AllergyWatch®

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

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Asthma: It's All in the Genes!

INFORMATION on variables influencing susceptibility to asthma is critical to realizing preventive, diagnostic, and therapeutic advances. Studies of the genetics of asthma have implicated the prostanoid DP receptor gene (*PTGDR*) on chromosome 14q22.1--in a mouse model, the PTGDR had to be present for the asthmatic phenotype to emerge. Genetic variants of *PTGDR* were analyzed for their association with asthma susceptibility.

Asthma patients and controls were screened for variants of *PTGDR* using single-strand conformational polymorphism analysis with specific oligonucleotide primers. Gene sequencing studies identified four new *PTGDR* single nucleotide polymorphisms (SNPs): T-549C, C+367A, G+894A, and G+1044A, in addition to the previously reported T-197C and C-441T variants. Combinations of *PTGDR* variants affecting transcription for disease association were evaluated in case-control studies including 518 white and 80 black patients with asthma (and 175 and 45 nonasthmatic controls).

Four common and unique three-SNP haplotypes were identified, with varying capacity to support *PTGDR* transcription and differing DNA-binding-protein affinities. In both racial groups, individual SNPs showed significant associations with clinical asthma. On multivariate analysis, subjects having at least one copy of the low-transcriptional-efficiency haplotype were at lower risk of asthma--odds ratio 0.55 for whites and 0.32 for blacks--than those with no copies.

The results strongly support the concept that *PTGDR* is a gene affecting asthma susceptibility. In both white and black Americans, combinations of gene variants associated with impaired expression of *PTGDR* are linked to reduced asthma risk. Population-based studies will be needed to determine how much of the total asthma risk can be attributed to these gene variants and their ability to predict asthma risk.

COMMENT: *Asthma is thought to be caused by a combination of environmental and genetic ele-*➤➤

CONTENTS

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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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ments. Approximately ten genes with their polymorphisms have been found to promote (or protect from) susceptibility to asthma. This genetic variability helps to explain the clinical variability of the disease, and why the search for a single asthma gene is futile. Various combinations of the ten-or-so genes are likely to explain the clinical expressions. This study confirms the role for a gene encoding for a receptor for prostaglandin D2. The accompanying editorial supplies brilliant perspective on all of this complexity.
R. J. M.
Oguma T, Palmer LJ, Birben E, et al: Role of prostanoid DP receptor variants in susceptibility to asthma. N Engl J Med. 2004;351:1752-1763; Cookson W, Moffatt M: Making sense of asthma genes (editorial).
N Engl J Med. 2004;351:1794-1796. ♦♦

Acid Suppression Linked to Pneumonia Risk

ACID-suppressing drugs--especially H_2-receptor antagonists (H_2RAs) and proton pump inhibitors (PPIs)--are very widely used by patients with gastric symptoms. By raising the gastric pH, these drugs may lead to decreased elimination of pathogens from the oral cavity. A population-based study examined the possible relationship between acid-suppressing drugs and community-acquired pneumonia.

A Dutch general practice data base covering 1995 through 2002 was used to analyze a population of over 364, 683 patients with at least 1 year's worth of data. Over a mean follow-up of 2.7 years, the patients had a total of 5,551 first episodes of pneumonia. Eighteen percent of episodes were confirmed by either radiographic or microbiologic testing. Overall, 5.3% of patients were exposed to H_2RAs or PPIs. The incidence of pneumonia was 2.45/100 person-years among patients using acid-suppressive drugs, compared with 0.6/100 for nonexposed patients. Unadjusted relative risk of pneumonia in the exposed group was 4.47.

A nested case-control analysis, including 475 exposed patients and 4,690 matched controls, found no evidence of confounding by the indication for acid-suppressive therapy. On analysis by drug category, adjusted relative risks were 1.89 for current PPI users and 1.63 for current H_2RA users, compared with those who had stopped using these medications. A dose-response relationship was apparent for current PPI users, less so for H_2RA users. Overall, 42% of pneumonia risk was attributable to PPI use and 37% to H_2RA use.

Users of acid-suppressive medications appear to be at increased risk of community-acquired pneumonia. The relationship appears particularly strong for PPIs, including a significant dose-response association. This may be an important concern among patients at increased risk of infection, such as those with asthma or chronic obstructive pulmonary disease.

COMMENT: *Most clinicians accept an association between gastroesophageal reflux and airway symptoms, particularly cough, hoarseness, sensation of postnasal drip, and wheeze. We often treat subjects with persistent airway symptoms with acid suppression. The increased occurrence of pneumonia associated with acid suppression makes the decision to treat possible gastroesophageal reflux more challenging.*
D. K. L.
Laheij RJF, Sturkenboom MCJM, Hassing R-J, et al: Risk of community-acquired pneumonia and use of gastric acid-suppressive drugs.
JAMA. 2004;292:1955-1960. ♦♦

How Important Is Early Allergen Exposure?

EARLY allergen exposure is generally thought to affect the risk of childhood allergic disease. Despite the implications for disease prevention, few prospective studies have examined this assumption. This 5-year follow-up study assessed the effects of early childhood allergen exposure on the risk of allergic sensitization or asthma.

Beginning in 1993, all women seen for antenatal care at three English general practices were asked to take part in a longitudinal study of childhood asthma. The 625 enrolled children accounted for 94% of all those eligible. Levels of house dust mite and cat allergen were measured in home dust samples collected when the children were 8 weeks old. At 5.5 years, 552 children were available for follow-up, including skin prick testing for sensitization to house dust mite and cat and maternal reports of wheezing.

Skin prick tests showed allergic sensitization to dust mite or cat in approximately 10% of the children. Atopic wheezing was present in 7%. Neither sensitization nor wheezing at age 5 showed a monotonic relationship with home allergen levels in infancy. However, for both dust mite and cat and for both outcomes, the exposure-response relationships increased sharply at lower exposure levels then flattened out at higher levels. Parental allergies and being first-born appeared to modify these relationships.

This prospective study of normal children suggests that exposure to allergens during infancy has no linear effect on atopic sensitization or wheezing at age 5. For both outcomes, the risks appear to increase at very low levels of allergen exposure, only to attenuate or even decrease at high levels. Including the effects of parental atopy and birth order, the results highlight the importance of both genetic and environmental factors. On its own, reducing home allergen levels is unlikely to reduce the rate of childhood allergic disease and may even increase the risk of sensitization.

COMMENT: *It is generally assumed that the risk of childhood respiratory allergies is related to allergen exposures in early life. The extent of this effect is still actively debated. Cullinan et al. present only the second cohort study to report exposure outcomes for sensitization and atopic wheezing in children. Contrary to the German Multicenter Allergy Study, no significant relationships between allergen exposure and either sensitization or wheeze were found. The difference may lie in the fact that the German study was weighted with high-risk children, in whom the strongest dose-response relationship was noted. The U.K. study appears more representative of the general population, in which allergen exposure is less likely to have had a health impact.*
E. J. B.

Cullinan P, MacNeil SJ, Harris JM, et al: Early allergen exposure, skin prick responses, and atopic wheeze at age 5 in English children: a cohort study.
Thorax. 2004;59:855-861. ♦♦

Nasal Corticosteroids Ineffective in Sinusitis Recurrence

PATIENTS with nasal polyps and chronic rhinosinusitis are commonly treated with topical corticosteroids, before and after surgery. However, questions remain about their effectiveness after functional endoscopic sinus surgery (FESS).

The trial included 162 adults with chronic rhinosinusitis or nasal polyps undergoing FESS, including systemic corticosteroids during the perioperative period. Postoperatively, patients were randomized to receive 1 year of treatment with fluticasone propionate aqueous nasal spray, 400 or 800 µg twice daily; or placebo. Patients with recurrent or persistent disease were withdrawn from the trial, though not from statistical analysis.

Functional endoscopic sinus surgery was associated with sharp reductions in total symptom scores. However, postoperative treatment had little or no effect on disease recurrence or persistence. In both fluticasone dose groups, more than 50% of patients were withdrawn from the trial--nonsignificantly higher than in the placebo group. There were also no significant differences detected in subgroup analyses, including patients with nasal polyps, those with high symptom scores preoperatively, and those with no history of sinus surgery.

This randomized trial questions the benefits of steroid therapy after FESS for patients with chronic rhinosinusitis and nasal polyps. Even with a treatment period up to 1 year, fluticasone propionate aqueous nasal spray yields no significant reduction in disease recurrence and persistence, compared with placebo.

COMMENT: *In a game of word association, the first word that comes to mind with "chronic sinusitis" is "frustration." Despite the progress we have made in understanding the immunologic mechanisms involved and refining surgical technique, we really have not come very far toward helping patients with this disease. This well-controlled study from The Netherlands suggests that even high-dose nasal steroids are unable to prevent the recurrence of symptoms in the first year following sinus surgery. The fact that roughly half of patients relapsed in the first postoperative year also reminds us of the importance of exhausting nonsurgical options first.*
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. ♦♦

Increased Asthma Risk with Wheezing in Infancy

THERE are few data on the long-term outcomes of wheezing in infants. A Finnish research group previously reported on the prevalence of asthma at age ➤➤

10 among 127 children hospitalized for bronchiolitis or pneumonia at age 2. Here they report on asthma and other outcomes in the same group of patients at age 18 to 20.

At a median age of 10 months, 83 patients were hospitalized for bronchiolitis and 44 for pneumonia. Eighty-eight of these patients were available for follow-up, median age 19 years; forty-five controls were available as well. Asthma was defined in terms of physician diagnosis and patient self-report. Other assessments included lung function studies, methacholine challenge, home peak expiratory flow monitoring, and skin prick testing to inhalant allergens.

In young adulthood, physician-diagnosed asthma was present in 30% of patients who had bronchiolitis in infancy and 15% of those who had asthma, compared with 11% of controls. Self-reported asthma was also more frequent in the bronchiolitis and pneumonia groups. On methacholine challenge testing, bronchial reactivity was somewhat more frequent in the two patient groups; severe hyperreactivity was found in 3 patients, all from the bronchiolitis group. Lung function values were generally within normal limits, but more likely to be abnormal among patients in the bronchiolitis group. Skin prick testing showed higher reactivity to dog and cat allergen among subjects in the bronchiolitis group. Bronchiolitis was a significant risk factor for asthma, independent of smoking and atopy.

Infants hospitalized for bronchiolitis or pneumonia remain at increased risk of asthma through their teen years. Early childhood wheezing also appears to predict lung function abnormalities. Atopy is a risk factor for asthma and bronchial reactivity, though not for abnormal lung function results.

COMMENT: *These Finnish researchers report data from a prospective cohort of children hospitalized for either bronchiolitis or pneumonia when less than 2 years old in 1981 and 1982. Ten years ago, they reported that the prevalence of asthma was 15% between the ages of 8 and 10 years in those with a history of bronchiolitis and 7% in the group who had pneumonia. Over the last 10 years those prevalence numbers have doubled, with asthma developing in 30% of children presenting with bronchiolitis and 15% of the pneumonia group, compared with just 11% of controls. Weaknesses of the study include the relatively small sample size of 127 original patients, with one-third dropping out. Strengths include the extensive analysis including skin test data, rigorous definitions of asthma, and long-term follow-up. The bottom line was an increased risk for asthma and impaired lung function, independent of the development of atopy, in patients hospitalized for wheezing before 2 years of age.*
S. M. F.

Piippo-Savolainen E, Remes S, Kannisto S, et al: Asthma and lung function 20 years after wheezing in infancy: results from a prospective follow-up study.
Arch Pediatr Adolesc Med. 2004;158:1070-1076. ♦♦

The "United Airway" Extends to the Ear!

THE united airway concept suggests a continuum of involvement of the upper and lower airways in allergic disease. Previous studies have suggested that patients with allergic disease are at increased risk of otitis media with effusion (OME), mainly through the effects of Th2 cytokines and their receptors. This study simultaneously examined the inflammatory status of the ear and upper airway in children with OME.

The analysis included 45 children undergoing tympanostomy tube placement for OME at the same time as adenoidectomy for adenoid hypertrophy. At surgery, samples of middle ear effusion fluid, eustachian tube mucosa, and adenoid tissue were obtained for assessment of cellular and cytokine profiles by immunohistochemistry and in situ hybridization. Based on skin prick testing, 24% of the children were classified as atopic.

The middle ear effusions of atopic children had higher percentages of eosinophils, T lymphocytes, and interleukin (IL)-4 and IL-4 mRNA+ cells, compared with nonatopic children. In contrast, middle ear fluid from atopic children had lower percentages of neutrophils and IFN-γ-positive cells. Similar patterns were apparent on comparison of eustachian tube and adenoid tissue samples.

Atopic children with OME show evidence of allergic inflammation in the middle ear, as well as in the nasopharynx. The pattern of inflammation is similar to that observed in the respiratory tract in allergic disease, but different from that in nonatopic children. These results suggest that the unified airways concept should be extended to include the middle ear as well as the upper and lower airways.

COMMENT: *In this cleverly designed study, 45 children undergoing myringotomy with PE tubes and adenoidectomy had cellular and cytokine profiles from tissue samples from both sides of the eustachian tube. Allergy skin testing (AST) was also performed during anesthesia to determine atopic status. The allergic children, with at least one positive AST, had significantly higher levels of eosinophils, T lymphocytes, and IL-4 mRNA+ cells--which are characteristic of allergic inflammation--compared to nonatopic controls. Controls also tended to have higher levels of neutrophils and IFN-γ mRNA. The results support the concept that the middle ear has an immunologic response that is similar to that of the upper and lower airways in allergic patients. The theory of the unified airway is now extended to the middle ear.*
S. M. F.

Nguyen LHP, Manoukian JJ, Sobol SE, et al: Similar allergic inflammation in the middle ear and the upper airway: evidence linking otitis media with effusion to the united airways concept.
J Allergy Clin Immunol. 2004;114:1110-1115. ♦♦

Once Again, Breast Is Best!

SOME studies, but not all, suggest that breast-feeding reduces the risk of childhood asthma and allergy. Previous reports from a large Swedish birth cohort indicated that breast-feeding exclusively for at least 4 months reduced asthma risk by age 2. Four-year follow-up results in the same cohort are reported.

The prospective study included 4,089 children born in Stockholm during 1994-96. The children were followed up regularly through age 4, with asthma defined by parental report. Complete follow-up data were available in 3,619 children.

Median duration of exclusive breast-feeding in the study cohort was 6 months. At age 4, 7% of children met the study definition of asthma. For children breast-fed exclusively for at least 4 months, asthma prevalence was 6.4%, compared to 9.1% for those with shorter durations. The associated odds ratio (OR) was 0.72; a somewhat stronger effect was noted after exclusion of children who wheezed during lactation, OR 0.64. The protective effect of breast-feeding was stronger for children without a family history of allergic disease, compared to those with such a history: OR 0.58 vs 0.73, respectively.

The results strengthen the conclusion that exclusive breast-feeding for at least 4 months reduces the risk of asthma through age 4. The effect seems strongest for children with no family history of allergy. Breast-feeding may also reduce asthma severity.

COMMENT: *This is an update report from the ongoing prospective Swedish birth cohort study that presents data on children at 4 years of age. The retention was impressive, with a 90% response rate of the initial 4,089 children. There was a remarkable reduction in risk of asthma at 4 years of age in children exclusively breast-fed for at least 4 months, OR 0.58. Even children with a family history of allergies benefited from breast-feeding, OR 0.73. It was interesting that there was no significant protective effect of breast-feeding on the development of allergic sensitization as measured by RAST in 88% of the cohort. There was also a trend toward a benefit of breast-feeding on peak flow values in the children with extended, exclusive breast-feeding--at least 4 months. This data can help us counsel our patients about the potential benefits of exclusive nursing of newborns for at least the first 4 months.*
S. M. F.

Kull I, Almqvist C, Lilja G, et al: Breast-feeding reduces the risk of asthma during the first 4 years of life.
J Allergy Clin Immunol. 2004;114:755-760. ♦♦

Much More on SLIT

ACCESS to subcutaneous immunotherapy (SIT) is restricted in the United Kingdom. This has led to interest in the use of sublingual immunotherapy (SLIT) as an alternative treatment for allergic rhinitis. This randomized, placebo-controlled trial evaluated the benefits of SLIT for patients with seasonal allergic rhinitis (SAR) uncontrolled by standard medications.

The feasibility study included 186 adult patients with SAR that was not well-controlled despite nasal steroids and/or oral antihistamines. After a year on usual treatment, patients were randomized to receive 2 years of active SLIT with grass pollen extract; 1 year of SLIT and 1 year of placebo; or 2 years of placebo. Treatment continued from February through January of each year. The main study outcome was symptom scores recorded on daily diary cards.

After the first year, hay fever symptoms did not differ significantly for patients receiving active SLIT vs placebo. However, patients receiving 2 years of SLIT showed significant benefits at the end of the second year: they were 6.8-fold more likely to have reductions in rhinorrhea and 2.4-fold more likely to have reductions in sneezing. Rescue medication use decreased to a greater extent in the SLIT groups, although nasal steroid use was unchanged. Side effects were more frequent with SLIT, mainly occurring during dose escalation.

For patients with SAR that does not respond to conventional drug treatment, SLIT yields significant improvements in symptoms. However, the benefits do not appear until the second season of SLIT; side effects are common but generally mild. Long-term follow-up studies of SLIT for patients with hay fever are needed.

Smith H, White P, Annila I, et al: Randomized controlled trial of high-dose sublingual immunotherapy to treat seasonal allergic rhinitis.
J Allergy Clin Immunol. 2004;114:831-837. ♦♦

FOR patients with allergic disease, SLIT offers an attractive alternative to subcutaneous immunotherapy. In children, both forms of immunotherapy may reduce the risk of developing asthma. A short-term, coseasonal SLIT protocol was evaluated for its effect on asthma risk and other outcomes in children with hay fever.

The randomized, open, controlled trial included 113 children, mean age 7.7 years, requiring treatment for allergic rhinoconjunctivitis. For all patients, grass pollen was the only clinically significant allergen. One group received SLIT using an extract of mixed grass pollens, with buildup and maintenance phases for three consecutive pollen seasons. Controls received standard symptomatic care.

The cumulative dose of major allergen grass group 5 was approximately 40 µg over a 4-month treatment period. Outcomes did not differ significantly between groups during the first year of treatment. However, in the second and third years, children in the SLIT group used less medication and had somewhat lower symptom scores. Also beginning in the second year, subjective symptom evaluation scores were better with SLIT. Children receiving symptomatic care were more likely to develop asthma by year 3: relative risk 3.80.

For children with seasonal allergic rhinitis, three seasons of SLIT are associated with a reduced risk of asthma. This form of immunotherapy also improves medication use and symptom scores compared with symptomatic treatment, although these benefits are not realized until the second year. The results add to the concept that treating allergic rhinitis helps prevent allergic asthma.

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COMMENT: *These two reports from European allergists investigate the use of high-dose SLIT to treat seasonal allergic rhinitis in children and adults. The adult study, which was placebo-controlled, reported the benefit of SLIT after 2 years of co-seasonal treatment for spring-summer hay fever in adults. There was no significant difference between the actively treated group and controls after the first year, but improvement was impressive by the second year with SLIT. This was similar to the improvement in symptoms after 2 years of treatment in the pediatric study from Italy. Although this study was not placebo-controlled, the children were treated for 3 years and had benefits both in rhinitis symptom improvement and reduction in asthma, compared to a cohort group of controls. The bottom line is that these reports add to the convincing literature on the benefits of SLIT: similar to parenteral aqueous allergen immunotherapy, SLIT reduces both the symptoms of allergic rhinitis and the risk of asthma in children. Our needle-phobic patients would appreciate the option to use SLIT if it truly is immunologically equivalent.*
S. M. F.
Novembre E, Galli E, Landi F, et al: Coseasonal sublingual immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis. **J Allergy Clin Immunol**. 2004;114:851-857. ♦♦

CLINICAL trials and experience have validated the use of SLIT for treatment of allergic disease. Questions still remain, including the magnitude of SLIT's clinical efficacy and its ability to prevent further allergic disease. These issues were addressed in a randomized trial conducted in a "real-life" clinical setting.

The study included 511 patients seen at an Italian allergy clinic--all had allergic rhinitis, with or without intermittent asthma. In a 2:3 ratio, they were randomized to receive 3 years of treatment with medications only or with medications plus SLIT. Symptoms and medication use were assessed each year during periods of allergen exposure. Before and at the end of treatment, the patients underwent pulmonary function testing, methacholine challenge, and skin prick testing.

Dropout rates were similar: 15% on SLIT and 12% on medications only. Patients with SLIT had progressive reductions in clinical score, from a mean of 147.0 at baseline to 72.9 in year 1, 68.3 in year 2, and 54.7 in year 3. Controls, in contrast, had no significant reduction. Adherence was good, and systemic adverse effects were rare. The SLIT group also had a significant reduction in methacholine challenge positivity. The rate of new cutaneous sensitization was 5.9% with SLIT, compared with 38% in the control group.

This allergy clinic trial supports the benefits of SLIT added to medication for allergic rhinitis, with or without asthma. In addition to reducing symptoms and medication use, SLIT reduces bronchial hyperreactivity and new skin sensitizations.

COMMENT: *These authors addressed the impact of SLIT on the magnitude of clinical efficacy, changes in bronchial hyperreactivity, adherence to treatment, and preventive effects. They studied 511 subjects with allergic rhinitis (with or without asthma) on pharmacotherapy alone or drugs plus SLIT over a 3-year period. SLIT reduced clinical symptom scores by 50%, with associated significant decreases in methacholine reactivity, good adherence, and a preventive effect on the onset of additional skin sensitization. Side effects were minimal. It is becoming increasingly difficult to ignore the efficacy of this distinctly European approach.* (See ***AllergyWatch*** Nov/Dec 2004, p 10.)
E. J. B.
Marogna M, Spadolini I, Massolo A, et al: Randomized controlled open study of sublingual immunotherapy (SLIT) for respiratory allergy in real life: clinical efficacy and more. **Allergy**. 2004;59:1205-1210. ♦♦

EIB Treatments Have Differing Effects on Gas Exchange

PATIENTS receiving short-acting β_2-agonists may develop airway obstruction, perhaps related to ventilation/perfusion imbalance. No studies have examined the effects of long-acting β_2-agonists, such as salmeterol, on ventilation/perfusion balance. The cysteinyl leukotriene inhibitor montelukast does not appear to cause ventilation/perfusion mismatch in patients with exercise-induced bronchospasm (EIB). This study compared the effects of salmeterol and montelukast on cardiopulmonary exercise economy and physical performance in patients with EIB.

The study included 18 adult asthma patients with EIB. In randomized, crossover fashion, they received oral montelukast 10 mg/d and inhaled salmeterol 50 µg bid. After 5 days on each treatment, the patients completed treadmill exercise tests for comparison of gas exchange, physical performance, and lung function parameters.

Most exercise parameters did not differ significantly between treatments, including pulmonary function during exercise, time to exhaustion, Borg score, lactate levels, and oxygen uptake. Most other respiratory variables and heart rate were similar as well.

However, oxygen pulse was significantly higher after montelukast than after salmeterol at two time points: after running at 80% of maximal oxygen uptake and 6 minutes into running at 60%. There was also a significant difference in mean peak postexercise decline in FEV_1, which occurred at 2 minutes after the run to exhaustion: 10.0% after montelukast vs 16.2% after salmeterol.

In patients with EIB, most measures of lung function, gas exchange, and exercise economy are similar after short-term treatment with montelukast or salmeterol. However, montelukast is associated with a higher oxygen pulse at certain times, suggesting a more favorable effect on gas exchange at moderate exercise. Further study is needed to assess the therapeutic implications of this difference.

COMMENT: *The mechanism of EIB has been debated for decades, as has the best way to prevent exercise-induced symptoms. While various treatment approaches are effective, we all have patients in whom pro-* ➤➤

phylaxis has failed. And while the effects of long-acting inhaled β-agonists and leukotriene antagonists have been compared ad nauseum using traditional spirometric and immunologic endpoints, this study compared the drugs' effects on a variety of other physiologic measurements that are important in EIB. As expected, the drugs had similar effects on most endpoints. However, gas exchange during exercise (as measured by oxygen pulse) was significantly better after montelukast than salmeterol. Although the clinical significance of this finding is unclear, it certainly is provocative and deserving of further study.
S. A. T.
Steinshamn S, Sandsund M, Sue-Chu M, Bermer L: Effects of montelukast and salmeterol on physical performance and exercise economy in adult asthmatics with exercise-induced bronchoconstriction.
Chest. 2004;126:1154-1160.

♦♦

How Many Asthma Patients Really Have GERD?

PATIENTS with asthma have particularly high rates of gastroesophageal reflux disease (GERD), which may act as an asthma trigger. Even when esophageal pH monitoring is used, reported prevalences of GERD among asthma patients vary widely. The prevalence of GERD was assessed in a clinical population of asthma patients.

The study included a random sample of 149 adult patients receiving inpatient or outpatient care for asthma at six Finnish hospitals. All underwent 24-hour esophageal pH monitoring and completed a questionnaire regarding lung and stomach symptoms. Pulmonary function testing was performed as well.

Ninety patients consented to participate. Seventy-five patients with an FEV_1 of greater than 45% predicted underwent methacholine challenge testing, which showed bronchial hyperresponsiveness in 69%. Esophageal pH monitoring detected abnormal acid reflux in 36% of patients. However, 25% of patients with documented reflux did not have typical symptoms of GERD.

In contrast, 52% of patients reported typical GERD symptoms. Of these, just 51% had reflux detected on esophageal pH monitoring.

Objective testing documents GERD in more than one-third of a clinical sample of asthma patients. However, many of these patients do not have typical GERD symptoms. Another group of asthma patients report GERD symptoms without evidence of abnormal acid reflux. The results raise the possibility that mild GERD accompanying asthma could be caused by asthma medications or by asthma itself, whereas GERD may exacerbate asthma only in more severe cases.

COMMENT: *To achieve adequate asthma control, one must often evaluate and treat comorbid conditions. Gastroesophageal reflux disease is present in approximately 30% of asthma patients. Although 47 of the 90 patients in this study had typical reflux symptoms, only 24 had abnormal acidic reflux documented by 24-hour esophageal pH monitoring. Conversely, 25% of patients with a positive pH probe were free from symptoms of GERD. This begs the question: Can we justify empiric treatment based on a history of typical gastroesophageal symptoms alone, or is pH monitoring necessary for all asthmatics with suboptimal control?*
T. L. H.
Kiljander TO, Laitinen JO: The prevalence of gastroesophageal reflux disease in adult asthmatics.
Chest. 2004;126:1490-1494.

♦♦

β_2-Receptor Genotype Affects Albuterol Response

THERE is ongoing debate over possible adverse effects of regular albuterol use. Polymorphisms of the β_2-adrenergic receptor may influence the response to inhaled albuterol--retrospective studies suggest adverse effects in patients with the common Arg/Arg genotype.

This randomized, genotype-stratified trial included two groups of 41 patients with mild asthma who were not receiving any controller medication. One group had the Arg/Arg genotype at the sixteenth amino-acid position of the β-adrenergic receptor, while the other group had the Gly/Gly genotype. In crossover fashion, patients received 16 weeks of scheduled treatment with albuterol and 16 weeks of placebo. Asthma control was compared by morning peak expiratory flow rate (PEFR), within and across genotype groups.

Four patients in the Arg/Arg group dropped out before randomization. During a run-in period, when patients took ipratropium bromide instead of albuterol as rescue medication, morning PEFR increased by 23 L/min in patients with the Arg/Arg genotype, compared to a nonsignificant 2 L/min increase in the Gly/Gly group. During the albuterol period, morning PEFR in Arg/Arg patients was 10 mL/min lower than during the placebo period. In contrast, Gly/Gly patients had a 14 L/min increase during albuterol treatment. Similar genotype-related differences were apparent in FEV_1, symptoms, and medication use.

This randomized trial confirms that patients with the Arg/Arg genotype have adverse effects during regular albuterol treatment. Morning PEFR increases when regular albuterol is stopped, but does not decline when albuterol treatment is started. The one-sixth of patients with this β_2-adrenergic receptor genotype may benefit from alternative treatments.

COMMENT: *Two previous large studies showed little change in asthma control when β_2-agonists were used regularly rather than as needed. However, other relatively large studies have shown deterioration in one or more aspects of asthma control. The question as to whether differences observed could be attributed to β_2-adrenoceptor polymorphisms is addressed in this careful prospective investigation. Israel et al. found that patients with the Gly/Gly 16 genotype improved with salbutamol but not placebo, while those with the Arg/Arg 16 genotype improved with placebo but not salbutamol. It is concluded that patients with the* ➤➤

Arg/Arg 16 genotype can have clinical deterioration with use of short-acting β_2-agonists. Should all patients with asthma undergo genotyping? This may be premature, but data in this study should be confirmed and widened to address long-acting β-agonists and the concomitant use of inhaled steroids.
E. J. B.
Israel E, Chinchilli VM, Ford JG, et al: Use of regularly scheduled albuterol treatment in asthma: genotype-stratified, randomized, placebo-controlled cross-over trial. **Lancet**. 2004;364:1505-1512. ♦♦

High CRP Linked to Respiratory Function and Bronchial Responsiveness

C-reactive protein (CRP) is a key marker of inflammation, and may play an active role in development of atherosclerosis. Patients with cardiovascular risk factors have increased rates of impaired respiratory function, although the mechanism of this association is unknown. The relationship between bronchial hyperresponsiveness (BHR) and CRP was studied in a general population sample.

The analysis included 259 adults from the European Community Respiratory Health Survey. With adjustment for smoking and other factors, mean FEV_1 was 3.29 L/s for subjects in the highest tertile of serum CRP, compared with 3.50 L/s for those in the lower tertiles.

Based on a 20% or greater decrease in FEV_1 in response to less than 4 mg of methacholine, BHR was present in 41.9% of subjects in the high-CRP group, compared with 24.9% of those with lower CRP levels. The associations were independent of smoking, asthma, and other factors.

High serum CRP is independently associated with lower FEV_1 and increased BHR. The findings strengthen the possibility that systemic inflammation contributes to both respiratory impairment and BHR.

COMMENT: *C-reactive protein is a major marker of inflammation in humans. Its hepatic synthesis is largely regulated by interluekin-6. Prior studies have linked impaired respiratory function with cardiovascular risk factors. These authors evaluated the relationship between BHR and systemic inflammation via its surrogate, CRP levels. A reduced FEV_1 and higher frequency of BHR were strongly associated with high CRP levels. The pathogenesis of this association is unknown and must await further study. It is interesting to speculate whether it could relate to higher or more chronic exposure to some environmental irritant or infectious agent.*
E. J. B.
Kony S, Zureik M, Driss F, et al: Association of bronchial hyperresponsiveness and lung function with C-reactive protein (CRP): a population based study. **Thorax**. 2004;59:892-896. ♦♦

Birch Pollen Peptide Vaccine: A New Approach to Immunotherapy?

THE major birch pollen antigen, Bet v 1, is an important cause of allergic disease. Vaccination using allergen-specific blocking antibodies is a potentially advantageous alternative to specific immunotherapy. This report describes the development of a B cell epitope-derived, peptide vaccine against Bet v 1.

Based on the three-dimensional structure of Bet v 1, the investigators selected and synthesized six allergen-derived peptides of 25 to 32 amino acids in length. Together, the peptides resembled the primary structure of the allergen itself, without the residual secondary or tertiary structure. In a basophil histamine-release assay, even high concentrations of the peptides--alone or together--induced no histamine release. In contrast, complete recombinant Bet v 1 induced histamine release in dose-dependent fashion.

Immunization of rabbits with the peptides induced allergen-specific IgG. In studies using sera from birch-allergic patients, preincubation with peptide-induced rabbit IgG blocked binding of IgE to Bet v 1 in 57 of 60 samples. Further experiments in mice found that peptide-specific IgG antibodies blocked Bet v 1-induced allergic reactions. Peptide vaccination inhibited allergen-induced degranulation of rat basophil leukemia cells almost completely, suggesting induction of blocking antibodies to inhibit the immediate allergic response.

The study illustrates a B cell epitope-based approach to the design of safe and potentially effective allergy vaccines, based on knowledge of the allergen's structure. The peptide-induced antibodies achieved in this study strongly block IgE binding to Bet v 1 in sera from patients with birch pollen allergy. Using this approach, it may be possible to give peptide vaccines in high doses without danger of anaphylactic side effects.

COMMENT: *This fascinating study demonstrates that adjuvant-bound birch allergen peptide fragments around 30 amino acids long are able both to induce specific IgG "blocking antibody" and to prevent specific IgE sensitization in mice. In birch-allergic humans, these peptides did not elicit immediate or late skin test reactions, nor did they induce basophil histamine release. The obvious next step is to perform a human immunotherapy trial. This strategy may avert the T-cell-mediated adverse reactions observed with prior "peptide" immunotherapy projects because of the use of adjuvant. Stay tuned.*
S. A. T.
Focke M, Linhart B, Hartl A, et al: Non-anaphylactic surface-exposed peptides of the major birch pollen antigen, Bet v 1, for preventive vaccination.
Exp Allergy. 2004;34:1525-1533. ♦♦

Sensitization Affects Lung Function Only With Allergen Exposure

THE data on the effects of pet exposure on the risk of allergic sensitization and asthma are unclear. The effects of early pet exposure and current allergen exposure on sensitization and lung function at age 3 were examined in a birth cohort study.

The analysis was based on a British birth cohort of 1,085 children, of whom 498 had complete follow-up data at age 3. Assessments included skin prick testing; lung function studies, including plethysmographic measurement of specific airway resistance (sR_{aw}); and assessment of exposure to dust mite, cat, and dog allergen.

Pet ownership--dog, cat, or both--was unrelated to sR_{aw}. Forty-seven percent of children had regular contact with pets at age 3, while 6% had no pet contact. There was no significant difference in geometric mean sR_{aw} values between these two groups: 1.10 vs 1.09 kPa/s.

Sensitization to one or more allergens was present in 20.3% of children, and was associated with reduced lung function. For children sensitized to cat, sR_{aw} was unrelated to level of cat allergen exposure. For those sensitized to dog, there was a significant and positive correlation between sR_{aw} and dog allergen level, with lung function decreasing at higher levels of exposure. Sensitized children with high levels of exposure to the allergen they were sensitized to had a geometric mean sR_{aw} of 1.20 kPa/s, compared with 1.08 kPa/s for children who were not sensitized and not exposed; 1.07 for sensitized children with high allergen exposure; and 1.12 for sensitized children who were not exposed.

This study documents decreased lung function among 3-year-olds who are sensitized and exposed to high levels of the sensitizing allergen. If there is no allergen exposure, sensitization appears to have little effect on lung function. Lung function at age 3 is unrelated to pet ownership during early life. If there is any relationship between pet ownership and asthma, it is probably not mediated by lung function.

COMMENT: *These British researchers used a relatively new technique of measuring sR_{aw} in preschool children using whole-body plethysmography. The children were followed prospectively from birth; endpoints included allergic sensitization, home allergen levels and sR_{aw} measured at 3 years old. Of the 1085 children born into the study, lung function and other data were analyzed for 498. Interestingly, lung function was not significantly affected by pet ownership in children without allergic sensitization or in allergic children without pet exposure. On the other hand, there was a significant reduction in sR_{aw} in sensitized children who were exposed to pets at home. This study suggests that allergen sensitization and exposure may be clinically relevant, even in infants.*
S. M. F.

Lowe L, Woodcock A, Murray CS, et al: Lung function at age 3 years: effect of pet ownership and exposure to indoor allergens.
Arch Pediatr Adolesc Med. 2004;158:996-1001. ♦♦

Study Shows Impact of Pneumococcal Vaccine

STREPTOCOCCUS pneumoniae is a major cause of infectious disease, including meningitis, pneumonia, and otitis media. Children under 2 and the elderly are most frequently affected. In 2000, routine administration of pneumococcal conjugate vaccine (PCV) was recommended for U.S. children. This study evaluated the impact of PCV vaccination on pneumococcal disease in children in two states.

The ecologic analysis used Medicaid data for the state of Tennessee and a commercial insurance database for upstate New York. The Tennessee data included more than 440,000 child-years for children under age 2 and nearly 590,000 child-years for a comparison group of 3- to 5-year-olds. The New York data included about 44,000 and 78,000 child-years, respectively. At baseline, medical visits for pneumonia and invasive pneumococcal disease were higher in Tennessee, while visits for otitis media were higher in New York.

In both regions, total disease rates decreased significantly after the introduction of PCV. The overall rate of pneumococcal pneumonia and invasive pneumococcal disease decreased by 19 to 33 per 1,000 children per year, while the otitis media rate decreased by 125 to 430 per 1,000 children per year. For pneumonia and invasive disease, emergency department (ED) visits decreased by 8 per 1,000 children and outpatient visits by 12 per 1,000 in Tennessee, while outpatient visits decreased by 33 per 1,000 in New York. Substantial reductions in ED and outpatient visits for otitis media were also noted in both states.

The introduction of PCV appears to have significantly reduced rates of pneumococcal disease in American children. In just a few years, substantial reductions have been achieved not just in invasive disease, but also in pneumococcal pneumonia and otitis media.

COMMENT: *As an older but still practicing physician, it still amazes me to read about rapid changes in disease incidence after a specific vaccine has been safely introduced to the public! This study involves over 400,000 children, aged 3 to 5 years, in Tennessee and upper New York State. It is estimated that since 2000, when routine administration of a pneumococcal conjugate vaccine was introduced in the United States, 42% of the Tennessee and 53% of the New York State children received at least three injections. When the impact of such preventive therapy was analyzed in 2001-02, significant reduction in the rates of pneumonia (18% to 31%) and otitis media (6% to 20%) were observed. Over time, as more children are immunized, an even bigger success story can be anticipated!*
J. A. A.

Poehling KA, Lafleur BJ, Szilagyi PG, et al: Population-based impact of pneumococcal conjugate vaccine in young children.
Pediatrics. 2004;114:755-761. ♦♦

Patients Can't Tell When MDI Canisters Are Empty

PATIENTS using pressurized metered-dose inhalers (MDIs) may use inaccurate means of testing whether their canisters are empty, such as shaking or estimating their weight. Few patients seem actually to count the number of actuations delivered.

The authors asked 50 asthma patients who regularly used MDIs how they knew when it was time to replace their inhaler. Seventy-two percent said they knew a canister was empty when it no longer made a sound when actuated. Some said they replaced a canister when it was "old," such as "after a month or so." A few patients responded that they were supposed to place the canister in water, and that it would float when empty. However, none had actually used the floatation technique. Just half of patients shook the canister before actuation.

In a further study, the authors evaluated the floatation patterns of MDI canisters when full and at various levels of depletion. All canisters had many more actuations than listed by the manufacturer. This was especially true for canisters containing chlorofluorocarbon propellant, for which shaking before actuation significantly increased the number of "puffs." No floatation pattern reliably depicted whether canisters were empty or full. About one-fourth of the time, water blocked the valve opening.

Asthma patients do not know and use reliable methods of determining when MDI canisters are empty. This may cause them to use canisters for much longer than intended. The floatation test does not accurately reflect the contents of canisters. For now, counting and recording doses seems to be the only accurate method of determining when canisters have been depleted.

COMMENT: *MDI therapy for asthma is one of the most convenient ways for patients to administer their medication. Unfortunately, we know that many patients have trouble using their inhalers correctly. Now a study from Wake Forest demonstrates that children with asthma and their parents cannot accurately tell when their inhaler is empty. This could lead to patients wasting medication by throwing it away too soon or using an empty inhaler with the risk of flare-up. The authors also point out "floating the canister" is not accurate in assessing if the inhaler is empty. Even water can clog the valve, making the inhaler inoperable. It appears that one has to count puffs to keep an accurate log on the amount of medication in the canister until counting devices are developed for MDIs.*
T. L. H.
Rubin BK, Durotoye L: How do patients determine that their metered-dose inhaler is empty?
Chest. 2004;126:1134-1137. ♦♦

Inhaled Steroids May Cause Cutaneous Side Effects

EASY skin bruising is a recognized complication of high-dose corticosteroid therapy, particularly in older adults. This side effect has been linked to impaired adrenal function. This study evaluated rates of bruising among patients taking an inhaled steroid for chronic obstructive pulmonary disease (COPD).

The analysis included 1,116 patients with mild to moderate COPD from the Lung Health Study II. All were current or recent smokers--63% were men, and the mean age was 56 years. In the trial, patients were randomized to receive inhaled triamcinolone acetonide, 1,200 µg/d, or placebo for 3.5 to 4.5 years. Skin changes--including bruising, skin rashes, and slow healing--were assessed by periodic questionnaires.

Easy bruising was reported by 11.2% of compliant patients in the triamcinolone group, compared with 3.5% in the placebo group. Slow healing was also more likely to be reported in the steroid group, 2.4% vs 0.5%. Skin rashes were slightly less frequent in patients taking triamcinolone. Rates of bruising seemed highest for older men assigned to triamcinolone who were compliant with inhaler use.

A subset of patients underwent assessments of adrenal function and bone mineral density. None of these variables was significantly related to bruising.

Patients with COPD taking moderate to high doses of inhaled corticosteroids may have increased rates of bruising and slow skin healing. These side effects may be useful markers of systemic toxicity resulting from inhaled steroid use, especially in older patients. However, the cutaneous effects appear unrelated to suppressed adrenal function or bone loss.

COMMENT: *Much concern regarding safety profiles surrounds moderate-to-high doses of inhaled corticosteroids. One organ often not mentioned is the skin. This study reminds us that the easy bruising and delayed wound healing that we see with oral corticosteroids can also occur with inhaled corticosteroids. In addition, the authors examined the association between skin bruising and markers of systemic toxicity, such as suppression of adrenal function or loss of bone mineral density. No association was identified.*
T. L. H.
Tashkin DP, Murray HE, Skeans M, et al: Skin manifestations of inhaled corticosteroids in COPD patients: results from Lung Health Study II.
Chest. 2004;126:1123-1133. ♦♦

Study Finds 23% Rate of Allergic Rhinitis in Western Europe

FEW studies have specifically examined the rate of allergic rhinitis in Europe. A population-based survey was performed to assess the prevalence of allergic rhinitis in Western European countries, including "clinically confirmable" but undiagnosed cases.

Telephone interviews were conducted with random adult subjects in Belgium, France, Germany, Italy, Spain, and the United Kingdom, with a target of 1,600 subjects per country. Of 9,646 respondents, 19% self-reported allergic rhinitis (physician-diagnosed in 13%). The self-reported rate of current asthma was 6.4%, including 22% of those with physician-diagnosed allergic rhinitis. ➤➤

Clinical visits were made by 726 of respondents who screened positive for allergic rhinitis. Of 724 completed examinations, the diagnosis of allergic rhinitis was confirmed in 411, a rate of 57%. Of these confirmed cases, 45% of patients did not have a previous physician diagnosis of allergic rhinitis. The overall prevalence of allergic rhinitis in Western Europe was estimated at 23%, ranging from 17% for Italy to 29% for Belgium.

The results confirm the high prevalence of allergic rhinitis in Western Europe, but suggest that nearly half of clinically confirmable cases have not been diagnosed. Patients whose allergic rhinitis is undiagnosed tend to have less severe symptoms, but could still benefit from accurate diagnosis and appropriate treatment.

COMMENT: *Many are claiming that the incidence and prevalence of allergic rhinitis in western society is continually increasing due to a range of environmental factors, from overly clean domiciles to increased psychologic stress. However, U.S. studies vary significantly, based on the specific population and region studied. This ambitious epidemiologic study revealed similar findings in western European countries, with rates varying from 17% in Italy to 29% in Belgium. The study design confirmed in Europe what has also been demonstrated in the United States--that is, clinical allergic rhinitis is still underdiagnosed. Given the significant social and financial burdens that the illness entails, this study further supports the notion that the trained allergy specialist provides a more sensitive diagnostic acumen to those with characteristic nasal symptoms.*

G. D. M.

Bauchau V, Durham SR: Prevalence and rate of diagnosis of allergic rhinitis in Europe.
Eur Respir J. 2004;24:758-764. ♦♦

Adding Montelukast to Desloratadine Improves Outcomes in Chronic Urticaria

CHRONIC urticaria (CU) is a common, disabling, and unpredictable condition. The main treatment is nonsedating H1-receptor antagonists, especially desloratadine. This trial evaluated the effects of adding the leukotriene inhibitor montelukast to desloratadine for the treatment of CU.

The randomized, double-blind trial included 81 patients with chronic urticaria: 58 women and 23 men, mean age 35.7 years. After a 1-week placebo run-in period, patients were randomized to receive 6 weeks of treatment with oral desloratadine, 5 mg, plus placebo; desloratadine plus montelukast, 10 mg; or placebo only. The study ended with a 1-week placebo washout period. Symptoms of pruritus, wheals, and urticaria were recorded in patient diaries.

Both active treatment groups had significant improvement in total CU symptoms, with good maintenance at follow-up. The extent of improvement was greater with desloratadine plus montelukast, compared with desloratadine alone: total symptom score decreased by a mean of 88.5% in the combination group compared with 69% in the desloratadine-only group. The only outcome that was not superior with desloratadine plus montelukast was number of urticarial episodes. Combination treatment also yielded greater improvement in urticaria quality of life.

Adding montelukast to desloratadine improves symptom control in patients with CU. Benefits appear within 3 weeks and are well-maintained thereafter. These two types of medications may have complementary effects on the mechanism of CU.

COMMENT: *Antihistamines and leukotriene antagonists have each separately been shown to improve symptoms in CU. These agents are commonly used in combination for CU, despite only limited supporting data. In this study, the addition of montelukast to desloratadine improved symptoms considerably compared with desloratadine alone, and this effect was sustained throughout the 8-week duration of the study. Since many allergists treat CU with high-dose antihistamines, it would also be useful to compare this desloratadine/montelukast combination to high-dose second-generation antihistamine treatment.*

S. A. T.

Nettis E, Colanardi MC, Paradiso MT, Ferrannini A: Desloratadine in combination with montelukast in the treatment of chronic urticaria: a randomized, double-blind, placebo-controlled study.
Clin Exp Allergy. 2004:34:1401-1407. ♦♦

Patients with Anaphylactoid Reactions to NSAIDs Tolerate COX-2 Inhibitors

STUDIES have shown that selective cyclo-oxygenase (COX)-2 inhibitors can be safely used by patients with nonsteroidal anti-inflammatory drug (NSAID)-sensitive asthma and urticaria-angioedema. Controlled challenges with the COX-2 inhibitors rofecoxib and celecoxib were performed in patients with NSAID-induced anphylactoid reactions.

Controlled oral challenges were performed in 33 patients receiving emergency care for anphylactoid reactions after using an NSAID. There were 19 women and 14 men, mean age 45 years. The reactions included skin reactions in all patients, laryngeal edema in 73%, hypotension in 39%, and GI effects in 15%.

At least 1 month after these episodes, the patients underwent challenge with rofecoxib or celecoxib. If no reaction occurred, successive challenges were given with meloxicam, paracetamol, and nonselective COX-1/COX-2 inhibitors. Patients with significant respiratory, nasoocular, cutaneous, or anaphylactoid reactions were considered positive responders.

The patients underwent a total of 115 challenges. All patients tolerated rofecoxib and/or celecoxib, as well as a potent, nonselective COX inhibitor other than the one responsible for their anaphylactoid reaction. All 23 patients who initially reacted to dipyrone or prophyphenazone were able to tolerate celecoxib, which has structural similarity to other pyrazole derivative agents.

Patients with a history of NSAID-induced ana- ➤➤

phylactoid reactions can tolerate treatment with selective COX-2 inhibitors. The study finds no evidence of cross-reactivity among pyrazole deriviatives. Oral challenges remain the best way to identify a safe NSAID for use in patients who need treatment and have had this type of reaction.

COMMENT: *With the recent removal of rofecoxib (Vioxx) from the U.S. marketplace, allergists should be aware of the data on other COX-2 challenges. These authors and others have shown that most COX-1-sensitive patients can tolerate COX-2. Cautious, monitored introduction seems to be the current clinical wisdom.*
A. M.
Quiralte J, Delgado J, de San Pedro BS, et al: Safety of the new selective cyclooxygenase type 2 inhibitors rofecoxib and celecoxib in patients with anaphylactoid reactions to nonsteroidal anti-inflammatory drugs.
Ann Allergy Asthma Immunol. 2004;93:360-364. ♦♦

ALLERGY AND IMMUNOLOGY REVIEWS OF NOTE

COMMENT: *This succinct review outlines the fundamentals of Hymenoptera sting allergy, its diagnosis, and its treatment. I intend to use it as the basis for patient education and consent for immunotherapy in my office.*
R. J. M.
Freeman T: Hypersensitivity to Hymenoptera stings.
N Engl J Med. 2004;351:1978-1984. ♦♦

COMMENT: *Most American clinicians strongly counsel smoking asthma patients and/or family members to stop smoking because of risk of worsening asthma. Implicit in the counsel is the promise of asthma improvement once smoking is stopped. This review examines the risks of smoking in asthma and benefits of quitting, put into the context of pathophysiologic as well as therapeutic differences between smoking and nonsmoking asthma patients. The rationale for a different therapeutic approach to the asthma patient who cannot/will not quit smoking is also discussed.*
G. D. M.
Thomson NC, Chaudhuri R, Livingston E: Asthma and cigarette smoking.
Eur Respir J. 2004;24: 822-833. ♦♦

COMMENT: *This well-written review summarizes novel treatments under study for allergic disease. It provides a concise update on the status of many new and exciting areas of research.*
A. M.
Stokes J, Casale TB: Rationale for new treatments aimed at IgE immunomodulation.
Ann Allergy Asthma Immunol. 2004;93:212-217. ♦♦

COMMENT: *This excellent review of pollen-related food allergy focuses on the lipid transfer proteins, which are the allergens thought to be responsible for the life-threatening forms of this syndrome. The authors discuss the foods containing the cross-reacting proteins, as well as the geographic distribution of these allergens.*
S. A. T.
Salcedo G, Sanchez-Monge R, Diaz-Perales A, et al: Plant non-specific lipid transfer proteins as food and pollen allergens.
Clin Exp Allergy 2004;34:1336-1341. ♦♦

COMMENT: *These authors present an update on the glucocorticoid receptor gene as well as the expression and regulation of its gene products, namely GRα and GRβ, as well as alterations in pathologic states.*
E. J. B.
Pujols L, Mullol J, Torrego A, Picado C: Glucocorticoid receptors in human airways.
Allergy. 2004;59:1042-1052. ♦♦

American College of
Allergy, Asthma & Immunology
85 West Algonquin Road, Suite 550
Arlington Heights, IL 60005-4425