AllergyWatch®

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

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

Volume 10, Number 6 November- December 2008

SLIT: Not Ready for Prime Time

SEVERAL studies have evaluated the clinical efficacy of sublingual immunotherapy (SLIT) for allergic rhinitis and asthma in children and adults. It has been suggested that safety is a key advantage of SLIT; however, severe cases of anaphylaxis have recently been reported in patients receiving SLIT. Data from a prospective study were analyzed to assess systemic adverse effects among patients receiving a standardized SLIT extract.

The analysis included 43 children and adolescents, median age 11 years, participating in an open-label study of SLIT. All had allergic rhinitis; 63% had asthma as well. All patients were sensitized to one or more allergens, mainly house dust mite. The patients received SLIT consisting of increasing doses of a standardized allergen; after 26 weeks of treatment, the average accumulated dose was 7,200 U. Adverse events were assessed using the criteria of the European Academy of Allergy and Clinical Immunology's position paper on immunotherapy.

During the study, 4 patients had immediate systemic reactions to SLIT, a rate of 9%. One patient had a late systemic reaction, for a rate of 2%. Overall, seven systemic reactions occurred in a total of 23,154 SLIT doses. Six were rated grade 2, causing wheezing or worsening of nasal symptoms. There was one grade 3 reaction, consisting of angioedema and urticaria.

The results suggest an 11% rate of systemic reactions among patients receiving standardized SLIT. All of the reactions in this small sample were rated grade 2 or 3. Larger, randomized, placebo-controlled studies will be needed to identify patients at high risk of systemic reactions, the role of allergen dose, and the safety of mixed allergen extracts.

COMMENT: *The debate concerning SLIT continues with both excitement and some apprehension. Efficacy seems to differ in studies performed in North America compared to Europe. Most of the benefits have been demonstrated with standardized, single-allergen therapy. There is a risk of systemic reactions, including anaphylaxis, making home administration a concern.* ➤➤

CONTENTS

The American College of Allergy, Asthma & Immunology expresses its appreciation to Schering-Plough for its unrestricted grant in support of the publication of *AllergyWatch*®.

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
- Pediatric Allergy and Immunology

"*AllergyWatch®*" is an official publication and a registered trademark of The American College of Allergy, Asthma & Immunology and is published six times per year in one volume. Subscription rates: U.S., Individual $90.00 Outside the U.S.: $120.00, Residents, Fellows, Students within the U.S.: $65.00, outside the U.S., add $18.00, bulk subscription pricing available upon request of the publisher. Send subscription inquiries to *AllergyWatch®*,85 West Algonquin Road, Suite 550, Arlington Heights, IL, 60005. Address editorial enquiries to: *AllergyWatch®*, c/o Anthony Montanaro, MD., Editor, The Oregon Health Sciences University, 3181 S.W. Sam Jackson Park Road, PV 320, Portland, Oregon 97201-3098. Telephone (503) 494-8531. ISSN 1521-2440.

Two things are clear to me: more data are needed and SLIT is not ready for prime time.
D. K. L.
Rodríguez-Pérez N, Ambriz-Moreno MJ, Canonica GW, Penagos M: Frequency of acute systemic reactions in patients with allergic rhinitis and asthma treated with sublingual immunotherapy.
Ann Allergy Asthma Immunol. 2008;101:304-310. ♦♦

Just Say 'NO'

REGULAR disease monitoring is an important part of guidelines for asthma management. A wide range of severity indicators have been used--including symptoms, spirometry, exacerbations, and exhaled nitric oxide--but little is known about how these measures are related to each other. The interrelationships among asthma severity indicators were assessed in a primary care sample.

The prospective study included 267 adult asthma patients, mean age 51.6 years, from five Scottish primary care clinics. The patients' mean FEV_1 was 86.3% of predicted. The investigators collected data on symptoms, use of reliever and maintenance medications, spirometric measurements, British Thoracic Society treatment step, and exhaled NO. Exacerbations were assessed for 12 months before and 3 months after a scheduled clinic visit.

The patients experienced a total of 157 exacerbations, resulting in unscheduled health care contacts or oral corticosteroid therapy, during the study period. Factors positively associated with exacerbation rate during the 12 months preceding the scheduled clinic visit included inhaled corticosteroid dose, treatment step, and symptom score. The only measure negatively associated with exacerbations was exhaled NO.

For patients with frequent exacerbations receiving higher doses of inhaled corticosteroids, the mean exhaled NO level was 19.7 ppb, compared to 40.4 ppb for patients with mild asthma not receiving corticosteroids. However, exhaled NO was not sensitive in identifying patients who experienced exacerbations in the 3 months after the clinic visit. At a cutoff value of 20 ppb, sensitivity was 66.7% and specificity 51.9%.

The results suggest that, in primary care patients with asthma, spirometric parameters, measures of airway inflammation, and symptoms are not strongly correlated with each other. Patients with severe asthma have paradoxically low exhaled NO levels, reflecting their use of high-dose inhaled corticosteroids. The findings question the value of exhaled NO for asthma monitoring in this patient population.

COMMENT: *These data from a general practice setting confirm my impressions concerning the measurement of exhaled NO in clinical practice. I use exhaled NO in subjects with respiratory symptoms without a diagnosis of asthma, before methacholine challenge in subjects with cough and an unclear diagnosis, and when adherence issues with inhaled corticosteroids are suspected. I do not think that exhaled NO will be used for routine monitoring even with less expensive portable devices. Time will tell.*
D. K. L.
Menzies D, Jackson C, Mistry C, et al: Symptoms, spirometry, exhaled nitric oxide, and asthma exacerbations in clinical practice.
Ann Allergy Asthma Immunol. 2008;101:248-255.

THERE are continued questions as to whether and how exhaled nitric oxide measurement should be used in asthma monitoring. The adjunct use of exhaled NO in guiding asthma management was evaluated in a study of inner-city youth.

A total of 780 adolescent and young adult patients with persistent asthma were screened for participation in the study. The patients were drawn from low-income neighborhoods in 10 U.S. cities. After a 3-week run-in period on a standard treatment regimen, 546 patients were randomly assigned to two treatment monitoring groups. One group received standard treat-➤➤

ment, based on National Asthma Education and Prevention Program guidelines; the other group received standard treatment with adjunct monitoring of exhaled NO. Treatment continued for 46 weeks; the two groups were compared in terms of number of days with asthma symptoms, among other outcomes.

Mean number of days with asthma symptoms--based on patient recall, over the preceding 2 weeks--was about 1.9 days in both groups. Other symptom outcomes were similar as well, including pulmonary function and asthma exacerbations. Patients assigned to adjunct exhaled NO monitoring had a higher dose of inhaled corticosteroid: mean difference 119 µg/d. Adverse events were similar between groups.

In this study of inner-city patients with persistent asthma, a standard approach to disease monitoring--with or without exhaled NO monitoring--yields good disease control for most patients. The addition of exhaled NO measurement leads to an increase in inhaled corticosteroid dosage without improving disease control. For patients receiving guideline-based asthma management, exhaled NO monitoring appears to be of little clinical benefit.

COMMENT: *Measurement of exhaled NO as a tool for measurement of asthmatic inflammation is being promoted commercially. This long-term study, funded by the National Institutes of Health, demonstrated no added benefit in asthma outcomes when NO was measured, compared to usual guidelines. This study should put to rest the idea of widespread use of NO in managing asthma. Possible exceptions may be obese or atopic adolescents, in whom better control was demonstrated in a post hoc analysis. No to NO?*
S. F. W.
Szefler SJ, Mitchell H, Sorkness CA, et al: Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial.
Lancet. 2008;372:1065-1072. ♦♦

Inhaled Steroids Linked to Fracture Risk

MEASUREMENTS like bone mineral density do not seem to provide a good indicator of the risk of fracture associated with inhaled corticosteroid (ICS) therapy. A meta-analysis was performed to assess the association between ICS treatment and the risk of nonvertebral fracture in older adults.

A review of the literature identified five case-control studies of nonvertebral fracture and ICS use. All studies reported on at least two ICS doses as the dose of beclomethasone dipropionate (BDP) or equivalent, along with the odds ratios for fracture risk for each dose compared with no ICS. Meta-analysis included data on 43,783 cases and 259,936 controls.

The data suggested that nonvertebral fracture risk increased along with BDP dose. The random-effects odds ratio of risk for fracture was 1.12 for each 1,000 µg increase in BDP dose. Although significant, the magnitude of fracture risk associated with ICS was much smaller than for other risk factors (eg, history of falls).

Inhaled corticosteroid use is a significant risk factor for nonvertebral fracture in older adults. Particularly in patients with other risk factors--eg, a history of previous osteoporotic fractures--ICS use may be a significant contributor to risk.

COMMENT: *Osteoporosis is a well-known risk with systemic corticosteroids, but characterizing the risk with topical corticosteroids has been challenging. This meta-analysis found an association between nonvertebral fracture risk and increasing doses of inhaled corticosteroids. It is important for asthma specialists to be aware of this risk, especially in asthma patients with other osteoporosis risk factors and in young patients who will likely remain on inhaled corticosteroid for several decades. Also see the review of this topic by Qaseem etal. (Ann Intern Med. 2008;149:404-415), included in the issue's "Reviews of Note."*
S. A. T.
Weatherall M, James K, Clay J, et al: Dose-response relationship for risk of non-vertebral fracture with inhaled corticosteroids.
Clin Exp Allergy. 2008;38:1451-1458. ♦♦

Nut So Bad . . .

CHILDREN with nut allergies face some risk of severe or life-threatening reactions, causing anxiety for patients, parents, and others. Reports have suggested that children with nut allergies continue to have reactions, which may become more severe over time. Few studies have reported on the outcomes of patients treated at specialty allergy centers, including a comprehensive management plan.

The investigators report a prospective follow-up study of 785 children with peanut or tree nut allergy seen at an English allergy center. All were managed using a comprehensive approach, including detailed advice on nut avoidance, emergency medications based on published guidelines, training of family members in the use of emergency medications, and notification and training of the child's school.

The children's median age at baseline was 68 months. Mean follow-up was 5.3 years, for a total of 3,640 patient-years. The index reaction was to peanut in 69% of children and was rated mild in 66% of patients, moderate in 29%, and severe in 5%.

At follow-up, 90% of children were in the same reaction severity grade, or in a lower grade. Just one patient had a severe reaction during follow-up: a rate of 0.1%. The incidence of reactions was low among preschool children, with no severe reactions. Of 114 reactions during follow-up, just three were treated with a single intramuscular epinephrine injection. Seventy-eight percent were treated with oral antihistamines only and 5% with inhaled epinephrine; 14% required no treatment. Forty-eight percent of reactions were caused by the same nut as the index reaction and 19% by a different nut. Accidental reactions were more likely to be caused by contact rather than ingestion, and were always mild. About half of reactions occurred at home; most of the rest occurred at locations other than school. ➤➤

For children with peanut/tree nut allergy, specialist treatment with a comprehensive management plan yields good outcomes. Reactions occur infrequently during follow-up, and are generally mild. Rates of appropriate and effective treatment are very high.

COMMENT: *A child's nut allergy is a scary thing for parents. The consulting allergist has to artfully walk the fine line between appropriate precautionary education and causing neurosis and unhealthy fear. This study makes the point that, in a specialty allergy clinic, the outcomes are much more favorable than the previous literature indicates. It includes a short review of the whole subject of nut allergies, avoidance, and treatment. In the specialist's population, the low incidence of reactions beyond the index reaction will surprise you. Pat yourself on the back, and give this article to parents.*
R. J. M.
Clark AT, Ewan PW: Good prognosis, clinical features, and circumstances of peanut and tree nut reactions in children treated by a specialist allergy center.
J Allergy Clin Immunol. 2008;122:286-289. ♦♦

Localized Allergy May Explain Seasonal Idiopathic Rhinitis

PATIENTS who have symptoms of rhinitis but negative results on skin prick testing and specific IgE measurement may be classified as having idiopathic rhinitis (IR). It has been suggested that these patients may have a type of localized allergy, without systemic atopy. Some patients have seasonal symptoms, occurring in spring only, that improve with topical corticosteroids and oral antihistamines. The authors looked at markers of nasal inflammation and allergen responses in a group of Spanish patients with seasonal IR.

The investigators compared 32 patients with seasonal IR and 35 patients with persistent allergic rhinitis and pollen allergy. Assessments included nasal inflammatory mediators, nasal specific IgE, and nasal allergen provocation test (NAPT) responses to grass and olive pollen (common seasonal allergens in Spain).

Responses to NAPT were positive in 62.5% of patients with seasonal IR. Twenty of the 32 patients had a positive nasal response to grass pollen, while 4 also responded to olive pollen. For the IR patients with positive results on NAPT, the nasal leukocyte-lymphocyte profile was similar to that of patients with persistent allergic rhinitis and pollen allergy, and different from that of controls. Thirty-five percent of NAPT-positive IR patients had specific IgE measured in nasal lavage specimens.

Patients with seasonal IR have a pattern of nasal inflammation similar to that of patients with allergic rhinitis caused by seasonal allergies. Some of these patients also have positive responses to nasal allergen provocation and nasal specific IgE. These patterns should be considered when evaluating patients who have seasonal or persistent rhinitis with negative allergy test results.

COMMENT: *Skin test-negative (and ImmunoCAP-negative) allergic rhinitis represents a small but important subset of rhinitis patients. This study used pollen allergen provocation to demonstrate objective responses in subjects with a suggestive history but negative test results. Distinguishing these patients from those with vasomotor rhinitis and nonallergic rhinitis with eosinophilia syndrome is important, as they may benefit from specific environmental control recommendations and targeted pharmacotherapy. It is unknown whether immunotherapy would be beneficial.*
S. A. T.
Rondón C, Doña I, López S, et al: Seasonal idiopathic rhinitis with local inflammatory response and specific IgE in absence of systemic response.
Allergy. 2008;63:1352-1358. ♦♦

For ASA Desensitization, More Is Better

ASPIRIN desensitization has become an important part of treatment for patients with aspirin-exacerbated respiratory disease (AERD). There is ongoing debate over the necessary dose of aspirin, with studies reporting on daily doses ranging from 100 to 1,300 mg. This clinical trial compared two doses of aspirin for patients undergoing desensitization therapy for AERD.

The study included 14 patients with aspirin-sensitive asthma and nasal polyps; all had a positive aspirin provocation test. After initial desensitization, patients received a maintenance aspirin dose of either 100 or 300 mg of aspirin per day. Assessments included nasal polyps, symptoms, and olfactory function.

Nasal polyps recurred in all patients taking the 100 mg dose of aspirin. None had reduced need for asthma medications or improvement in pulmonary function. In contrast, nasal polyps did not recur in any patient taking the 300 mg dose. Three of seven patients reduced their asthma medications, and five had improvements in pulmonary function.

Subsequently, 39 patients with AERD received the 300 mg dose of aspirin after desensitization. The 1-year results were good, with freedom from polyps and improved sense of smell. None of the patients required nasal revision surgery at a median follow-up of 27 months.

This small open trial supports the use of a 300 mg daily maintenance dose of aspirin for patients with AERD after initial desensitization. This treatment avoids recurrent polyps and sinus revision surgery while improving sense of smell. In contrast, patients receiving a 100 mg dose of aspirin have continued nasal and pulmonary symptoms and a high rate of recurrent nasal polyps.

COMMENT: *Aspirin-exacerbated respiratory disease is often successfully treated with aspirin (ASA) desensitization. Maintaining the ASA-tolerant state requires daily dosing of ASA, although choosing the appropriate dose has been controversial. In this study, subjects treated with 300 mg daily fared better than those taking 100 mg. As with using ASA for cardiac prophy-*➤➤

laxis, more appears to be better for AERD.
S. A. T.
Rozsasi A, Polzehl D, Deutschle T, et al: Long-term treatment with aspirin desensitization: a prospective clinical trial comparing 100 and 300 mg aspirin daily.
Allergy. 2008;63:1228-124. ♦♦

Are ACE Inhibitors Safe during VIT?

PREVIOUS case reports have described severe systemic reactions in patients with venom allergy who were taking angiotensin-converting enzyme (ACE) inhibitors. The reactions have occurred in response to stings or to venom immunotherapy (VIT). A single-center experience was reviewed to assess the relationship between systemic reactions and ACE inhibitor therapy in patients undergoing VIT.

The study included all patients evaluated for Hymenoptera venom allergy at the authors' clinic between 2000 and 2005. Of 157 patients with venom-specific IgE, 79 received VIT. Seventeen of these patients were taking an ACE inhibitor at the same time they were undergoing VIT. Clinical characteristics and outcomes were reviewed, including systemic reactions to field stings or VIT.

The mean duration of the overlap between ACE inhibitor therapy and VIT was 30.9 months. Mean age was 56.2 years for patients taking ACE inhibitors, compared to 36.4 years for those not taking ACE inhibitors; mean duration of VIT was 72.3 versus 29.9 months, respectively. None of the patients taking ACE inhibitors had a systemic reaction to VIT, compared to 21% of those not taking ACE inhibitors. Field stings occurred in 12 of the patients taking ACE inhibitors; none had a systemic reaction.

For patients with Hymenoptera allergy receiving VIT, treatment with ACE inhibitors does not appear to increase the risk of systemic reactions. Further study is needed to establish the safety of ACE inhibitor treatment during VIT.

COMMENT: *There is debate about the possibility that ACE inhibitor therapy may increase the risk of anaphylaxis. This paper offers reassurance that ACE inhibitors do not increase this risk with venom immunotherapy. However, the jury is still out.*
D. K. L.
White KM, England RW: Safety of angiotensin-converting enzyme inhibitors while receiving venom immunotherapy.
Ann Allergy Asthma Immunol. 2008;101:426-430. ♦♦

Reviews Looks at Intradermal Testing for Inhalant Allergy

THERE is a long history of debate over the clinical use and diagnostic accuracy of intradermal skin testing (IDST), particularly for patients with suspected inhalant allergy. Surveys suggest that allergists vary widely in their use of IDST for aeroallergens. The authors present of review of the literature on the role of IDST in testing for inhalant allergy.

The available data show wide variations in the definitions of positive aeroallergen IDST test results and the IDST concentrations used. Allergists who perform these tests use dilutions ranging from 100- to 1,000-fold of the concentrated extract used for skin prick testing (SPT). Studies support the safety of IDST, especially in patients with negative results on SPT. In this situation, a positive result on IDST has only a low level of agreement with the results of in vitro and challenge tests. These positive IDSTs provide little additional information that is diagnostically useful. However, a negative IDST result in the same clinical situation has high negative predictive value.

Studies comparing the results of IDST with challenge reactions have been done for only a few inhalant allergens. The results of IDST are of little help in evaluating suspected cat or timothy grass allergy, but may be of value in diagnosing hypersensitivity to *Alternaria*. When ISDT is done using lower potency or nonstandardized allergens, it may be more likely to identify patients with lower levels of clinical sensitivity; thus positive results may be more clinically useful. In routine clinical use, IDST has only moderate concordance with the results of radioallergosorbent test and challenge studies.

The authors provide an update on the use of IDST for aeroallergens. The available evidence suggests that a positive result on IDST is of little diagnostic value in patients with a negative SPT. Further studies of IDST are needed using challenge models additional, lower potency or nonstandardized aeroallergens: especially dog, trees, weeds, and molds.

COMMENT: *Intradermal testing is still utilized by many allergy specialists, but its use is often criticized by others. I agree that we need more studies with less potent or nonstandardized vaccines. Furthermore, the lack of positive predictability with IDST is based primarily on acute, high-dose challenge studies. However, chronic exposure, such as with dust mite or other indoor allergens, has not been evaluated. More data are needed before I am convinced that IDST to inhalant allergens has no value.*
D. K. L.
Calabria CW, Hagan L: The role of intradermal skin testing in inhalant allergy.
Ann Allergy Asthma Immunol. 2008;101:337-347. ♦♦

No Increase in Pneumonia with PPI Therapy

RECENT reports have suggested that patients taking proton-pump inhibitors (PPIs) may be at increased risk of community-acquired pneumonia (CAP). Considering the widespread use of these drugs and the morbidity and costs of CAP, this issue has important public health implications. The link between PPI therapy and CAP risk was investigated using British primary care data.

The U.K. General Practice Database was used to identify 80,066 adult patients with an incident diag-➤➤

nosis of CAP between 1987 and 2002. A total of 799,881 controls--matched for practice site, calendar year, and duration of follow-up--were identified as well. The two groups were compared for PPI use within 30 days before the index date.

On logistic regression analysis, current exposure to PPIs was unrelated to the overall risk of CAP, or of CAP requiring hospitalization. However, patients who recently started PPI therapy were at significantly increased risk of CAP. Adjusted odds ratios for CAP were 6.53 for patients starting PPI therapy within the previous 2 days, 3.79 within 7 days, and 3.21 within 14 days.

However, longer-term PPI use was not a risk factor for CAP. This was so even in a separate analysis in which cases and controls were matched for the three most important confounding factors (number of general practice visits, number of hospitalizations, and current opiate use).

Current treatment with PPIs does not appear to be a risk factor for CAP. However, risk of CAP may be increased within the first few days or weeks after starting PPI therapy. There is no obvious explanation for the latter finding; the observational study cannot show any causal relationship.

COMMENT: *We use acid-suppressive therapy, particularly PPIs, for persistent respiratory symptoms including cough, throat clearing, hoarseness, and asthma. The new data are reassuring, since a prior study investigating an older population showed an increased risk of pneumonia. Concerns remain that chronic PPI therapy may reduce absorption of iron and calcium and could contribute to anemia or osteoporosis.*
D. K. L.

Sarkar M, Hennessy S, Yang Y-X: Proton-pump inhibitor use and the risk for community-acquired pneumonia.
Ann Intern Med. 2008;149:391-398. ♦♦

Acetaminophen Linked to Childhood Asthma

IT has been suggested that acetaminophen (called paracetamol in Britain) might affect the risk of asthma. Previous studies have linked exposure to acetaminophen in utero, during childhood, and in adulthood to an increased rate of asthma. This question was addressed using data from Phase Three of the International Study of Asthma and Allergies in Childhood.

The analysis included data on 205,487 children, aged 6 to 7 years, drawn from 73 centers in 31 countries. Parents provided data on symptoms of asthma and other allergic diseases. The study questionnaire also assessed a wide range of potential risk factors, including use of acetaminophen for fever during the first year of life and the frequency of acetaminophen use during the past year.

The rate of asthma symptoms at age 6 to 7 years was significantly increased for children who received acetaminophen for fever during the first year of life: odds ratio 1.46. More recent exposure was also associated with increased asthma symptoms: odds ratios were 1.61 for children classified as medium users of acetaminophen and 3.23 for high users. The population risk of severe asthma symptoms attributable to acetaminophen use was estimated at 22% to 38%. Both in infancy and at age 6 to 7, acetaminophen use was also associated with increased symptoms of rhinoconjunctivitis and eczema.

Acetaminophen use may be a significant risk factor for asthma and other allergic diseases in children. The findings suggest a dose-response relationship between asthma and acetaminophen exposure, both in infancy and later in childhood, in a worldwide sample. Further research is needed to guide recommendations for the use of acetaminophen in infants and children.

COMMENT: *Finding that paracetamol (acetaminophen) conveys a higher risk of asthma and other atopic symptoms may have future implications for treatment of fever. The power of this study is that the risk factors extended over virtually all 30 countries and including a sample of more than 200,000 children.*
S. F. W.

Beasley R, Clayton T, Crane J, et al: Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6-7 years: analysis from Phase Three of the ISAAC programme.
Lancet. 2008; 372: 1039-1048. ♦♦

Affect Influences Asthma Control in Children

EMOTIONAL distress is common in patients with asthma, with studies reporting increased rates of depression in asthmatic patients of all ages. It has been suggested that depression and negative affect might be associated with reduced adherence with controller medications, and thus with poorer asthma control. The relationship between negative affect and disease control was evaluated in asthmatic children.

The study included 104 children and adolescents, aged 8 to 18 years, receiving inhaled corticosteroids (ICS) for asthma. The children and their parents completed independent assessments of the child's asthma symptoms, as well as questionnaires evaluating negative affect and sadness. Electronic monitoring devices were used to assess adherence with prescribed ICS use; health events were assessed from medical records.

The average adherence rate was 40%. Higher negative affect scores for the children and their parents were associated with more frequent reported asthma symptoms. Children with higher anxiety and depression scores missed more school days. Adherence with ICS was not related to child- or parent-reported symptoms, but was associated with prednisone burst therapy. The parents' negative affect was a predictor of prednisone bursts, even after controlling for adherence.

Negative affect has a significant impact on asthma control in children. These effects do not appear to be mediated by decreased adherence with ICS therapy. ➤➤

Affect may influence children's and parents' perceptions of asthma symptoms, the investigators suggest.

COMMENT: *This study considers the interplay between affect and adherence on asthma control in children. Although overall adherence was poor--with less than 40% of prescribed ICS actually used--adherence was not the sole determinant of control. Perception of asthma severity and depression were also important factors influencing control of asthma symptoms. The emotional state of both child and parent should be considered when evaluating asthma symptoms.*
S. M. F.
Bender B, Zhang L: Negative affect, medication adherence, and asthma control in children.
J Allergy Clin Immunol. 2008;122:490-495. ♦♦

Cesarean Delivery Increases Risk of Atopy, But Not Asthma

Rates of cesarean section have increased dramatically in the United States. Cesarean delivery has been linked to lasting alterations in the neonatal intestinal flora. In some studies, but not all, these changes have been associated with changes in atopy and/or allergy. A longitudinal study of the relationship between cesarean delivery and risk of childhood atopy and allergy is reported.

The study included 432 children with a parental history of asthma or allergies, drawn from the Epidemiology of Home Allergens and Asthma Study. The children were followed up from birth to age 9. The effects of mode of delivery on rates of physician-diagnosed asthma, wheezing, allergic rhinitis, and naso-ocular symptoms were assessed by logistic regression analysis. Atopy was evaluated by skin-prick testing or specific IgE measurement.

With adjustment for covariates, atopy was twice as common for children delivered by cesarean section: odds ratio 2.1, compared to those with vaginal delivery. There was also a significant association between cesarean delivery and allergic rhinitis, odds ratio 1.8. However, mode of delivery was unrelated to the risk of asthma or wheezing. Birth weight was the only other prenatal or perinatal factor significantly related to the risk of atopy or allergy.

Children delivered by cesarean section appear to be at increased risk of atopy and allergic rhinitis at age 9. However, there is no apparent relationship with asthma or wheezing. The observed associations with cesarean delivery might be related to the lack of contact with the mother's vaginal or fecal flora, or reduced or absent exposure to labor.

COMMENT: *Previous studies comparing the prevalence of atopy with mode of delivery have been inconclusive. These Boston researchers used prospective data from children born to allergic parents and found that cesarean section delivery is associated with twofold greater odds of allergic rhinitis compared to vaginal birth children. Interestingly, this was not found with asthma. The authors speculate that this predisposition may be explained by the lack of contact with maternal vaginal/fecal flora or reduced labor.*
S. M. F.
Pistiner M, Gold MR, Abdulkerim H, and others. Birth by cesarean section, allergic rhinitis, and allergic sensitization among children with a parental history of atopy.
J Allergy Clin Immunol. 2008;122:274-279. ♦♦

Age at Starting Daycare Affects Wheezing Risk

IN evaluating the hygiene hypothesis, contact with other children at home or in daycare is a useful indirect measure of exposure to infections. However, few studies using these variables have considered the whole spectrum of childhood wheezing phenotypes. This issue was addressed using data from a prospective, population-based cohort study.

The analysis included data from a British birth cohort study of childhood asthma and allergy. When the children were 5 years old, parents provided information on asthma and allergy symptoms. Most of the children underwent plethysmography to assess lung function and skin tests to assess allergic sensitization. Symptom outcomes were compared for children entering daycare at differing ages, and for children with differing numbers of older siblings.

Current wheezing was reported for 22% of the children, while 28% had evidence of allergic sensitization. On multivariate analysis, independent risk factors for wheezing included sensitization, odds ratio (OR) 2.47; male sex, OR 1.49; maternal asthma, OR 1.72; and maternal smoking during pregnancy, OR 2.15.

Children who entered daycare after 6 months of age were at reduced risk of current wheezing: ORs were 0.25 for children starting daycare between 6 and 12 months, and 0.65 for those starting daycare after 12 months. Children who started daycare between 6 and 12 months were also less likely to have persistent wheezing; daycare attendance had no effect on lung function. Starting daycare before age 6 months was linked to a higher risk of atopy, OR 2.47. Rhinoconjunctivitis was less likely for children with older siblings, OR 0.72. Other allergic disease outcomes were unrelated to sibship.

For children reaching school age, early exposure to other children in daycare is associated with a reduced risk of current wheezing. The risk of wheezing appears lowest for children starting daycare between age 6 to 12 months. Attending daycare and having older siblings may have different effects on different allergic disease phenotypes.

COMMENT: *The hygiene hypothesis is once again confirmed by this large, prospective, birth cohort study, which demonstrated that attending a nursery reduced the risk of persistent wheezing in children at 5 years. The protective effect was strongest when the children entered the nursery between 6 and 12 months of age.* ➤➤

These data suggest that the timing of exposure to day-care may be important.
S. M. F.
Nicolaou NC, Simpson A, Lowe LA, et al: Day-care attendance, position in sibship, and early childhood wheezing: a population-based birth cohort study.
J Allergy Clin Immunol. 2008;122:500-506. ♦♦

It's Not All about the Titer

IN addition to total and specific IgE levels, the IgE repertoire of patients with allergy includes the IgE affinity for allergen and IgE clonality. However, it is not currently possible to isolate individual IgE antibodies from patient sera. This hinders understanding of how the individual patient's IgE repertoire affects the occurrence and severity of allergic symptoms. This in vitro study examined the influence of IgE repertoire on effector cell degranulation.

Antibody shuffling techniques were used to develop a panel of recombinant IgE (rIgE) antibodies specific for house dust mite allergen Der p 2. Surface plasmon resonance mapping technology was then used to characterize these rIgE antibodies in terms of Der p 2 affinity and epitope specifcity. Human basophils were sensitized to rIgE antibodies in varying combinations. Basophil degranulation after challenge with Der p 2 was assessed using flow cytometry.

The experiments led to the production of 32 Der p 2-specific rIgEs, which bound nine different Der p 2 epitopes with affinities ranging from 0.0358 to 291 nM. When rIgE-sensitized basophils were exposed to Der p 2, several different factors were associated with an increased basophil degranulation response. In addition to high total IgE concentration and higher concentration of allergen-specific versus non-allergen-specific IgE, these factors included a more even concentration of allergen-specific IgE clones, increased IgE affinity for allergen, and increased IgE clonality (ie, a higher number of allergen epitopes recognized by the IgE repertoire).

Many different aspects of the IgE repertoire influence the effector cell degranulation response to allergen, the new findings suggest. More detailed knowledge of the composition of the IgE repertoire could aid in clinical assessment of allergic status in individual patients. In addition, information on the development of IgE clonality, individual IgE antibody affinity, and IgE concentrations might help in studying the factors contributing to the atopic march.

COMMENT: *Using a panel of well-characterized recombinant IgE antibodies, these researchers elucidated how individual components of the complex IgE repertoire affect in vitro degranulation. Changes in the concentration, specific activity, affinity and clonality of the IgE antibody all work together to trigger effector cell activation. Consequently, although sera from allergic patients might have similar allergen-specific IgE titers, there may still be a difference in their ability to elicit allergen degranulation. This has implications for diagnostic testing.*
S. M. F.
Christensen LH, Holm J, Lund G, et al: Several distinct properties of the IgE repertoire determine effector cell degranulation in response to allergen challenge.
J Allergy Clin Immunol. 2008;122:298-304. ♦♦

Asthma ED Visits Drop after Smoking Ban

EXposure to secondhand tobacco smoke is linked to increased rates and severity of asthma in children and adults. Many communities have enacted or are considering laws banning smoking in public places. Changes in asthma-related emergency department (ED) visits after implementation of smoke-free legislation were studied.

The analysis included data on ED visits for asthma at four hospitals in Lexington-Fayette County, Kentucky, before and implementation of smoke-free legislation. Age-adjusted rates of asthma-related visits were calculated, with adjustment for seasonality, secular trends over time, and demographic factors.

On adjusted analysis, the rate of ED visits for asthma decreased by 22% after the smoking ban. The decline in ED visits was 24% among adults (aged 20 years or older), compared to 18% in children and adolescents.

This study documents a significant drop in asthma-related ED visits after implementation of a smoke-free law in one Kentucky county. The improvement is greater in adults, but still significant in children. The study cannot demonstrate any causal effect.

COMMENT: *Numerous studies have demonstrated convincing evidence that public smoking bans improve health in a number of diseases, including asthma. This study from Kentucky reports an impressive 22% reduction in ED visits for asthma in the initial 32 months after the law was changed to ban smoking in public places. Smoke-free public health efforts can improve asthma outcomes.*
S. M. F.
Rayens MK, Burkhart PV, Zhang M, et al: Reduction in asthma-related emergency department visits after implementation of a smoke-free law.
J Allergy Clin Immunol. 2008;122:537-541. ♦♦

Cluster Analysis Identifies Differing Asthma Phenotypes

REFRACTORY asthma is a heterogeneous condition that varies in its clinical, physiology, pathologic, and molecular characteristics. Some unified approach is needed to incorporate these domains into a system for classification of clinical asthma phenotypes. A multivariate mathematical technique called k-means cluster analysis was used to develop a system of classifying patients with asthma into phenotypic groups.

The investigators applied the k-means cluster analysis technique to independent populations of asthma patients. Clusters were compared within a primary care population of 184 patients with predominantly mild ➤➤

to moderate asthma versus a secondary care population of 187 patients with refractory asthma. Differences in clinically relevant outcomes between clusters were then compared with a third population of 68 patients with predominantly refractory asthma. The third population of patients were clustered at baseline into a randomized trial of two treatment approaches: a strategy aimed at minimizing eosinophilic inflammation versus standard care.

In both the primary care and secondary care populations, k-means cluster analysis identified two patient clusters: an early-onset atopic cluster and an obese, noneosinophilic cluster. Among patients with refractory asthma, two distinct clusters of patients with discordance between symptoms and eosinophilic airway expression were identified: an early-onset symptom-predominant cluster and a late-onset inflammation-predominant cluster.

In the clinical trial, patients from both discordant clusters benefited from the inflammation-guided approach. For the inflammation-predominant cluster, this approach led to a significant reduction in the frequency of severe exacerbations: 0.38 per patient per year, compared with 3.53 per patient per year with standard care. For the symptom-predominant cluster, the inflammation-guided approach led to a significant reduction in inhaled corticosteroid dose: mean difference 1,829 µg beclomethasone equivalent per day.

The k-means cluster analysis technique may offer a useful new approach to evaluating the multiple dimensions contributing to differences in asthma phenotype. The identified subgroups differ in their clinical responses to differing treatment approaches. Further study is needed to evaluate long-term changes in cluster membership, as well as the implications for research into the molecular and genetic basis of asthma.

COMMENT: *This very interesting article allows for a thoughtful approach to determine which patients can be managed primarily by a symptom-based approach and which patients need measurement of surrogate markers of eosinophilic inflammation to guide monitoring their steroid dose in a down-titration fashion or to help prevent inflammation. I also recommend the accompanying editorial by Saglani and Bush (Am J Respir Crit Care Med. 2008;178:437-440).*
B. E. C.

Haldar P, Pavord ID, Shaw DE, et al: Cluster analysis and clinical asthma phenotypes.
Am J Respir Crit Care Med. 2008;178:218-224. ♦♦

With or Without Atopy, Wheezing Children Have Same Pathology

CHILDREN with atopic asthma are likely to have persistent wheezing into adulthood. In contrast, for nonatopic children, wheezing most often resolves by adolescence. These differences, described in epidemiologic studies, suggest a difference in the pathologic characteristics of the two groups. This study compared the airway pathologic findings of atopic versus nonatopic children with wheezing.

The investigators analyzed clinical bronchial biopsy specimens from three groups of children and adolescents: 18 nonatopic children with multitrigger wheezing, 20 atopic children with multitrigger wheezing, and 17 controls with neither atopy nor wheezing. Median ages were 4 to 5 years. A wide range of airway pathologic features were compared among groups, including epithelial loss, basement membrane thickness, angiogenesis, inflammatory cell counts, and subepithelial cytokine-positive cells.

Surprisingly, there was little or no difference in the airway pathologic features of wheezing children with versus without atopy. Biopsy specimens from both groups showed increased epithelial loss, basement membrane thickening, increased blood vessel numbers, and eosinophilia, compared to control specimens. Wheezing children also had increased expression of cytokines, with a highly significant difference in interleukin (IL)-4-positive cells and a marginal difference in IL-5-positive cells. There were also few differences on comparison of children with mild versus moderate asthma and of younger versus older children.

The airway pathology of wheezing in atopic children is essentially the same as that in nonatopic children. The findings suggest that all children with bronchodilator-responsive wheezing have pathologic features of asthma, whether or not they are atopic. Further study is needed to define the evolution of symptoms in nonatopic children with asthmatic airway pathology.

COMMENT: *This landmark study helps us to continue to understand the observations reported by Saglani et al, as reviewed in previous issues of* AllergyWatch. *(See Am J Respir Crit Care Med. 2005;171:722-727 and 2007;176:858-864.) This evolving knowledge helps us better understand that a similar physiologic process is present, which may have pertinent indications for treatment.*
B. E. C.

Turato G, Barbato A, Baraldo S, et al: Nonatopic children with multitrigger wheezing have airway pathology comparable to atopic asthma.
Am J Respir Crit Care Med. 2008;178:476-482. ♦♦

More Clarity on Reactions to Cephalosporins

HYPERSENSITIVITY reactions to cephalosporin antibiotics may be classified as immediate or nonimmediate. Nonimmediate reactions generally consist of minor rashes, but may lead to anxiety and changes in antibiotic prescribing. The investigators assessed the value of various tests for diagnosing sensitivity reactions to cephalosporins, including comparison of immediate and nonimmediate reactions.

The investigators analyzed the findings of 148 children with hypersensitivity reactions to cephalosporins. The children were seen at two Italian centers between 1999 and 2007; most reacted to cefaclor or ceftriaxone. Those with immediate reactions (within 1 hour) underwent immediate-reading skin tests with penicillin reagents and the implicated cephalosporins, along ➤➤

with specific IgE measurements and challenge tests. For children with nonimmediate reactions (after 1 hour), evaluation consisted of patch tests, delayed-reading skin tests, and challenges.

One hundred five children had nonimmediate reactions, mainly urticaria and maculopapular reactions. Forty-three had immediate reactions, ranging from erythema to anaphylaxis. None of the children with nonimmediate reactions had positive results on patch tests or delayed skin tests; only 1 had an immediate positive reaction to skin testing with penicillin reagent. Challenge testing was performed in 96 children with nonimmediate reactions. Just 1 patient reacted to cefaclor suspension, but was able to tolerate cefaclor capsule.

In contrast, 33 of 43 children with immediate reactions had positive results on immediate-read skin tests. The remaining 10 patients were able to tolerate subsequent cephalosporin challenges and/or therapeutic courses. On re-evaluation, 1 child was skin test-positive for both the implicated cephalosporin and for penicillin reagents. The results suggested IgE-mediated hypersensitivity in 79% of the children with immediate reactions.

Very few children with nonimmediate reactions to cephalosporins have true IgE-mediated hypersensitivity reactions. In contrast, about 80% of those with immediate reactions to cephalosporins do have IgE-mediated reactions. The authors' experience highlights the value of cephalosporin skin testing in diagnostic evaluation.

COMMENT: *One area where we desperately need ongoing studies and data is drug allergy. While data are good for penicillin testing (when this was commercially available), similar standardization and data are lacking for non-penicillin antibiotics. This study of European children sheds light on the high likelihood that immediate (within 1 hour) cephalosporin responses are IgE-mediated. In contrast, nonimmediate reactions are unlikely to be IgE-mediated, with a very low rate of reproducing symptoms on challenge.*
K. R. M.

Romano A, Gaeta F, Valluzzi RL, et al: Diagnosing hypersensitivity reactions to cephalosporins in children.
Pediatrics. 2008;122:521-527. ♦♦

CLINICAL TIDBITS

Hearing Loss Common in Antibody Deficiencies

ACUTE otitis media (AOM) is one of several infectious problems commonly seen in patients with primary antibody deficiency disorders. Recurrent AOM can lead to hearing loss. This study looked for evidence of hearing loss in patients with primary antibody deficiencies. The study included 25 patients with X-linked agammaglobulinemia (XLA) and 22 with common variable immunodeficiency (CVID). Median age at symptom onset was 12 months in the XLA group and 33 months in the CVID group; current age was 15 and 25 years, respectively. Audiologic testing revealed sensorineural hearing loss in 38% of patients: 28% with XLA and 50% with CVID. The hearing loss was bilateral in 12 of 18 cases.

Children with primary antibody deficiency disorders are at high risk of hearing loss. These patients should undergo complete audiologic evaluation at diagnosis and follow-up. More data is needed on the contribution of AOM to hearing loss in these patients.

COMMENT: *Among the considerations in patients with humoral immunodeficiencies, one that might be overlooked is hearing impairment. As these patients are prone to develop recurrent otitis media, it is logical that this complication might occur. An additional consideration might include an as-yet undefined genetic predisposition for hearing loss in this population.*
K. R. M.

Berlucchi J, Soresina A, Redaelli De Zenis LO, et al: Sensorineural hearing loss in primary antibody deficiency disorders.
Pediatrics. 2008;153:293-296. ♦♦

New Hypoallergenic Amino Acid Infant Formula

EXTENSIVELY hydrolyzed formula (EHF) is recommended for use in infants who are allergic to or intolerant of cow's milk formula. When feeding with EHF is unsuccessful, amino acid-based formulas (AAF) may be used. The authors evaluated a new AAF developed to provide a mix of essential and nonessential amino acids, as well as docosahexanoic acid and arachidonic acid, similar to that of breast milk.

In an initial study, 165 healthy formula-fed infants were randomly assigned to receive the new AAF or a casein EHF. At up to 120 days, there was no difference in growth between the two groups of infants. Both formulas were safe and well tolerated.

In a second study, 32 infants with documented cow's milk allergy received the new AAF to confirm hypoallergenicity. A double-blind, placebo-controlled food challenge, open challenge, and 7-day feeding period were completed in 29 infants. There were no allergic reactions to any of the three challenges.

The results support the safety and hypoallergenicity of the new AAF. The new formula provides a useful alternative for infants and children with cow's milk allergy and other food allergies.

COMMENT: *While breast-feeding is preferable for infant feeding, having additional choices for multiply food-allergic infants is important. Those who require use of amino acid-based formulas now have an additional, safe option, which also supplements arachidonic and docosahexaenoic acids to levels commonly found in human breast milk.*
K. R. M.

Burks W, Jones SM, Berseth CL, et al: Hypoallergenicity and effects on growth and tolerance of a new amino acid-based formula with docosahexaenoic acid and arachidonic acid.
Pediatrics. 2008;153:266-271. ♦♦

Controversial Approach to Stem Cell Transplantation for Immunodeficiency

THE only known cure for chronic granulomatous disease is allogeneic hematopoietic stem cell transplantation from an HLA-matched donor. The authors report on a child who had severe X-linked chronic granulomatous disease with no HLA-identical sibling. After careful consideration of the ethical and psychologic issues, the parents opted to undergo in vitro fertilization in the hope of giving birth to a suitable HLA-identical donor.

In vitro fertilization was performed with the use of X-enriched spermatozoa, with preimplantation genetic diagnosis to select female, HLA-identical embryos. After two cycles, two such embryos were identified and transferred into the uterus. The result was a successful singleton pregnancy, with birth of a healthy baby girl. There were inadequate cell numbers in cord blood, so conventional stem cell transplantation was performed when the girl was 1 year old and her affected brother was nearly 6. Transplantation resulted in stable donor chimerism and immunologic reconstitution in the brother.

In vitro fertilization with preimplantation genetic diagnosis and female sex selection offers a potential source of HLA-identical stem cells for children with chronic granulomatous disease. This procedure raises challenging questions related to cost, medicolegal issues, and ethical and psychologic concerns.

COMMENT: *This is the first reported case of X-linked chronic granulomatous disease treated by in vitro fertilization. Female gender typing and HLA-matching led to the birth of a healthy, unaffected sister who later became the patient's stem cell donor. In Switzerland where this occurred, preimplantation genetic diagnosis is banned, except for HLA typing. Technologic advances may make this therapeutic consideration possible for (wealthy) parents of affected children who are otherwise unable to find a suitable stem cell donor. Such an approach has been used to treat other genetic disorders, including Wiskott-Aldrich syndrome and Fanconi's anemia. Careful consideration should be given to the myriad psychologic and ethical issues arising from such a complex decision. Further consensus/guidelines are needed from the world scientific community.*
K. R. M.

Reichenbach J, Van de Velde H, De Rycke M, et al: First successful bone marrow transplantation for X-linked chronic granulomatous disease by using preimplantaion female gender typing and HLA matching.
Pediatrics. 2008;122:e778-782. ♦♦

Omalizumab for Chronic Autoimmune Urticaria

THERE is evidence of autoimmunity in about 45% of patients with chronic urticaria. A trial of anti-IgE therapy with omalizumab in this subgroup of patients with chronic autoimmune urticaria (CAU) is reported.

The experience included 12 patients with CAU, confirmed by a basophil histamine release assay and autologous skin test. All patients had continued symptoms despite 6 weeks of treatment with antihistamines. After 4 weeks of placebo treatment, all patients received treatment with omalizumab, with dosage based on the patient's body weight and IgE level. Treatment was given every 2 to 4 weeks for 16 weeks.

The mean Urticaria Activity Score (on a 0-to-9 scale) decreased from 7.50 at baseline to 2.66 during the last 4 weeks on omalizumab. Urticaria symptoms resolved completely in 7 of 12 patients. Four patients had continued urticaria with some improvement; only one patient had no response. Benefits were also noted in terms of rescue medication and quality of life. There were no adverse effects.

Omalizumab is a promising treatment for CAU that does not respond to antihistamines. Further studies are needed, including patients with other forms of chronic urticaria.

COMMENT: *Chronic urticaria is difficult to treat. This study using omalizumab in 12 subjects suggests a favorable response. However, the study did not have a control group, and chronic urticaria is usually a self-limited disorder. We can be optimistic about this treatment, but must await a placebo-controlled trial before using such an expensive drug off-label.*
R. J. M.

Kaplan AP, Joseph K, Maykut RJ, et al: Treatment of chronic autoimmune urticaria with omalizumab.
J Allergy Clin Immunol. 2008;122:569-573. ♦♦

REVIEWS OF NOTE

COMMENT: *This article approaches potential vaccine allergic reactions from a pediatrician's standpoint, and at the same time is a terrific review of available data for those of us asked to evaluate children for such allergic reactions. Highly recommended reading.*
K. R. M.

Wood RA, Berger M, Dreskin SC, et al: An algorithm for treatment of patients with hypersensitivity reactions after vaccines.
Pediatrics. 2008;122:e771-e777. ♦♦

COMMENT: *This review of inflammation in asthma takes an interesting perspective regarding the yin and yang of self-limited vs persistent disease.*
S. A. T.

Van Hove CL, Maes R, Joos GF, Tournoy KG: Chronic inflammation in asthma: a contest of persistence vs resolution.
Allergy. 2008;63:1095-1109. ♦♦

COMMENT: *Medications used to manage chronic obstructive pulmonary disease (COPD) have potential safety concerns. In this case-control study in patients with recently diagnosed COPD, ipratropium was associated with increased cardiovascular deaths, whereas inhaled corticosteroids were associated with reduced risk for cardiovascular death. The authors state that the possible association between ipratropium and elevated risk for all-cause and cardiovascular death needs further study.* ➤➤

M. F.
Lee TA, Pickard S, Au DH, et al: Risk for death associated with medications for recently diagnosed chronic obstructive pulmonary disease.
Ann Intern Med. 2008 149:380-390. ♦♦

COMMENT: *This excellent paper reviews previous studies on omalizumab therapy in allergic rhinitis, either as monotherapy or in combination with immunotherapy. The authors discuss a proof-of-concept trial with omalizumab in nasal polyposis, which in case of a positive therapeutic response would pave the way for anti-IgE treatment approaches for severe nonatopic lower airway disease. The review notes that nasal polyp scores were significantly improved in the group treated with omalizumab, with a reported a correlation between nasal polyp severity and total serum IgE. The authors caution that the high costs of treatment with omalizumab, the high frequency of allergic rhinitis and nasal polyps, and the current lack of data concerning the safety of long-term use of omalizumab should be considered.*
M. F.
Verbruggen K, Van Cauwenberge P, Bachert C: Anti-IgE for the treatment of allergic rhinitis - and eventually nasal polyps?
Int Arch Allergy Immunol. 2009;148:87-98. ♦♦

COMMENT: *Daily we use corticosteroids in the appropriate management of allergic disease. We cannot promote this therapy without being knowledgeable of the potential risks and of the strategies to minimize these risks. Osteoporosis is a life-altering side-effect that may result from inhaled corticosteroid therapy over the long-term and will occur if oral corticosteroid therapy is used. We can debate the magnitude of this risk, but we should be aware of the most effective means of diagnosing and treating osteoporosis in the patients entrusted to our care.*
D. K. L.
Qaseem A, Snow V, Shekelle P, et al: Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians.
Ann Intern Med. 2008;149:404-415. ♦♦

COMMENT: *I am convinced the overlap of obesity, chronic respiratory symptoms including asthma, fatigue and sleep apnea is a clinical presentation that we are seeing in clinic more often than we recognize. This group of investigators is in the vanguard in the assessment of sleep-disordered breathing in asthma, including pediatric asthma. Stay tuned for more information.*
D. K. L.
Alkhalil M, Schulman ES, Getsy J: Obstructive sleep apnea syndrome and asthma: the role of continuous positive airway pressure treatment.
Ann Allergy Asthma Immunol. 2008;101:350-357. ♦♦

COMMENT: *This is a concise review delineating the diagnosis, immunology and treatment of common variable immunodeficiency. Although written for primary care, it is complete and annotated for allergists.*
S. F. W.
Park MA, Li JT, Hagan JB, et al: Common variable immunodeficiency: a new look at an old disease.
Lancet. 2008;372:489-502. ♦♦

COMMENT: *We are close to having realistic treatments for acute attacks of hereditary angioedema. As usual, new answers bring more questions. How will bradykinin inhibitors compare with C1 inhibitor replacement, and will the recombinant molecule be as effective as the plasma-derived one? Who should get long-term prophylaxis versus acute treatment for attacks? This article reviews the subject nicely.*
R. J. M.
Zuraw BL: Hereditary angioedema.
N Engl J Med. 2008;359:1027-1036. ♦♦

COMMENT: *Allergists should understand climate change and be advocates for the mediation of greenhouse gas effects and other interventions that can potentially curb the crisis of global warming, which is causing increases in allergic respiratory disease.*
S. M. F.
Shea KM, Truckner RT, Weber RW, Peden DB: Climate change and allergic disease.
J Allergy Clin Immunol. 2008;122:443-453. ♦♦

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