function testing in children with CF were evaluated.

The study included 60 children with CF and mild to moderate lung disease: mean FEV_1 15% predicted. Each patient underwent HRCT, and the scans were scored according to a standardized system assessing the size and extent of bronchiectasis, mucous plugging, peribronchial thickening, parenchymal changes, and hyperinflation. The resulting HRCT scores were correlated with the children's FEV_1 and other pulmonary function values.

The HRCT scans showed bronchiectasis in 35% of children with CF, mucous plugging in 15%, and air trapping in 63%. Just one-fourth of the children showed no HRCT abnormality. Correlations between HRCT and pulmonary function variables were rated fair to moderate, although the HRCT appearance sometimes differed markedly from the pulmonary function results. Of 37 children with normal pulmonary function tests, ➤➤

30% had bronchiectasis while 14% had bronchiectasis in at least four lobes.

In children with CF and mild to moderate pulmonary involvement, the pulmonary abnormalities demonstrated by HRCT scans vary widely. Bronchiectasis and other morphologic abnormalities may be seen even in patients with normal pulmonary function results. An accompanying editorial highlights the potential of HRCT in evaluating treatments for very early CF lung disease.

COMMENT: *It is not unusual for the allergist treating young asthmatics to have some patients who also have CF. The pulmonary status of these patients is often judged objectively, through serial office pulmonary function parameters--especially the FEV_1. It now appears that an additional sensitive measurement of CF disease status would be the use of serial high-resolution CT. In this important study of 6- to 10-year-old children with CF, 30% of the patients with normal pulmonary function had significant evidence of bronchiectasis. As the editorial points out, using HRCT at a younger age (before 6 years) could also help in diagnosis and in early institution of preventive measures, since it offers a noninvasive, objective tool before children can properly perform pulmonary function tests.*
J. A. A.
Brody AS, Klein JS, Molina PL: High resolution computed tomography in young patients with cystic fibrosis: distribution of abnormalities and correlation with pulmonary function tests. J Pediatr. 2004;145:32-38; and McColley SA: Cystic fibrosis lung disease: when does it start, and how can it be prevented? (editorial).
J Pediatr. 2004;145:6-7. ♦♦

Antibiotics for Infants Don't Increase Risk of Early Childhood Asthma

PREVIOUS studies have linked antibiotic use during childhood with the later development of asthma. One potential mechanism is a shift toward a Th2-predominant immune response in children who use antibiotics frequently. The relationship between antibiotic use in infancy and asthma in early childhood was evaluated in a birth cohort study.

The longitudinal study included 4,408 children born in 1992 or 1993 and continuously enrolled in a Boston HMO through the first 5 years of life. The number of courses of oral antibiotics given during the first year of was evaluated as a predictor of health care visits for asthma by age 5.

Antibiotic use in infancy was significantly related to the presence of asthma at age 1 to 2 years, after adjustment for sex and lower respiratory illnesses. Compared to children receiving no antibiotics, odds ratios for asthma were 1.9 for those receiving 1 or 2 courses of antibiotics, 1.6 for those receiving 3 or 4 courses, and 2.1 for those receiving 5 or more courses. However, antibiotic use in the first year of life was unrelated to asthma developing between the ages of 2 and 5 years.

Antibiotic treatment for infants during the first year of life does not appear to lead to the development of early childhood asthma. Instead, the findings suggest that children with asthma are more likely to receive frequent courses of antibiotics in early life. The authors note several limitations with their study, including the lack of data on parental asthma and allergies.

COMMENT: *The majority of previous studies have reported an association between antibiotic use in early life and subsequent asthma. This has led some to speculate that early antibiotic use leads to immune deviation toward the Th2 phenotype. This longitudinal study followed children from birth to age 5, showing an association between antibiotic use in the first year of life and asthma diagnosed prior to age 2. However, the association did not hold for asthma diagnosed after age 2. These results argue against a cause/effect relationship between antibiotic use and asthma.*
S. A. T.
Celedón JC, Fuhlbrigge A, Rifas-Shiman S, et al: Antibiotic use in the first year of life and asthma in early childhood.
Clin Exp Allergy. 2004,34:1011-1016. ♦♦

REVIEWS OF NOTE

COMMENT: *This is an excellent, succinct review that covers all aspects of chronic cough--pathophysiology, differential diagnosis, workup, and new therapeutic strategies. It is at once a good teaching tool for staff and colleagues, as well as a reference for specific workups when it has been awhile since seeing patients with chronic cough. This is highly recommended reading.*
G. D. M.
Morice AH, and committee members: The diagnosis and management of chronic cough.
Eur Respir J. 2004;24: 481-492. ♦♦

COMMENT: *In past years, all patients had to do to get an antibiotic was self-diagnose a "sinus infection." But if they said they had a "cold," it was assumed to be viral and no antibiotic was used. In reality, the symptoms are identical. Only 0.5% to 2.0% of all URIs ultimately develop into bacterial infections. This review article summarizes "best practices" for this most common malady.*
R. J. M.
Piccirillo JF: Acute bacterial sinusitis.
N Engl J Med. 2004;351:902-910. ♦♦

COMMENT: *It appears that acute asthma in young children may be better treated with bronchodilators using a metered-dose inhaler with a valve holding chamber device rather than using "wet nebulization." What is different about this review is that the former technique was more helpful in the moderate to* ➤➤

severe groups of patients, compared to those with mild asthma. However, the accompanying editorial calls attention to possible overinterpretation of these results. Although the strength of meta-analysis is an increase in sample size (combining the results of many studies), a marginal effect in several studies may be overemphasized. Other known weaknesses of this type of analysis include definite differences between studies and the potential for publication bias. These problems can confuse the casual reader.
J. A. A.
Castro-Rodriguez JA, Rodrigo GJ: β-Agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis. J Pediatr. 2004;145:172-177; and Smyth RL, Jones A: Treatment of acute wheezing episodes in young children (editorial).
J Pediatr. 2004;145:151-152. ♦♦

COMMENT: *For many years, the dedicated members of the Section on Allergy and Immunology of the American Academy of Pediatrics have sponsored an annual "Synopsis Book." This year, 75 of the "best" recent articles relevant to allergic and immunologic diseases in children are reviewed by 24 of our fellow allergist-immunologists and published by* Pediatrics*--which is generally read by practicing general pediatricians. I can't think of a more worthwhile advertisement for the value of our specialists to primary care physicians. Let's give the Section and the reviewers a round of applause-well done!*
J. A. A.
Wood RA, ed: Synopsis book: best articles relevant to pediatric allergy and immunology.
Pediatrics. 2004;114(suppl):517-554. ♦♦

COMMENT: *Chronic urticaria can be a frustrating problem for both patients and their physicians. Dr. Kaplan, one of the world's leading experts, has prepared this wonderful review that provides a synopsis of the latest research. The article elucidates the complex interactions of the various immunologic factors that are frequently responsible for this condition.*
S. M. F.
Kaplan A: Chronic urticaria: pathogenesis and treatment.
J Allergy Clin Immunol. 2004;14:465-474. ♦♦

COMMENT: *The authors present a very useful review of the available literature on sputum analysis in asthma. They review the correlation with induced sputum with bronchial biopsy and bronchoalveolar lavage and point out the benefits and limitations of all these studies.*
A. M.
Kim CK, Hagan JB: Sputum tests in the diagnosis and monitoring of asthma.
Ann Allergy Asthma Immunol. 2004;93:112-122. ♦♦

COMMENT: *The current studies emphasize the importance of inhaled corticosteroids as first-line asthma therapy. In the last 20 years there have been tremendous strides in asthma medications. Evidence supports the use of inhaled corticosteroids at low or medium doses in the patient with persistent asthma. Additional therapies, primarily long-acting beta$_2$-agonists, have helped patients remain on manageable doses of inhaled corticosteroids. The role of anti-IgE is still unclear, and further clinical experience may help to define this medication's place in antiasthma therapy.*
A. L. L.
Sin DD, Man J, Sharpe H, et al: Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis.
JAMA. 2004;292:367-376. ♦♦

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