AllergyWatch®

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

A Publication of The American College of Allergy, Asthma & Immunology

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Experts Disagree on the Validity of Immunotherapy for Allergic Asthma

COMMENT: *In these unique pro/con editorials, two internationally known experts "square off" on the topic of immunotherapy for allergic asthma. While Dr. Adkinson points to the limitations of supporting data, Dr. Bousquet highlights the benefits that clinical allergists have observed for years. Regardless of your bias, this makes interesting and provocative reading.*
A. M.
Bousquet J: Immunotherapy is clinically indicated in the management of allergic asthma.
Am J Respir Crit Care Med 164:2139-2140, 2001.
Adkinson NF Jr: Immunotherapy is not clinically indicated in the management of allergic asthma.
Am J Respir Crit Care Med 164:2140-2142, 2001. ♦♦

New Information on Childhood Asthma That Regresses: What You See May Not Be What You Get!

MANY patients with childhood asthma go into remission as they age, while other patients do not develop asthma until adulthood. Longitudinal studies are needed to identify factors affecting the course of atopy and asthma from adolescence through young adulthood. Follow-up data from an Australian population study were used to assess patterns of onset and remission during adolescence and to identify relevant risk factors.

The population-based study included a random sample of 718 children, aged 8 to 10 years at baseline, living in one Australian town. The children were evaluated six times at 2-year intervals from 1982 to 1992, then again in 1997. Each examination included assessment of atopy, airway hyperresponsiveness (AHR), and wheezing over the past year. The current analysis focused on 498 subjects who were evaluated at least three times. ➤➤

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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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According to baseline and follow-up data, 13.7% of subjects had late-onset atopy and 12.4% had late-onset wheezing. In contrast, only 3.2% had atopy that went into remission while 5.6% had wheezing that went into remission. Significant risk factors for onset of wheezing were atopy at age 8 to 12, odds ratio (OR) 2.8; and parental history of asthma, OR 2.0. Children with AHR at age 8 to 12 were more likely to have persistent wheezing, OR 4.3.

Girls were more likely to have late-onset AHR, whereas boys were more likely to have late-onset atopy. The OR was 1.9 for both of these associations.

Few patients develop new-onset AHR during adolescence, these longitudinal data suggest. However, adolescents are at continued risk of new-onset atopy and wheezing. Childhood atopy, particularly at age 8 to 10 years, is a significant risk factor for the onset of wheezing.

COMMENT: *This interesting study focuses on examination of risk factors for persistence of wheeze and for late-onset wheeze. The subjects were a cohort of 8- to 10-year-old children who were extensively investigated--on at least three and up to seven occasions--between 1982 and 1992. More than one-third had recent wheeze on at least one occasion, and although remission did occur, the rate of remission was less than the incidence of new cases. This is food for thought when we tell patients/parents much of asthma remits at puberty. In an excellent editorial, Russell raises a number of interesting questions: Why is being female a risk factor for late-onset bronchial hyperreactivity, but being male is a risk factor for late-onset atopy?*
E. J. B.

Xuan W, Marks GB, Toelle BG, et al: Risk factors for onset and remission of atopy, wheeze, and airway hyperresponsiveness.
Thorax 57:104-109, 2002.

◆◆

CHILDREN with asthma often seem to "outgrow" their disease, but previous studies have shown continued pulmonary function abnormalities and bronchial hyperresponsiveness among patients with asthma in remission. Airway inflammatory markers were measured in children with apparently "outgrown" asthma.

Two groups of 35 children undergoing elective surgical procedures were studied. One group with apparently outgrown asthma, ie, a history of previous wheezing but no symptoms within the past year and no drug treatment. Children in the other group had no history of wheezing or atopy. Nonbronchoscopic bronchoalveolar lavage was performed as the children were undergoing anesthesia.

Median eosinophil percentage value was 0.36% in 25 children with apparently outgrown atopic asthma, compared with 0.10% for children in the control group (and 0.21% for those with apparently outgrown viral asthma). The duration of remission was unrelated to the level of airway eosinophilia.

Children with a history of atopic asthma in apparent remission may still have evidence of significant airway inflammation, even though they are no longer wheezing. The presence of continued airways eosinophilia may be a risk factor for future relapse in children who have "outgrown" their asthma. For asthma symptoms to persist, some other component of airway inflammation may need to be present, besides elevated eosinophils.

COMMENT: *It is not uncommon for adult patients presenting with recent-onset asthma to have a history of asthma as a child. Airway abnormalities have been noted in asthmatic children in remission, but the level of airway inflammation has not been documented. These investigators used bronchoalveolar lavage fluid (obtained before a scheduled routine surgical procedure) from 35 children with a history of asthma that had been in clinical remission for varying times, as well as from 35 age-matched controls with no history of asthma. They demonstrated significant airway eosinophilia in the asthmatic compared with the control children, which may portend an increased risk of asthmatic re-emergence in adult life. Such a notion, if confirmed by other studies, could influence decisions about duration of anti-inflammatory therapy in clinically asymptomatic* ➤➤

patients with a history of asthma.
G. D. M.
Warke TJ, Fitch PS, Brown V, et al: Outgrown asthma does not mean no airways inflammation.
Eur Respir J 19:284-287, 2002. ♦♦

Study Tracks Changes in Asthma Treatment Over Time

THE population-based Saskatchewan Health data base was used to examine changes in the intensity of asthma treatment over time. The analysis included 13,671 patients, aged 5 to 44 years, who received anti-asthma medication. Patients were prospectively followed up for a mean of 4.1 years. Intensity of asthma treatment was classified as mild, intermediate, or severe at baseline and during successive 12-month periods.

Initial asthma treatment met the study definition of mild in 48.7% of patients, intermediate in 44.1%, and severe in 7.1%. About half of patients receiving treatment appropriate for mild asthma were less than 15 years old. During follow-up, just 3% of patients whose treatment was initially in the mild category moved to the severe category. Within the severe group, more than half of patients under 15 were reclassified into the mild group during follow-up, compared with about one-fourth of patients over 15.

Patients initially receiving treatment for severe asthma had a high rate of previous hospitalization for asthma. Patients who were in the severe category through 3 years of follow-up were about 16 times more likely to be hospitalized for asthma than those whose asthma was in remission.

Most patients who do not require intensive asthma treatment in the first year of therapy will not require intensified treatment during the subsequent 3 to 5 years. Among patients with initially severe asthma, intensity of treatment often decreases over time, particularly for young patients. The results support recent data suggesting that asthma is usually not a progressive disease, especially in patients younger than age 15 at onset.

COMMENT: *Suissa and his colleagues provide valuable insights from further study of the computerized data base of the Saskatchewan Health group. This study provides reassurance that asthma is not a progressive disease in most patients. This is especially true for those younger than 15 years of age at onset of treatment.*
E. J. B.
Ernst P, Cai B, Blais L, Suissa S: The early course of newly diagnosed asthma.
Am J Med 112:44-48, 2002. ♦♦

New Insights into Identification of High-Risk Asthma Patients

THERE is concern that treatment with β_2-agonists might mask the effects of increased airway inflammation in asthma by altering the patient's ability to perceive symptoms. The effects of bronchodilator therapy--including both short-acting and long-acting β_2-agonists--on patient perceptions of airway obstruction were assessed in a randomized, placebo-controlled trial.

The study included 128 asthma patients, mean age 35 years. Mean FEV_1 was 86% of predicted; the geometric mean concentration causing a 20% decrease in FEV_1 on histamine testing (PC_{20}) was 0.97 mg/mL. Patients were randomized to receive 12 weeks of treatment with the short-acting β_2-agonist salbutamol, the long-acting agent formoterol, or placebo. Histamine challenges were performed at baseline and every 4 weeks. On each occasion, breathlessness was assessed using a modified Borg scale.

For patients with initially low bronchial hyperresponsiveness, PC_{20} decreased from 5.26 to 1.94 mg/mL during short-acting β_2-agonist therapy. However, on analysis of repeated measures, the course of time to perception of a 20% reduction in FEV_1 did not differ significantly between groups. This was so for the study sample overall and for patients with initially high vs low bronchial responsiveness (PC_{20} lower vs higher than 2 mg/mL).

Chronic β_2-agonist therapy does not alter patient perceptions of bronchoconstriction in response to histamine challenge. Symptom perception through 12 weeks of treatment is similar for patients receiving a short- vs long-acting β_2-agonist or a placebo. Even when bronchial hyperresponsiveness increases, perception of bronchoconstriction is unchanged. The study did not assess the effects of treatment on airway inflammation.

COMMENT: *This article addresses the long-held concern about the possible effects of β_2-agonists on perception of symptoms--especially dyspnea. The study looked at 168 patients with mild to moderate asthma were persistently challenged with histamine in the presence of daily short-acting (albuterol) or long-acting (salmeterol) β_2-agonists. Perhaps surprisingly, there were no significant differences between either β_2-agonist and perception of dyspnea. These data suggest no adverse effect of regular β_2-agonist use from the perspective of altered perceptions.*
G. D. M.
van Schayck CP, Bijl-Hofland ID, Cloosterman SGM, et al: Potential masking effect on dyspnoea perception by short- and long-acting β_2-agonists in asthma.
Eur Respir J 19:240-245, 2002. ♦♦

A key objective of asthma treatment is to identify patients at high risk of life-threatening asthma attacks. Previous studies have found that patients who experience near-fatal asthma attacks have reduced ability to perceive dyspnea. This study examined perception of dyspnea (POD) in patients with asthma, who were subsequently followed up for life-threatening asthma attacks.

The study sample comprised 113 consecutive outpatients with stable asthma. Initial POD was assessed by having the patients breath against a progressive load at mouth pressures up to 30 cm H_2O. At each minute, the patients rated their sensation of difficulty breathing on a modified Borg scale. The occurrence of asthma hospitalizations and fatal or near-fatal asthma attacks were assessed during follow-up of up to 24 months. ➤➤

Compared with a group of normal controls, POD was high in 15% of asthma patients, in the normal range in 59%, and lower than normal in 26%. Patients in the low POD group tended to be older, and were more likely to be female, and had a longer duration of asthma. Patients with low POD were more likely to have severe asthma than those with normal POD, though asthma severity was no different for patients with low vs high POD. During follow-up, all asthma events--including emergency visits, hospitalizations, and fatal and near-fatal asthma attacks--were more frequent in the low POD group than in the normal or high POD group.

More than one-fourth of patients with stable asthma have lower than normal POD, the findings suggest. Low POD is associated with certain patient characteristics and with an increased risk of subsequent serious asthma attacks. Measurement of POD may play an important role in assessing patient risk and in preventing deaths from asthma.

COMMENT: *Dyspnea is a subjective measure of asthma severity and consequently asthma morbidity and mortality. Asthmatic patients clearly experience different thresholds of dyspnea, with some patients being unaware as the work of breathing increases. Because asthma patients with a low perception of dyspnea are at increased risk of life-threatening asthma, identification of airway inflammation is critical. Should we be working to develop a simple tool to assess the level of perception of dyspnea?*
A. L. L.

Magadle R, Berar-Yanay N, Weiner P: The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea.
Chest 121:329-333, 2002. ♦♦

Anti-IgE Plus SIT Has Additional Benefits in Seasonal Allergic Rhinitis

SPECIFIC immunotherapy (SIT) is a potentially effective treatment for allergic rhinitis. Treatment with the monoclonal anti-IgE antibody omalizumab reduces IgE-mediated symptoms caused by any allergen, and has been found beneficial in patients with seasonal allergic rhinitis and allergic asthma. The effects of combination therapy with SIT and anti-IgE for seasonal allergic rhinitis were assessed.

This randomized, double-blind trial was conducted over sequential birch and grass pollen seasons in Germany. The subjects included 221 children, aged 6 to 17 years, with seasonal allergic rhinitis. Patients were assigned to receive 24 weeks of SIT-birch or SIT-grass, starting before pollen season and continuing throughout. In addition, they were assigned to receive anti-IgE at the same time. Outcomes were assessed by intention to treat, including daily symptom severity scores and rescue medication use.

Across the two pollen seasons, median symptom load was reduced by 48% in patients receiving anti-IgE rather than placebo. This was so for patients receiving SIT-birch and SIT-grass. Compared with patients receiving unrelated (ie, birch) SIT plus placebo during grass season, symptom loads were reduced by 45% for patients receiving birch-SIT plus anti-IgE, by 32% for those receiving SIT-grass plus placebo, and by 71% for those receiving SIT-grass plus anti-IgE.

Safety evaluation showed no serious adverse events related to anti-IgE. Eczema occurred only in patients assigned to placebo, with no cases among those assigned to anti-IgE. The rate of injection site reactions was similar between the two types of treatment.

For patients with seasonal allergic rhinitis, the combination of SIT and anti-IgE appears to have significant benefits in addition to those of SIT alone. The additional benefit is observed during both birch and grass pollen season, whether or not the patient is receiving SIT coverage for the specific allergen. The additive efficacy of this approach reflects the complementary modes of action: active immunization for SIT vs passive immunization with anti-IgE.

COMMENT: *These European researchers present a large multicenter study that demonstrated an additive effect of monoclonal anti-IgE with SIT in children and adolescents with seasonal allergic rhinitis. Although the treatment was of short duration--only 24 weeks--there was impressive improvement in symptom scores, particularly among patients in the SIT grass pollen-treated group who also received anti-IgE. Surprisingly, there was no difference in the incidence of local reactions to immunotherapy in either group. It was of interest that none of the patients receiving anti-IgE with SIT had any eczema lesions, although eczema was reported in 7 patients on SIT alone. There may be a role for combining the two treatments, particularly in patients with multiple allergic sensitivities.*
S. M. F.

Kuehr JK, Brauburger J, Zielen S, et al: Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis.
J Allergy Clin Immunol 109:274-280, 2002. ♦♦

Specific Immunotherapy Reduces Asthma Risk in Children with Seasonal Rhinoconjunctivitis

CHILDREN with allergic rhinitis are at risk of developing asthma. Specific immunotherapy (SIT) is an effective treatment for pollen allergy. This randomized trial evaluated the efficacy of SIT in preventing asthma and reducing bronchial hyperresponsiveness in children with seasonal allergic rhinoconjunctivits.

The study included 205 children, mean age 10.7 years, from six European pediatric allergy centers. All had grass and/or birch pollen allergy causing symptoms of seasonal allergic rhinoconjunctivitis, but no other clinically relevant allergies. Hay fever symptoms were rated moderate to severe, although none of the patients required daily treatment for asthma at baseline. After stratification for methacholine responsiveness and other factors, one group received 3 years of SIT while the other group was left untreated. Both groups were allowed limited symptomatic medication, ie, loratadine, levocabastine, sodium cromoglycate, and nasal ➤➤

budesonide. The patients were followed up for the development of asthma, both on clinical grounds and by peak flow monitoring. During pollen season and during the winter, methacholine provocation testing was performed.

At baseline, 124 patients were allergic to grass, 43 to birch, and 41 to both grass and birch. Twenty percent of patients had mild asthma symptoms during pollen season, which would likely have gone unrecognized if the children had not participated in the study.

Children receiving SIT had a significant reduction in conjunctival sensitivity, compared with controls. Bronchial provocation testing showed a PC_{20} of less than 2 mg/mL during the first birch season in 48% of patients, during the first grass season in 37%, and during the first winter in 33%. One-fourth of children had no response to the highest methacholine concentration during pollen season while one-third had no response during the winter.

Mean PC_{20} values during pollen season increased from 10.4 mg/mL to 14.9 ng/mL in the SIT group. In the control group, PC_{20} was 11.1 ng/mL at baseline and 12.2 ng/mL at the end of the study. Among children initially free of asthma, the rate of clinical asthma symptoms at the end of 3 years was significantly lower in the SIT group: odds ratio 2.52. Two of 40 children with asthma at baseline were free of asthma at the end of the study.

For children with seasonal allergic rhinoconjunctivitis, SIT can reduce the risk of subsequent asthma. This finding suggests that allergic rhinoconjunctivitis and allergic asthma may be regarded as different manifestations of the same disease. The patients in this study had a high rate of bronchial hyperresponsiveness at baseline, despite having a negative history of asthma requiring daily medication.

COMMENT: *In 1968 Johnstone and Dutton presented a paper that addressed the question, Does SIT prevent asthma in children with allergic rhinitis? The allergy community has been waiting over 30 years for another prospective study of immunotherapy in children to address this question. These European researchers present a well-controlled, well-designed investigation which clearly shows that SIT, given for 3 years, can prevent the development of asthma in children with allergic rhinitis. In the discussion, the authors raise the point that there may be a continuum between allergic rhinitis and allergic asthma, and that they may be different manifestations of the same disease. This article will probably be cited frequently in future discussions about allergic children.*
S. M. F.

Möller C, Dreborg S, Ferdousi HA, et al: Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-Study).
J Allergy Clin Immunol 109:251-256, 2002. ♦♦

NHANES III Data Show Obesity Is a Risk Factor for Childhood Asthma

As the prevalence of childhood asthma continues to increase, more information is needed on the contribution of asthma risk factors. Data from the Third National Health and Nutrition Examination Survey (NHANES III) were used to estimate the current U.S. prevalence of childhood asthma, to assess the relevant risk factors, and to identify subgroups of children at particularly high risk.

Data for NHANES III were collected between 1988 and 1994 at 89 mobile examination centers across the United States. The current analysis included a nationally representative sample of 12,388 children aged 2 months through 16 years. Current asthma was defined as a caregivers' report that their child had been diagnosed as having asthma by a doctor. Two complementary data analysis approaches were used to identify high-risk population subgroups.

The prevalence of current asthma was 6.7%, with a 95% confidence interval of 5.6% to 7.8%. On multivariate analysis, significant risk factors were parental history of asthma or hay fever, odds ratio (OR) 4.00; body mass index at the 85th percentile or higher, OR 1.94; and African-American ethnicity, OR 1.64.

Signal detection analysis identified two groups of children as being at the highest risk of current asthma: children aged 10 years or older who had a parental history of asthma and allergy and a body mass index at the 85th percentile or higher, asthma rate 31.0%; and African-American children aged 10 years or younger who had a positive parental history, asthma rate 15.6%.

The data document a 6.7% prevalence of asthma among U.S. children. The findings support previous results in adults showing that obesity is an independent risk factor for asthma; the nature of this relationship is uncertain. Risk of asthma is highest among children whose parents have a history of asthma or hay fever. The cross-sectional study provides no information on the causal nature of these associations. More research is needed to assess the effects of targeted interventions.

COMMENT: *The NHANES III collected data from 12,000 children and adolescents from 1988 to 1994. The data confirm an increasing prevalence of asthma, 6.7%, compared with similar data collected 10 years earlier, when the prevalence was 4.3%. One of the most interesting conclusions was the confirmation of the strong association between obesity and asthma. We should probably be counseling our overweight patients about weight control as well as medication compliance and environmental controls.*
S. M. F.

Rodríguez MA, Winkleby MA, Ahn D, et al: Identification of population subgroups of children and adolescents with high asthma prevalence: findings from the Third National Health and Nutrition Examination Survey.
Arch Pediatr Adolesc Med 156:269-275, 2002. ♦♦

Most Infants with Cow's Milk Allergy Can Tolerate Soy Formula

COW'S milk allergy is a common problem in infants. Because of the potential for soy intolerance, these babies are often switched to extensively hydrolyzed protein formulas, rather than soy formulas. A previ- ➤➤

ous study suggested a high rate of soy intolerance among children with non-IgE-associated cow's milk allergy, but there have been no prospective studies of this issue. This randomized trial compared soy formula vs extensively hydrolyzed formula for infants with documented allergy to cow's milk, including follow-up to age 2 years.

The study included 170 infants, mean age 7 months, with cow's milk allergy. Except for 4 patients with a history of anaphylaxis, the diagnosis was confirmed by double-blind, placebo-controlled food challenge (DBPCFC). The babies were randomized to an extensively hydrolyzed formula or a soy protein-based formula Through age 2, the children were followed up for the occurrence of allergy or other reactions. If a reaction to the assigned formula was suspected, this was confirmed by DBPCFC using both study formulas. At diagnosis and at age 1 and 2, IgE antibodies to cow's milk and soy protein were measured.

Parents of infants assigned to the soy formula group were more likely to suspect adverse reactions than parents of infants assigned to hydrolyzed formula: 28% vs 11%. The rate of confirmed reactions to the study formulas was 10.0% in the soy formula group and 2.2% in the hydrolyzed formula group. Reactions to soy were equally likely among babies with IgE-associated and non-IgE-associated cow's milk allergy. The rate of adverse reactions to soy was 25% in infants less than 6 months old, compared with 15% in those aged 6 to 12 months.

Most infants with documented allergy to cow's milk formula can tolerate a soy protein-based formula, the randomized trial concludes. Few cases of IgE-associated soy allergy are observed. The study's major limitation is a high number of doubtful delayed reactions on DBPCFC.

COMMENT: *It's an old adage, "The questions remain the same, but (over time) the answers change." In the United States, current recommendations for infants who react to cow's milk-based formula are to place them on a casein hydrolyzed formula,* not *a soy formula. This well-designed study from Finland is the first controlled, prospective investigation on the subject, and it shows that soy formula is well-tolerated by most cow's milk formula-sensitive children.*
J. A. A.

Klemola T, Vanto T, Juntunen-Backman KJ, et al: Allergy to soy formula and to extensively hydrolyzed whey formula in infants with cow's milk allergy: a prospective, randomized study with a follow-up to the age of 2 years. **J Pediatr** 140:219-224, 2002. ♦♦

Celecoxib Linked to Fatal Allergic Vasculitis: Case Report

THE selective cyclo-oxygenase-2 (COX-2) inhibitors, such as celecoxib, have come into widespread use for the treatment of arthritis. Aside from their lower rate of adverse GI effects, these medications carry the same side effects as other nonsteroidal anti-inflammatory drugs, including cutaneous reactions. A patient who died of allergic vasculitis related to celecoxib treatment is reported.

The 52-year-old man was started on celecoxib 200 mg/d for treatment of cervicobrachial neuralgia. On day 8, he developed a maculopapular rash and urticaria on his chest and arms, progressing to angioedema. Celecoxib was stopped and treatment with prednisolone and cetirizine initiated. However, a few days later, the patient was hospitalized with diarrhea, hyperthermia, circulatory failure, and acute purpuric dermal necrolysis. Laboratory findings included metabolic acidosis, rhabdomyolysis, disseminated intravascular coagulation, and kidney and liver failure, with no evidence of infection or chronic inflammatory disorders.

Plasma C3 and C4 concentrations showed a sharp, transient decrease, but plasma histamine was normal. The findings of skin biopsy were consistent with leukoclastic vasculitis. The skin lesions gradually became purpuric and necrotic, progressing to diffuse cutaneous necrolysis. The patient died of acute multiple organ failure 8 days after admission. Autopsy findings included diffuse microvascular thrombosis and necrolysis of the skin and digestive tract mucosa.

This is the first reported case of fatal allergic vasculitis associated with celecoxib treatment. Possible mechanisms include an allergic reaction to celecoxib or interference with endothelial prostacycline synthesis, leading to widespread local thrombosis.

COMMENT: *Many of us have been reassured by the landmark study of Stevenson and Simon related to the safety of rofecoxib in aspirin-sensitive patients. However, me must keep in mind that those observations do not exclude the possibility of IgE- or non-IgE-mediated reactions. This is especially true with celecoxib, which is a sulfur-containing compound. Sulfur drugs and compounds containing sulfur have been previously associated with severe adverse reactions similar to what is described in this case report.*
E. J. B.

Schneider F, Meziana F, Chartier C, et al: Fatal allergic vasculitis associated with celecoxib.
Lancet 359:852-853, 2002. ♦♦

Study Compares Potency of Levocetirizine with Other Second-Generation Antihistamines

CETIRIZINE has emerged as a widely used second-generation antihistamine, offering high potency, minimal metabolism, and a low rate of side effects. Its R-enantiomer levocetirizine has high affinity and selectivity for H_1 receptors and is also minimally metabolized. Levocetirizine was compared with several other current antihistamines for potency and other characteristics in healthy volunteers.

Eighteen healthy men participated in the randomized, double-blind, placebo-controlled crossover study. None took antifungals or other prescription drugs for 14 days before the study. The medications compared were levocetirizine 5 mg, ebastine 10 mg, fexofenadine 180 mg, loratadine 10 mg, and mizolastine 10 mg. To evaluate anti-H_1 activity, the wheal-and-flare response to epicutaneous histamine dihydrochloride was assessed at frequent intervals within 24 hours. ➤➤

On evaluation of area under the curve for histamine-induced wheal and flare, levocetirizine had the greatest potency and most consistent effectiveness of all drugs studied. Ebastine, fexofenadine, and mizolastine all had comparable effects; loratadine was the least potent. All subjects had greater than 95% inhibition of the wheal response at some time after taking levocetirizine. Fexofenadine had the next greatest inhibitory response, followed by mizolastine and ebastine. All of the study drugs were well tolerated.

Of the five second-generation antihistamines studied, levocetirizine is the most potent in inhibiting the wheal-and-flare response to histamine skin prick testing. The response to levocetirizine is maximal within 4 hours, and remains so up to 12 hours. As the most active enantiomer of the widely used drug cetirizine, levocetirizine is expected to be a very useful antiallergy medication.

COMMENT: *This study is one of the first to examine the potential clinical benefit of levocetirizine. This enantiomer of cetirizine appears to have significant benefits compared with other currently available antihistamines. Further study will be required to determine the short- and long-term safety of this drug. If indeed it is nonsedating, levocetirizine will be a valuable addition to our treatment armamentarium.*
A. M.
Grant JA, Riethuisen J-M, Moulaert B, DeVos C: A double-blind, randomized, single-dose, crossover comparison of levocetirizine with ebastine, fexofenadine, loratadine, mizolastine, and placebo: suppression of histamine-induced wheal-and-flare response during 24 hours in healthy male subjects.
Ann Allergy Asthma Immunol 88:190-197, 2002. ♦♦

Can Dry Cleaning Eliminate Cat Allergen from Wool?

CAT allergen is readily carried on wool clothing, which may play an important role in the distribution of Fel d 1 allergen to cat-free environments. Efforts to remove allergen from the clothing of cat owners may be helpful in reducing such distribution and resulting indirect exposure to cat allergen. The effectiveness of dry cleaning in removing cat allergen from wool fabrics was evaluated.

The investigators prepared 80 x 100 cm wool squares and placed them in the baskets of male cats for 1 week. The squares were then cut in half, and one half from each pair was commercially dry cleaned. High-volume sampling of the paired specimens was then performed to compare levels of Fel d 1 allergen.

All exposed wool squares showed high levels of Fel d 1; no allergen was detected on unexposed, control squares. Dry cleaning significantly reduced the amount of Fel d 1 on exposed samples, but did not eliminate the allergen completely. Three of five nonexposed wool squares had detectable levels of Fel d 1 after they were dry cleaned.

Dry cleaning is effective in removing most of the Fel d 1 allergen from cat-exposed wool fabrics. However, some allergen remains after cleaning. Furthermore, nonexposed fabrics may become contaminated with Fel d 1 during the dry cleaning process.

COMMENT: *The almost ubiquitous presence of cat allergen in our general environment is a potential contributor to allergic symptoms in highly sensitive subjects without knowledge of exposure to cats. This paper describes the effects of dry cleaning on levels of cat allergen on wool, a fabric demonstrated to be effective in transferring cat allergen. The good news is that dry cleaning significantly reduces cat allergen. The bad news is that the allergen is not completely eliminated and, in the process of dry cleaning a fabric with cat allergen, the allergen is transferred in low amounts to other fabrics. Paranoia is to be avoided, but we must be aware of the possibility of contact with this potent allergen. I do not believe the data suggest we need cat-free dry cleaners.*
D. K. L.
Liccardi G, Russo M, Barber D, et al: Efficacy of dry-cleaning in removing Fel d 1 allergen from wool fabric exposed to cats.
Ann Allergy Asthma Immunol 88:301-305, 2002. ♦♦

Add-on Montelukast Has Benefits in Aspirin-Intolerant Asthma

A subgroup of patients with asthma are intolerant of aspirin and other nonsteroidal anti-inflammatory drugs, with associated rhinosinusitis and nasal polyposis. This randomized trial examined the effects of adding a leukotriene antagonist to conventional glucocorticosteroid therapy in patients with aspirin-sensitive asthma.

The European/U.S. multicenter trial included 80 patients with aspirin-sensitive asthma, with a mean FEV_1 of 70% predicted at baseline. All patients were receiving conventional asthma controller therapy, with 90% receiving moderate- to high-dose glucocorticosteroids. The patients were randomized to receive 4 weeks of treatment with montelukast 10 mg once daily or placebo. Outcomes assessment included weekly pulmonary function testing, asthma symptom scores, and asthma-specific quality of life.

In patients receiving montelukast, FEV_1 improved by a mean of 10.2%, compared with the placebo group. The montelukast group also had significantly greater improvement in morning and evening peak expiratory flow rate--by a mean of 28.0 and 23.1 L/min, respectively. Patients receiving montelukast had greater improvements in asthma-specific quality of life, particularly in the emotional domain. The benefits of montelukast were consistent across patient subgroups--including those with allergic rhinitis or exercise-induced bronchoconstriction--and were unrelated to baseline urinary leukotriene E_4 level. One patient in the placebo group withdrew because of headaches.

Adding montelukast to conventional asthma controller therapy has significant benefits for patients with aspirin-intolerant asthma. This trial shows improvement in several parameters among aspirin-intolerant patients with relatively severe asthma and moderate to high doses of glucocorticosteroids. More study is needed to compare the effects of antileukotriene ➤➤

drugs in aspirin-tolerant and aspirin-intolerant asthma patients, matched for disease severity and baseline treatment.

COMMENT: *In this multinational study of aspirin-sensitive asthmatics, the addition of montelukast to inhaled corticosteroids appeared to improve multiple clinical parameters. While leukotriene antagonist monotherapy in such patients with FEV_1 values of 50% to 80% has been disappointing, add-on therapy can be very useful.*
A. M.
Dahlén S-E, Malström K, Nizankowska E, et al: Improvement of aspirin-intolerant asthma by montelukast, a leukotriene antagonist: a randomized, double-blind, placebo-controlled trial.
Am J Respir Crit Care Med 165:9-14, 2002. ♦♦

Subjects with Gastroesophageal Reflux Have High Rates of Asthma and Sleep Apnea Symptoms

PREVIOUS studies have suggested a relationship between gastroesophageal reflux (GER), and pulmonary disease. The association between GER and asthma may be causal in nature, perhaps resulting from aspiration of the stomach contents or from vagally mediated bronchoconstriction. The relationship of nocturnal GER with sleep-disordered breathing, asthma, and respiratory symptoms was assessed in a population-based study.

A structured interview, lung function measurements, and allergy tests were performed in 2,661 young adults (aged 20 to 48 years) from three northern European countries. Most were randomly selected, while 459 patients with reported asthma were included as well. The questionnaire included a question about GER, defined as heartburn or belching after going to bed.

Nocturnal GER was reported at least once weekly by 4.6% of subjects. The prevalence of respiratory symptoms and asthma was elevated 2- to 3-fold for subjects reporting GER. Most of the relationships between GER and respiratory symptoms persisted after adjustment for other variables, including risk factors for sleep-disordered breathing. Nine percent of subjects reporting GER symptoms had physician-diagnosed asthma, compared to 4% of those without GER. The concomitant presence of GER and asthma was associated with significantly increased body mass index and a higher rate of various sleep-related symptoms.

This study finds an increased rate of asthma and respiratory symptoms among young adults reporting nocturnal GER. Nocturnal GER is also associated with in increased prevalence of obstructive sleep apnea symptoms. For patients with sleep apnea, narrowing or occlusion of the upper airway during sleep may lead to increased intrathoracic pressure and thus to respiratory symptoms. The study's main weakness is its reliance on patient self-report of nocturnal GER symptoms, which is not strongly related to objective evidence of GER.

COMMENT: *Nocturnal GER is a "hot" topic in the world of respiratory illness, especially asthma and obstructive sleep apnea. Although these investigators identify subjects on the basis of self-reporting, they show a significant increase in most respiratory symptoms among subjects with reported nocturnal GER. Changes in intrathoracic pressure with these respiratory illnesses may increase nocturnal GER and in turn lead to worsening of asthma and obstructive sleep apnea.*
A. L. L.
Gislason T, Janson C, Vermeire P, et al: Respiratory symptoms and nocturnal gastroesophageal reflux: a population-based study of young adults in three European countries. **Chest** 121:158-163, 2002. ♦♦

Long-Term Outcomes of Pigeon Breeder's Disease

PIGEON breeder's disease (PBD) is a type of hypersensitivity pneumonitis that may occur in acute, subacute, or chronic forms. Factors affecting clinical expression include host susceptibility, intensity and duration of pigeon antigen exposure, and nature of the antigen. Although the disease is common among pigeon breeders, there are few data on the frequency and circumstances of disease progression. The long-term outcomes of 18 patients with PBD are presented.

Eighteen pigeon breeders were referred for evaluation of suspected hypersensitivity pneumonitis caused by pigeon exposure. At presentation, 8 patients had acute PBD, with recurrent respiratory and systemic symptoms temporally related to pigeon exposure; 5 had subacute disease, with unremitting systemic and lower respiratory symptoms; and 5 had chronic disease, with dyspnea but not acute systemic symptoms, except during intense periods of pigeon exposure. Mean follow-up was 10.8 years after diagnosis.

Fourteen of the patients significantly reduced their exposure to pigeons, while 4 kept their birds. All 8 patients with acute PBD either regained or never lost normal pulmonary function. Four of five patients with subacute PBD had persistent symptoms, along with persistent mild restrictive or obstructive changes on spirometry. Lung function improved in 3 of the 5 patients were severe disease, but deteriorated in the other 2, who continued exposure to pigeons.

Long-term follow-up of patients with PBD shows good outcomes among patients with the mild form of this hypersensitivity pneumonitis. In contrast, patients with chronic PBD have persistent symptoms and airway obstruction. Pigeon breeder's disease has a complex immunopathology, associated with alveolar macrophage activation, T-lymphocyte responses, and various modulating factors.

COMMENT: *Hypersensitivity pneumonitis is one of those conditions that is studied in detail for scientific understanding of immunologic lung disease and to enhance chances of passing the Boards. However, it is not a condition that we frequently recognize in clinical practice. Long-term outcome data in affected sub-* ➤➤

jects are limited. This is unfortunate, as office-based clinicians may be more likely to see subjects with milder disease, which may not have been diagnosed with the first symptoms. This paper adds to the literature on the long-term effects of hypersensitivity pneumonitis, including subjects who continue to have some exposure to the causative antigen. The findings are somewhat reassuring in that many subjects do well. These patients with milder disease could be in your practice.
D. K. L.
Zacharisen MC, Schlueter DP, Kurup VP, Fink JN: The long-term outcome in acute, subacute, and chronic forms of pigeon breeder's disease hypersensitivity pneumonitis.
Ann Allergy Asthma Immunol 88:175-182, 2002. ♦♦

Fexofenadine Alone vs Montelukast Plus Loratadine for Allergic Rhinitis

PREVIOUS trials of treatment for seasonal allergic rhinitis (SAR) have shown that the combination of montelukast, a leukotriene receptor antagonist, and loratadine, a second-generation antihistamine, is more effective than either drug alone. Fexofenadine has recently been shown to have significant benefits over loratadine. This study compared fexofenadine alone with the combination of montelukast plus loratadine for the treatment of SAR.

The study included 37 patients, mean age 37 years, with symptoms of SAR and skin-test-confirmed grass pollen allergy. Patients with asthma were excluded; most patients were taking intranasal corticosteroids or oral antihistamines at baseline. During grass pollen season, patients received 2 weeks of treatment with fexofenadine 120 mg and with montelukast 10 mg plus loratadine 10 mg, in random order. Patients completed a 7- to 10-day placebo run-in and washout period before each treatment. Outcomes of interest included nasal peak inspiratory flow and symptom scores.

During the placebo periods, there were no differences in any of the variables studied, compared with baseline. Both active treatments brought significant improvements in nasal peak inspiratory flow and symptoms. Neither the objective nor subjective outcomes were significantly different between fexofenadine vs montelukast plus loratadine.

For patients with SAR, fexofenadine alone offers similar efficacy to the combination of montelukast plus loratadine. Both treatments improve nasal peak flow and symptoms, compared with placebo. Both treatments have a low rate of adverse effects and a rapid onset of action, achieving peak effect within 2 days.

COMMENT: *Fexofenadine alone fared very well compared with the combination of loratadine and montelukast in this industry-sponsored, head-to-head crossover study. As the accompanying editorial points out, since there were trends favoring the combination of loratadine and montelukast, a larger study might have identified a small advantage to this combination. Given the recently reported differences in the potency of second-generation antihistamines, it would be of interest to see if the combination of fexofenadine and montelukast is more effective than fexofenadine alone.*
S. A. T.
Wilson AM, Orr LC, Coutie WJR, et al: A comparison of once daily fexofenadine versus the combination of montelukast plus loratadine on domiciliary nasal peak flow and symptoms in seasonal allergic rhinitis. Clin Exp Allergy 32:126-132, 2002.
Sander C, Rajakulasingam K: Leukotriene receptor antagonists for the treatment of allergic rhinitis (editorial). **Clin Exp Allergy** 32:4-7, 2002. ♦♦

Nocturnal Asthma Linked to Low Serum Cortisol Levels

NIGHTTIME symptoms are a problem for nearly half of asthmatic children. One possible contributing factor is the circadian decrease in serum cortisol level, which reaches its low point at about midnight and may lead to reduced suppression of airway inflammation. Endogenous serum cortisol levels were compared in asthmatic vs control children, and their relationship with nocturnal airflow limitation was assessed.

The study included 28 children with stable asthma who had increased airway responsiveness to histamine and used inhaled corticosteroids as maintenance medication. Eighteen healthy control children were studied for comparison. All children underwent measurement of cortisol and FEV_1 every 4 hours for 24 hours. In addition, blood eosinophils, airway response to methacholine, and adenosine-5'-monophosphate were measured at 4:00 a.m. and 4:00 p.m.

Cortisol level tended to be lower in asthmatic vs control children, with the difference becoming significant at 12:00 midnight. Ten of the asthmatic children had nocturnal asthma, defined as 15% or greater 24-hour variation in FEV_1. In this group, cortisol levels were significantly lower than in control children at 12:00 midnight, 8:00 a.m., and 12:00 noon. Median eosinophil numbers at 4:00 a.m. were significantly different between the three groups.

Among children with asthma, a higher 24-hour cortisol level was associated with a significant increase in FEV_1 percent predicted. In both the control group and among asthmatic patients without nocturnal asthma, greater 24-hour cortisol variation was associated with lower FEV_1 percent predicted at all time points. Cortisol measurements were not significantly related to the airway response to methacholine.

Serum cortisol levels appear to be related to overall FEV_1 level as well as to the nocturnal decline in FEV_1 in children with asthma. Higher serum cortisol is associated with better pulmonary function. Children with nocturnal asthma have lower cortisol levels than healthy children from midnight to noon. The authors emphasize, however, that many different factors can affect serum cortisol levels.

COMMENT: *The mechanisms for nocturnal symptoms of asthma have long been debated. One prevailing theory has been the known diurnal variation in serum cortisol levels, which reach a nadir in the middle of the night. The authors investigated whether this held true for children with asthma compared to controls.* ➤➤

They found that the levels were lower (at midnight) in the asthmatic children and correlated with decreased airflow, as children with nocturnal asthma had an even lower serum cortisol level and higher levels were correlated with better FEV_1 values. They also found that higher variations between morning and evening cortisol levels were correlated with lower FEV_1, even in children without nocturnal asthma. This provocative study further supports the role of adrenal dysfunction in nocturnal asthma in children. However, it does not specifically address whether this is a cause or possibly an effect of more severe disease, which requires more corticosteroids and thus alters the normal adrenal cycle.
G. D. M.
Landstra AM, Postma DS, Boezen HM, Van Aalderen WMC: Role of serum cortisol levels in children with asthma.
Am J Respir Crit Care Med 165:708-712, 2002. ♦♦

Study Identifies New "Pseudoallergens" Contributing to Chronic Urticaria

PREVIOUS reports have described cases of chronic urticaria elicited by pseudoallergic reactions (PARs) to medications, natural foods, and food additives. The authors have noted improvement in chronic urticaria symptoms in patients following a diet low in such pseudoallergens, with symptoms returning on challenge with pseudoallergen-rich foods. A group of patients with chronic urticaria and PARs were studied to identify new pseudoallergens in foods.

The study included 22 patients with chronic urticaria, associated with daily spontaneous wheal responses. The patients, mean age 48 years, had previously responded well to a pseudoallergen-free diet. The analysis focused on certain foods frequently reported as eliciting wheal responses in chronic urticaria: sun-ripened tomatoes, white wine, and herbs. The patients underwent oral provocation testing with field-grown tomatoes, organically grown white wine, and a mixture of herb extracts. Skin biopsies were obtained for evaluation of in vitro mast cell histamine release.

Whole tomato elicited a reaction in 76% of patients, a steam distillate in 45%, and residues in 15%. Fifty percent of patients reacted to food additives and 47% to herbs. Forty-four percent reacted to whole wine, 27% to a wine extract, and none to residue. None of the patients had positive results on skin-prick tests, and none had tomato-specific serum IgE. Tomato extract it self did not cause in vitro histamine release; rather, histamine release was enhanced after stimulation with substance P and C5a, but not with anti-IgE. No reactions were attributable to salicylic acid.

This study identifies aromatic volatile ingredients of certain foods as new pseudoallergens eliciting reactions in chronic urticaria. The most noteworthy finding is the occurrence of PARs to tomatoes. The mechanisms of these PARs remain undefined; further study is needed to determine the exact nature of various pseudoallergens in foods and their contribution to chronic urticaria.

COMMENT: *If chronic urticaria is only rarely an IgE-mediated disorder or food allergy, what then to make of clinical reports of dietary triggers? These authors studied 33 subjects in a subset of chronic urticaria patients who improved on a diet that restricted "pseudoallergens." Many then reacted to something in tomatoes, wine, herbs, and/or additives. In vitro analysis of the tomato responders' skin showed that the pseudoallergic phenomenon did not involve IgE or direct histamine release but could occur via aromatic volatile natural ingredients acting as cofactors with other endogenous histamine releasers. Therefore certain naturally occurring pseudoallergens may be involved in the triggering or maintenance of chronic urticaria.*
R. J. M.
Zuberler T, Pfrommer C, Specht K, et al: Aromatic components of food as novel eliciting factors of pseudoallergic reactions in chronic urticaria.
J Allergy Clin Immunol 109:343-348, 2002. ♦♦

Poor Correlation Between Sinus Pain and CT Findings

SINUSITIS is commonly diagnosed on the basis of clinical findings, such as facial pain and rhinorrhea. However, the correlation between clinically suspected sinusitis and the findings on sinus CT scanning is unclear. This issue was addressed in a prospective study of 200 consecutive paints with a clinical history of sinusitis.

The patients were all referred for paranasal sinus CT scanning by an otolaryngologist or internist. Before the imaging study, each patient completed a questionnaire regarding pain and other symptoms. The scans were read in blinded fashion by three radiologists, who scored for air/fluid levels, mucosal thickening, bony reactions, and other findings.

Questionnaire responses indicated some type of facial pain or headache in 82% of patients; the right temple or forehead was the most frequent site of maximal pain. On CT scanning, the maxillary sinus was the most commonly involved sinus. There was no significant relationship between the patient's pain symptoms and their CT findings. Mean number of facial or head pain sites was 5.88 for patients with a normal CT scan, compared with 5.45 for those with CT abnormalities.

In patients with clinical suspicion of sinusitis, reported pain is poorly correlated with the findings of paranasal sinus CT. Sinusitis should be managed on a clinical basis, with sinus CT reserved for evaluating the anatomy and extent of sinus disease in patients undergoing surgery. Potential limitations of this study include the use of one-time evaluation and reliance on standard imaging protocols.

COMMENT: *This well-designed study reminds us that many patients with "sinus headache" do not have paranasal sinusitis. The authors suggest that sinus CT should be reserved for patients with other physical signs or symptoms suggesting sinusitis.*
A. M. ➤➤

Mudgil SP, Wise SW, Hopper KD, et al: Correlation between presumed sinusitis-induced pain and paranasal sinus computed tomographic findings. **Ann Allergy Asthma Immunol** 88:223-226, 2002. ♦♦

U.K. Study Finds No Link Between Allergy and Infection/Antibiotic History in Children

THE so-called hygiene hypothesis suggests that the increasing prevalence of allergy is related to reduced exposure to infections and increase use of antibiotics during early life. Studies of this issue have yielded conflicting results, however. Data from a U.K. general practice data base were used to evaluate the association between allergic disease and children's exposure to infections and antibiotics.

The analysis was based on a historical birth cohort of more than 29,000 children seen in their general practitioner's office. Data were collected on the occurrence of infections in the cohort children and their siblings. The effects of these variables on the incidence of asthma, eczema, and hay fever were analyzed using Cox regression.

The greater the number of physician visits for nonallergic disease during the first year of life, the higher the subsequent incidence of allergic diseases. For patients in the highest quintile (ie, 14 or more consultations), hazard ratios (HRs) were 3.75 for asthma, 3.75 for eczema, and 3.87 for hay fever, compared with those in the lowest quintile (0 to 4 visits). Incidence of allergic disease was unrelated to either the children's personal infections or infections in siblings.

During the first year of life, 65% of children received at least one course of antibiotics while 8% had more than four courses. Children in the latter group had increased HRs for allergic diseases: 3.13 for asthma, 1.48 for eczema, and 2.12 for hay fever. However, these associations were reduced or eliminated by adjustment for consulting behavior.

In this birth cohort, infection history is not significantly related to the incidence of allergic diseases in young children. Children with heavy exposure to antibiotics have higher rates of allergic disease, but this may be partially explained by consulting behavior. Neither factor can explain the differing incidence of allergic disease in older vs younger siblings.

COMMENT: *After numerous articles supporting the "hygiene hypothesis," here is one that is contrary. The data base is large and the analysis appears to be sound, but the authors found no evidence that exposure to infections resulted in a reduced incidence of allergic disease. They did find an association of antibiotic use with the risk of developing allergies. This data base was collected from actual patient visits to their general practitioner, and not direct patient/parent questionnaires. The possibility of underreporting of infections is mentioned in the discussion, but is "adjusted" for consulting behavior and is not considered significant. The "hygiene hypothesis" remains a hypothesis, at least for now.*
S. M. F.

McKeever TM, Lewis SA, Smith C, et al: Early exposure to infections and antibiotics and the incidence of allergic disease: a birth cohort study with the West Midlands General Practice Research Database. **J Allergy Clin Immunol** 109:43-50, 2002. ♦♦

Patients With Persistent Asthma Show Reduced Lung Elastic Recoil

IN patients with asthma, persistent inflammation leads to airway remodeling, luminal narrowing, and airflow obstruction. The authors recently reported the unexpected finding of sharply reduced lung elastic recoil as a contributor to fixed expiratory airflow limitation in patients with chronic, stable asthma. The current study examined the course and mechanism of expiratory airflow limitation in a group of asthma patients with long-term follow-up.

The retrospective study included 21 patients with clinically stable, optimally treated asthma who had undergone follow-up lung function studies for longer than 5 years. Disease was classified as mild persistent asthma, FEV_1 greater than 80% predicted, in 4 patients; moderate persistent asthma, FEV_1 60% to 80% predicted, in 11 patients; and severe persistent asthma, FEV_1 less than 60% predicted, in 5 patients. For each patient, the investigators estimated the extent to which loss of lung elastic recoil contributed to reduction in maximum expiratory airflow over time.

Emphysema was minimal or absent and lung diffusion was normal in all patients. Patients with moderate persistent asthma and those with severe persistent asthma had sharp reductions in elastic recoil at total lung capacity, with values of 16 and 15 cm H_2O, respectively. In contrast, elastic recoil was well preserved in patients with mild persistent asthma, 22 cm H_2O. For patients with moderate to severe asthma, loss of elastic recoil explained 34% and 50% of the reduction in maximal expiratory airflow at 80% TLC and 70% TLC, respectively. Longitudinal FEV_1 results showed no change in lung function status over time for most patients.

Even with optimal medical therapy, long-term follow-up data show decreases in maximum expiratory airflow in patients with clinically stable, moderate to severe asthma. Loss of lung elastic recoil, occurring through some unknown mechanism, is an important contributor to this process. More research will be needed to clarify how loss of elastic recoil affects airway remodeling in persistent asthma.

COMMENT: *This report expands on the authors' previous observations from their long-term follow-up of clinic patients. The patients with moderate or severe airflow obstruction despite optimal therapy had a striking loss of elastic recoil. This challenges the current dogma that attributes fixed obstruction in longstanding asthma to permanent airway narrowing due to remodeling.*
S. A. T.

Gelb AF, Licuanan J, Shinar CM, Zamel N: Unsuspected loss of lung elastic recoil in chronic persistent asthma. **Chest** 121:715-721, 2001. ♦♦

REVIEWS OF NOTE

Tobin MJ: Asthma, airway biology, and nasal disorders in *AJRCCM* 2001.
Am J Respir Crit Care Med 165:598-618, 2002.

COMMENT: *An* outstanding *review of the literature published in* AJRCCM *last year. This is one to keep in your files for a quick reference on recently published data on either upper or lower airway diseases.*
A. M.

Spahn JD, Szefler SJ: Childhood asthma: new insights into management.
J Allergy Clin Immunol 109:3-13, 2002.

COMMENT: *What is the currently recommended approach for the management of the child with asthma? How should we be monitoring the success of therapy? What should we be using as first-line treatment for persistent asthma? Drs. Spahn and Szefler explain "between the lines" of the CAMP and other studies to help elucidate these issues. Although this wonderful review raises more questions than it answers, it should be a "must read" for anyone caring for children with asthma.*
S. M. F.

Berger WE: Monoclonal anti-IgE antibody: a novel therapy for allergic airways disease.
Ann Allergy Asthma Immunol 88:152-161, 2002.

COMMENT: *Anti-IgE will usher in a new era of allergic disease therapy. This is a thorough review of the efficacy of anti-IgE in allergic rhinitis and asthma. In addition, side-effect and safety data are summarized. Finally, the clinician/author suggests clinical situations in which anti-IgE may offer advantages over current therapy. This is a review that is must reading for clinicians who are not up to speed on this new concept of treatment.*
D. K. L.

Sabroe I, Lloyd CM, Whyte MKB, et al: Chemokines, innate and adaptive immunity, and respiratory disease.
Eur Respir J 19:350-355, 2002.

COMMENT: *The continuing "alphabet soup" of molecules that influence, mediate, and/or regulate allergic/asthmatic inflammation continues to escalate and creates the daunting task of trying to keep up with names and functions. A basic understanding of the categories of inflammatory mediators is necessary to appreciate the integration of various molecules into the big picture of allergic inflammation. The framework with which most allergists are now familiar is the Th1/Th2 paradigm. This has been used by the authors to construct an excellent brief review of chemokines, their basic classifications and functions. They expand the putative role of chemokines into innate immune responses as well, providing a sound physiologic rationale for these molecules as potential therapeutic targets.*
G. D. M.

Farrell RJ, Kelly CP: Celiac sprue.
N Engl J Med 346:180-188, 2002.

COMMENT: *Food allergies may assume many clinical forms. Celiac sprue is a type of food allergy that may occur in adults and children, may be subtle or overt and can be easily confused with other gastrointestinal and dermatologic disorders. Do you know the variable diagnostic utility of assays for antibodies to gliadin, endomysium, gluten, or wheat? Do you know how to recognize and treat "celiac crisis?" Do you know which other grains contain gluten? You will.*
R. J. M.

Vally H, Thompson PJ: Alcoholic drinks and asthma.
Clin Exp Allergy 32:186-191. 2002.

COMMENT: *This updated review of the effects of alcoholic beverages and asthma is a practical reference for all physicians who see patients with asthma.*
S. A. T.

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