AllergyWatch®

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

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Skin Tests at Age 2 Predict Wheezing at Age 12

IF early childhood factors associated with increased asthma risk could be identified, it might be possible to implement risk-reducing interventions. This study evaluated the relationship between skin prick test (SPT) results in toddlers with the risk of wheezing at age 12.

The birth cohort study included 620 children, with oversampling for family history of allergy. At age 6, 12, and 14 months, the children underwent SPTs for cow's milk, egg white, peanut, house dust mite (HDM), rye grass, and cat dander. Wheezing was assessed at frequent intervals up to age 2, and then at follow-up when the children were 12 years old. Associations between SPT results in infancy and early childhood and current wheezing at age 12 were assessed on multiple logistic regression analysis.

Early sensitization to HDM was an independent predictor of wheezing at age 12: the adjusted odds ratio was 3.31 for positive SPT at 1 year and 6.37 at 2 years. Of children with wheezing at age 1, the probability of wheezing at age 12 was 75% for those with early dust mite sensitization vs 36% for those without this sensitization.

Among 1-year-olds with eczema, the probability of wheezing at age 12 was 67% for those with early HDM sensitization versus 35% for those without. For children with both wheezing and eczema at age 1, the rate was 64% and 50%, respectively. Because of the small number of positive SPT results, no conclusions could be drawn regarding associations for other allergens.

Children who are sensitized to HDM at or before age 2 are more likely to have wheezing at age 12. The association is significant for both monosensitized and polysensitized children. Particularly in young children with early wheezing or eczema, SPT for HDM at age 1 or 2 might be a useful assessment for later risk of childhood asthma.

COMMENT: *Parents frequently ask if their child is at risk of developing asthma. Can we predict if that child will develop asthma? These Australian*➤➤

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The American College of Allergy, Asthma & Immunology expresses its appreciation to MERCK for its 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

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researchers reported data from the Melbourne Atopy Cohort, a birth cohort comprising 620 babies. They found that children monosensitized to HDM at 1 and 2 years old had at least a two times greater likelihood of wheezing illness at 12 years of age. This suggests that HDM sensitization is a harbinger of the development of asthma, irrespective of other potential allergenic sensitizations. Somewhat surprisingly, food allergens or multiple allergen sensitizations did not predict future wheezing illness.
S.M.F.
Lodge CJ, Lowe AJ, Gurrin LC, et al: House dust mite sensitization in toddlers predicts current wheeze at age 12 years.
J Allergy Clin Immunol. 2011;128:782-788. ♦♦

Higher Specific IgE May Predict More Severe Reactions to Peanut

ACCURATE predictors of the severity of reactions to food allergens are needed. There is evidence that, in patients with a history of severe reactions, a lower allergen dose is needed to elicit a positive response on double-blind placebo-controlled food challenge (DBPCFC). The eliciting dose of peanut DBPCFC was used as a measure of clinical sensitivity in evaluating risk factors for severe allergic reactions to peanut.

The researchers analyzed data on children at one Dutch medical center who had clinical reactions to peanut DBPCFCs between 2001 and 2009. Potential risk factors such as age, degree of sensitization, and concomitant atopic disease were evaluated for their relationship to the eliciting dose. The study included a total of 126 positive peanut DBPCFCs.

Three factors were independently associated with lower eliciting doses of peanut: age over 10 years, hazard ratio (HR) 1.89; peanut-specific IgE of 5.6 kU/L or greater (the lowest tertile), HR 2.03; and absence of atopic dermatitis, HR 0.45. Eliciting dose was unrelated to sex, presence of asthma or rhinitis, or the severity of past food reactions.

Lower eliciting doses on peanut DBPCFC are associated with older age, higher specific IgE level, and absence of atopic dermatitis. The effect of age may help to explain why adolescents have more severe reactions to peanut in daily life, compared to younger children. The results suggest that food-specific IgE levels may be positively correlated with the severity of reactions to foods.

COMMENT: *These Dutch researchers used peanut DBPCFCs in children with documented peanut allergy to determine predictive risk factors for severe allergic reactions. Not surprisingly, the degree of allergic sensitization--including higher specific IgE levels--predicted the eliciting dose of peanut during challenges. In fact, for each 1 kU/L increase in peanut-specific IgE, the risk of reacting to a specific eliciting dose increased by 1%. Predicting the severity of clinical reactions to foods following accidental ingestions is an important goal of food allergy research.*
S.M.F.
van der Zee T, Dubois A, Kerkhof M, et al: The eliciting dose of peanut in double-blind, placebo-controlled (DBPC) food challenges decreases with increasing age and specific IgE level in children and young adults.
J Allergy Clin Immunol. 2011;128:1031-1036. ♦♦

New Data on HRV and Asthma Exacerbations in Adults

THE link between upper respiratory viral illnesses and asthma exacerbations is better established in children than adults. It is unclear whether the viral replication and neutrophilic inflammation associated with human rhinovirus (HRV)-induced asthma exacerbations are the same as or different from that associated with HRV colds. Viral strain and load were

evaluated during naturally occurring colds in adult asthma patients.

The prospective study included 52 adults with asthma (and 14 controls), enrolled at the first sign of a cold. All underwent daily monitoring of symptoms, medication use, and peak expiratory flow until the cold resolved. Nasal lavage and induced sputum sampling were performed to measure viral copy number and inflammatory cell counts.

Of the 52 asthma patients, 25 experienced an exacerbation. The most frequent exacerbation-related exposure was the detection of HRV within the preceding 5 days. Infections with minor group A HRV were associated with a particularly sharp increase in exacerbation risk: 4.4 times higher than other types of infections.

In general, sputum neutrophil count and lower airway HRV burden were similar for asthmatic participants versus nonasthmatic, nonatopic controls. However, among asthma patients with HRV infection, sputum neutrophil counts were significantly increased for those with exacerbations. They were also more likely to have greater amounts of HRV detected in the sputum compared to nasal samples.

Human rhinovirus appears more important than other respiratory viruses as a cause of seasonal asthma exacerbations in adults. Minor group A HRV appears to be most strongly associated with exacerbations. Among asthma patients with HRV infection, sputum neutrophil counts appear higher in those with exacerbations versus routine colds, without major differences in HRV burden.

COMMENT: *Important differences are seen regarding the immunopathologic expression of asthma exacerbations in children and adults, especially with a persistent neutrophilic inflammatory pattern seen in adults. This continues to raise questions regarding differences in etiology and potential implications for therapy.*
B.E.C.

Denlinger LC, Sorkness RL, Lee W-M, et al: Lower airway rhinovirus burden and the seasonal risk of asthma exacerbation.
Am J Respir Crit Care Med. 2011;184:1007-1014. ♦♦

Asthma Questionnaires May Miss Uncontrolled Asthma in Children

THE Global Initiative for Asthma (GINA) and other recent guidelines recommend "step-up" therapy when needed to maintain good asthma control. It is unclear how GINA and other guidelines perform in detecting uncontrolled asthma. This study compared the GINA guidelines with the Childhood Asthma Control Test (C-ACT) and the Asthma Control Test (ACT) for detection of uncontrolled asthma in children.

Over a 4-week period, 145 children with asthma--84 aged 4 to 11 years and 61 aged 12 to 18 years--completed a web-based diary card on asthma symptoms, medication use, and activity limitations. Control status in a given week was assessed using GINA criteria. The children then completed either the C-ACT or ACT evaluating the previous 4 weeks. For both assessments, the cutoff score for uncontrolled asthma was 19 points.

Based on GINA criteria, 51% of the children had uncontrolled asthma while only 14% had complete asthma control. Median scores were 23 for C-ACT and 21 for ACT. For identification of patients with GINA-defined uncontrolled asthma, area under the receive operating characteristic curve was 0.89 for C-ACT and 0.92 for ACT. At the 19-point cutoff score, sensitivity in predicting uncontrolled asthma was 33% for C-ACT and 66% for ACT. Weeks with uncontrolled or partially controlled asthma were particularly associated with daytime symptoms and activity limitations.

The C-ACT and ACT show good agreement, compared to GINA criteria. However, based on GINA, about half of a large sample of children show uncontrolled asthma for at least 1 out of 4 weeks. Although specificity is high, C-ACT and ACT have low sensitivity in detecting uncontrolled asthma. At generally used cutoff points, C-ACT and ACT may underestimate the number of children with uncontrolled asthma.

COMMENT: *These authors attempt to validate commonly used asthma control instruments with the GINA guidelines. The lack of complete agreement is implicit based upon the significant variability of asthma. The lack of a question in either instrument related to the risk domain may be a contributing factor.*
B.E.C.

Koolen BB, Pijnenburg MWH, Brackel HJL, et al: Comparing Global Initiative for Asthma (GINA) criteria with the Childhood Asthma Control Test (C-ACT) and Asthma Control Test.
Eur Respir J. 2011;38:561-566. ♦♦

LABA Adverse Effects More Pronounced in Children

THERE are continued concerns regarding the safety of long-acting β-adrenergic receptor agonists (LABAs), with two randomized trials reporting increased rates of asthma-related deaths. Subsequent meta-analyses suggested that children were at highest risk of severe asthma outcomes related to LABAs. The U.S. Food and Drug Administration performed a meta-analysis to assess the long-term risk of LABAs in different age groups.

A literature search was performed to identify controlled clinical trials comparing risks with LABA use vs no LABA use. The review identified 100 studies including a total of 60,954 patients. The patients were placed in age groups: from 4 to 11 years, 12 to 17 years, 18 to 64 years, and older than 64 years.

On meta-analysis, the main outcome of interest was an asthma composite index consisting of asthma-related deaths, intubations, and hospitalizations. The effects of combined use of LABAs and inhaled corticosteroids (ICS) were analyzed as well.

The incidence of the asthma composite index was increased by 6.3 events per 1,000 patient years for all LABA users, compared to nonusers. The difference ➤➤

was greatest for children aged 4 to 11 years: 30.4 events per 1,000 person-years. The difference among age groups was significant, with younger age groups showing greater increases in LABA-related risk.

Subgroup analysis of patients with concomitant ICS and LABA use showed a similar pattern of results. However, analysis of patients who were assigned to ICS use as part of the study design found no significant difference by age.

This large meta-analysis suggests that children have the greatest excess risk of serious asthma-related events associated with LABA use. Further study of the use of LABAs in children is needed, including the effects of simultaneous treatment with ICS. The lack of a significant difference with "assigned" ICS treatment raises the possibility that risk might be decreased by giving ICS and LABA in a single inhaler.

COMMENT: *For LABA/ICS, this meta-analysis differentiates risk based on "concomitant" ICS use vs. "assigned" ICS use. Here, concomitant use is any use (frequency not specified) and assigned use is presumed to be regular use. Interestingly, these two LABA/ICS groups yielded differential risks of adverse events, with the "assigned" group having no increased risk with LABA. But, as the authors indicate, the "assigned" ICS user group was a smaller subset and was not a primary focus of the study. Data on the safety of LABA/ICS combination therapies still lag. To be continued!*
K.R.M.
McMahon AW, Levenson MS, McEvory BW, et al: Age and risks of FDA-approved long-acting β_2-adrenergic receptor agonists.
Pediatrics. 2011;128:e1147-e1154. ♦♦

Asthma and Glycemic Control in Children with Diabetes

ASTHMA, obesity, and diabetes are all rising in prevalence among young people. The link between poor glycemic control and complications of diabetes is well recognized. This study evaluated the possible impact of asthma on glycemic control in diabetic youth.

The researchers analyzed data on 1,683 young people with type 1 diabetes and 311 with type 2 diabetes, drawn from a population-based study of diabetic youth. The patients ranged in age from 3 to 21 years. Based on medical records and questionnaires, the prevalence of diabetes was 10.9% overall: 10.0% for youth with type 1 diabetes and 16.1% for those with type 2 diabetes.

Diabetic youth with asthma were more likely to be older, of racial/ethnic minorities, obese, and from single-family households. Among youth with type 1 diabetes, those with asthma had higher mean hemoglobin A1c levels: 7.77% versus 7.49% on adjusted analysis. Asthma was associated with an increased likelihood of poor glycemic control--especially among type 1 diabetics who were not receiving asthma medications. This association was weakened after adjustment for race/ethnicity.

This study suggests that diabetic youth may have an increased prevalence of asthma. In young people with type 1 diabetes, asthma appears to be linked to poor glycemic control, particularly if the asthma is untreated. Asthma medications, with their anti-inflammatory effect, may help to prevent the decline in lung function associated with poor glycemic control.

COMMENT: *This cross-sectional data analysis raises a number of questions. Is obesity the common, inflammatory, link between diabetes and asthma? Or could poor compliance with all treatments explain the observed association between poor asthma control and poor glycemic control? The finding of good glycemic control and regular use of asthma medications--including inhaled corticosteroids--seems somewhat counterintuitive.*
K.R.M.
Black MH, Anderson A, Bell RA, et al: Prevalence of asthma and its association with glycemic control among youth with diabetes.
Pediatrics. 2011;128:e839-ee847. ♦♦

One-Fourth of Asthma Exacerbations Caused by Medication Nonadherence

MANY studies have shown poor adherence with inhaled corticosteroid (ICS) therapy among patients with asthma. Changes in adherence to prescribed controller medications could be one explanation for symptomatic worsening of asthma. This study explored the association between changes in medication adherence over time and risk of asthma exacerbations.

The researchers used electronic prescription data on 298 patients, mainly African American, enrolled in a study of racial/ethnic differences in asthma phenotypes. The data were used to create a "moving average" of medication adherence for each patient and each day of follow-up. The association between this measure of adherence and asthma exacerbations--defined as oral corticosteroid treatment or asthma-related emergency department visit or hospitalization--was assessed.

During an average follow-up of 2 years, 46% of patients had at least one asthma exacerbation. Adherence to prescribed ICS therapy began to rise before the first exacerbation, and continued to increase thereafter. Although adherence was linked to fewer exacerbations, this was significant only for patients with adherence of greater than 75% of the prescribed dose: hazard ratio 0.61, compared to adherence of 25% or less. This pattern was observed mainly in patients without good baseline asthma control. Overall, nonadherence with ICS treatment accounted for an estimated 24% of asthma exacerbations.

The results suggest variations in ICS adherence occurring before and after asthma exacerbations, which likely contribute to some of these events. The data suggest that nearly one-fourth of exacerbations may be attributable to medication nonadherence. Very high adherence levels may be necessary to lower exacerbation rates.

COMMENTS: *Despite drastic improvements in asthma medication treatment options in the past 20 years--*

including the availability of highly potent and convenient ICS options--many of our patients simply do not take their medication as prescribed. Some literature supports the "on-demand" use of such medications. This study took on the challenge of quantifying nonadherence and correlating it with asthma outcomes. The results showed a strong association between asthma exacerbation and nonadherence with currently available ICS.
S.A.T.
Williams LK, Peterson EL, Wells K, et al: Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence.
J Allergy Clin Immunol. 2011;128:1185-1191. ♦♦

Roasting Peanuts Increases Degranulation Capacity of Ara h 1

ROASTING peanuts may affect their allergenicity via alterations in allergen structure leading to the Maillard reaction, in which free amino acids on proteins react with reducing sugars. To investigate these changes, the researchers developed a model of thermal treatment that mimicked the effects of roasting on peanuts.

The purified peanut allergens Ara h 1 and Ara h 2/6 were heated in the presence or absence of glucose, after which soluble proteins were extracted. To assess changes in allergenicity, IgE binding and degranulation capacities were studied using sera from patients with well-characterized peanut allergy.

Both Ara h 1 and Ara h 2/6 hydrolyzed in response to extensive heating at low moisture. Unlike Ara h 2/6, soluble Ara 1 from roasting in the presence of glucose formed large aggregates. The IgE-binding capacity of Ara h 1 was reduced 9,000-fold with heating in the presence of glucose versus 3.6-fold in the absence of glucose. Meanwhile, the capacity to elicit mediator release increased under both conditions. For Ara h 2/6 heated in the absence of glucose, both IgE-binding capacity and degranulation capacity decreased by 600- to 700-fold. These changes were significantly reduced in the presence of glucose.

Heating has opposite effects on the degranulation capacity of the peanut allergens Ara h 2/6 versus Ara h 1. The authors discuss the implications for component-resolved diagnostic approaches. The findings highlight the need to consider degranulation capacity as well as IgE binding when evaluating the effects of food processing on allergenicity.

COMMENT: *One theory proposed to explain the astounding increase in peanut allergy in the United States and Europe involves the presumed increase in peanut protein allergenicity due to roasting. In an attempt to lay the foundation for more accurate diagnostic testing for peanut allergy, these authors first subjected purified peanut proteins to a process that mimics roasting, and then evaluated both IgE binding and basophil release (degranulation capacity). Their "processed extract" remained allergenic but had different properties than native peanut proteins. Approaches like this may pave the way for a new generation of diagnostic testing reagents with improved specificity for peanut allergy.*
S.A.T.
Vissers YM, Adel-Patient K, Stahl Skov P, et al: Effect of roasting on the allergenicity of major peanut allergens Ara h 1 and Ara h 2/6: the necessity of degranulation assays.
Clin Exp Allergy. 2011;41:1631-1642. ♦♦

Beclomethasone HFA vs CFC for Long-Term Asthma Control

BECLOMETHASONE dipropionate is now available in an extrafine particular formulation with hydrofluoroalkane propellant (EF HFA-BDP). This product offers better total and small airway deposition, compared to large-particle beclomethasone with chlorofluorocarbon propellant (BDP-CFC). Based on short-term studies showing greater effects on pulmonary function, it has been suggested that EF HFA-BDP be prescribed at a lower dose.

The 1-year outcomes of EF HFA-BDP vs CFC-BDP were compared in a retrospective cohort study. A primary care database was used to identify asthma patients, aged 5 to 60, receiving their first inhaled corticosteroid (ICS) prescription or first ICS step-up dose with EF HFA-DBP. In both the initiation and step-up populations, patients were matched for demographic characteristics and asthma severity. Asthma control and exacerbation rates were compared between groups.

The study included 2,882 patients receiving EF HFA-BDP and 8,646 receiving CFC-BDP in the initiation population and 258 and 516 patients, respectively, in the step-up population. The adjusted odds of asthma control were higher with EF HFA-BDP: 1.15 in the initiation population and 1.72 in the step-up population. In both analyses, the median prescribed dose of EF HFA-BDP was half that of CFC-BDP.

Over 1 year of treatment, EF HFA BDP provides better asthma control than CFC-BDP, at half the dose. The results demonstrate the clinical significance of differences in ICS formulation, particle size, and deposition characteristics in a "real world" population of asthma patients.

COMMENT: *Catalyzed by environmental concerns associated with CFC propellants, the advent of the HFA metered-dose inhaler has changed our asthma controller armamentarium. This pharmaceutical industry-sponsored, retrospective matched cohort study helps validate the assumption that when using an HFA formulation, only half the microgram quantity of ICS is necessary to maintain asthma control compared to CFC inhalers. It is still unclear if using HFA vs CFC propellants alters the therapeutic index, and therefore it is premature to conclude that HFA products are superior to CFC products.*
S.A.T.
Barnes N, Price D, Colice G, et al: Asthma control with extrafine-particle hydrofluoroalkane-beclometasone vs. large-particle chlorofluorocarbon-beclometasone: a real-world observational study.
Clin Exp Allergy. 2011;41:1521-1532. ♦♦

The (Electronic) Nose Knows!

FIXED airway obstruction is a feature of both asthma and chronic obstructive pulmonary disease (COPD). The diagnostic distinction can be difficult to make, particularly in elderly patients. An "electronic nose" capable of performing metabolomic analysis of exhaled air was evaluated for use in differentiating between asthma and COPD.

The electronic nose was used for exhaled breath profiling in a cross-sectional study of 100 patients: 60 patients with asthma, 41 of whom had fixed airways obstruction; and 40 patients with COPD. The electronic nose created "breathprints" by measuring volatile organic compounds in standardized exhaled breath samples. External validity was tested using validation sets of newly recruited patients from a different hospital.

The breathprints created by the electronic nose showed good external validity, with 88% accuracy in distinguishing fixed asthma from COPD: area under the curve was 0.95, with sensitivity of 85% and specificity of 90%. In distinguishing asthma with fixed vs reversible airways obstruction, accuracy was 83%: area under the curve 0.93, with sensitivity of 91% and specificity of 90%. Accuracy was unaffected by smoking.

The electronic nose provides good accuracy in differentiating between asthma and COPD among patients with fixed airway obstruction. This may provide a useful new tool for ensuring correct diagnosis, and thus more appropriate treatment, in patients with obstructive airway diseases.

COMMENT: *Since asthma and COPD have different preferred treatments and prognoses, it's important to distinguish them from each other. These Dutch authors have developed an electronic nose, "e-nose," for analyzing substances in exhaled breath. From this validation study, it appears that the e-nose discriminates asthma from COPD, independent of history or lung function. This may become an important tool for managing elderly patients with asthma.*
S.A.T.

Fens N, Roldaan AC, van der Schee MP, et al: External validation of exhaled breath profiling using an electronic nose in the discrimination of asthma with fixed airways obstruction and chronic obstructive pulmonary disease.
Clin Exp Allergy. 2011;41:1371-1378. ♦♦

For Skin Prick Testing, IV Needles Are Hard to Beat

FEW recent, high-quality studies have compared the various tools used for skin prick testing. The authors assessed the sensitivity, reproducibility, and acceptability of the techniques of skin prick testing most commonly used in Europe.

The study compared four instruments used for skin prick testing: the 23G intravenous needle, the ALK Lancet, the Stallergenes (STG) Prick Lancet, and the Stallerpoint. Two different methods using the Stallerpoint were tested, for a total of five techniques. Sensitivity and reproducibility were assessed in 22 subjects by testing the positive control five times. Acceptability was assessed in single-blind fashion in 50 subjects.

Sensitivity was 100% with the intravenous needle, 96% for the ALK Lancet, and 98% for the STG Prick Lancet, compared to 20% and 57% for the Stallerpoint methods. The intravenous needle produced the largest mean wheals. The IV needle and the two metal lancets produced the best intrapatient reproducibility and acceptability.

The study shows significant differences in the results of different commonly used techniques of skin prick testing. Diagnostic performance and patient acceptability appear best with metal needles and/or lancets, particularly the 23G intravenous needle.

COMMENT: *The foundations of our specialty include prick skin testing as a safe, inexpensive, and highly accurate biological test for identifying specific IgE sensitization. In recent years there has been a push to change skin test methodology--not to improve accuracy, but rather to further increase its efficiency and also address theoretical safety concerns for technicians using "sharps." Meanwhile, there has been continued improvement in the previously inferior in vitro methods for measuring specific IgE. The results of this European study--which was not sponsored by a manufacturer of skin test supplies--remind us of just how good metal needles are for obtaining accurate prick skin test results.*
S.A.T.

Masse MS, Vallée AG, Chiriac A, et al: Comparison of five techniques of skin prick tests used routinely in Europe.
Allergy. 2011;66:1415-1419. ♦♦

FOCUS ON IMMUNOTHERAPY

In this issue, we focus on several recent papers providing important updates on allergen immunotherapy.

As We Knew... Systemic Reactions Are Rare with SCIT

SYSTEMIC and fatal reactions to subcutaneous immunotherapy (SCIT) are thought to be rare. However, the true rates of fatal reactions (FRs) and systemic reactions (SRs)--including delayed SRs--are unclear. These questions were addressed using 2 years of surveillance data.

The analysis included data contributed by members of the American Academy of Allergy, Asthma & Immunology and American College of Allergy Asthma & Immunology. In 2008 and 2009, members were surveyed regarding SCIT-related SRs, rated as mild (grade 1), moderate (grade 2), or severe anaphylaxis (grade 3). In 2009, respondents provided data on the use of epinephrine: time of onset was classified as early, within 30 minutes or less; or delayed, more than 30 minutes after SCIT injections.

Based on responses from a total of 630 practices, there were no reports of FRs in the first 2 years of the project. In data from 267 practices reporting on the timing of SRs, 14% of SRs were delayed onset (1,816 early-onset and 289 delayed-onset events). Delayed-onset SRs accounted for 15% of grade 1, 10% of grade 2, and 12.5% of grade 3 SRs. Rates of epinephrine treatment for early-onset SRs were 71% for grade 1, 67% for grade 2, and 94% for grade 3 reactions. For delayed-onset SRs, the rates were 56%, 67%, and 100%, respectively.

Based on 2 years of surveillance data, delayed-onset SRs to SCIT appear less common than previously reported. For grade 1 and 2 SRs, epinephrine treatment is more likely for delayed-onset versus early-onset events. Through 2 years, there have been no reported FRs to SCIT.

COMMENT: *This follow-up report from a surveillance program further supports the safety of SCIT for the treatment of atopic diseases. Although there are reports of SRs, no fatalities have been reported over the 2-year period from the time of program initiation. The study looked at the treatment of early- versus delayed-onset SRs, and reported less frequent treatment with epinephrine for mild or moderate forms of anaphylaxis and delayed forms of anaphylaxis. The authors recommend further study regarding the availability of self-injectable epinephrine for patients treated with SCIT, as well as patient education.*
V.H.-T.

Epstein TG, Liss GM, Murphy-Berendts K, Bernstein DI: Immediate and delayed-onset systemic reactions after subcutaneous immunotherapy injections: ACAAI/AAAAI surveillance study of subcutaneous immunotherapy--year 2.
Ann Allergy Asthma Immunol. 2011;107:426-431. ♦♦

Does Cluster Immunotherapy Have an Increased Rate of Systemic Reactions?

CLUSTER immunotherapy protocols provide an accelerated buildup period, allowing patients to reach maintenance doses within 1 month. However, this option is used in only a small percentage of patients, partly because of a perceived increase in the risk of systemic reactions. The rates of and risk factors for systemic reactions associated with aeroallergen cluster immunotherapy were evaluated.

The retrospective study included 441 patients receiving cluster immunotherapy at a large allergy group practice between 2008 and 2010. Local and systemic reactions were routinely graded and reported. Patient or protocol characteristics associated with reactions were analyzed as well.

Dust mite was the most common allergen included in the immunotherapy vaccines, followed by grass, tree, and weed pollen and cat and dog. Forty-eight patients had a systemic reaction during the buildup phase, for a rate of 10.9%. All but 4 of these patients discontinued cluster buildup; 75% eventually reached the maintenance dose.

About 38% of reactions were grade 1, 49% grade 2, 11% grade 3, and 2% grade 4. Rates of systemic reactions were higher for patients with physician-diagnosed asthma: 20% versus 7%. Risk was also higher for patients aged 21 to 40, female patients, and vaccine included grass pollen, weed pollen, and cat or dog allergen. The frequency of cluster doses was not a significant factor.

This experience shows an 11% rate of systemic reactions in a large sample of patients receiving aeroallergen cluster immunotherapy. The identified risk factors may aid in selecting patients for cluster immunotherapy protocols. Most systemic reactions are grade 1 or 2, and most patients with such reactions eventually reach the maintenance dose.

COMMENT: *Cluster immunotherapy offers the advantage of achievement of dose with an economy of time, but has the disadvantage of increased systemic reactions. Risk factors for these reactions include the use of grass, weed, cat, or dog allergens; female patients in the 21-to-40 age group; and presence of asthma. The young age group is most affected, with 1:10 concentrations most likely to cause reaction. Knowledge of these risk factors should enhance the safety of cluster immunotherapy.*
C.C.R.

Copenhaver CC, Parker A, Patch S: Systemic reactions with aeroallergen cluster immunotherapy in a clinical practice.
Ann Allergy Asthma Immunol. 2011;107:441-447. ♦♦

How Effective Is SCIT in Children?

PAST reviews of the effectiveness of subcutaneous immunotherapy (SCIT) in children have reached contradictory conclusions. The authors present an updated review of the evidence on SCIT in children, including the use of recommended quality assessment tools.

The review identified 31 articles published between 2006 and 2011. The studies presented high-quality data supporting the effectiveness of grass pollen SCIT in reducing the combined symptom medication score, as well as increasing the threshold on specific bronchial provocation testing. These outcomes were observed immediately as well as 7 years after the end of treatment. There were also data supporting improvements in the threshold of the specific bronchial provocation test and skin prick test reactivity.

Studies of SCIT for *Alternaria* allergy reported improvements in medication scores, combined symptom-medication scores, and quality of life, along with an increased threshold on nasal provocation testing. There was high-quality evidence showing benefits of house dust mite SCIT, including improvement in asthma symptom and medication scores and reduction in emergency department visits and skin test reactivity. There was also moderate evidence of improvement in pul-➤➤

monary function test results. Moderate evidence supported pollen SCIT for prevention of asthma, but only low to moderate evidence for long-term benefits. Data on prevention of new sensitizations were inconclusive.

Recent studies provide new data on the effectiveness of SCIT in children. There is now a solid body of evidence supporting SCIT for the treatment of pediatric allergy to grass pollen, *Alternaria*, and house dust mite. The evidence for sustained benefit is not as strong.

COMMENT: *The authors determine that "acceptable evidence" now exists demonstrating that grass pollen,* Alternaria, *and house dust mite subcutaneous immunotherapy is beneficial in the allergic pediatric population. Improvement is demonstrable using symptom and medication scores, skin testing, nasal and conjunctival challenge for allergic disease and emergency room visits for asthma even up to 12 years after termination with SCIT for pollen. However larger prospective controlled studies of longer duration are needed to validate the impact on new sensitization and on long-term outcomes.*
C.C.R.
Larenas-Linnemann DES, Pietropaolo-Cienfuegos DR, Calderón MA: Evidence of effect of subcutaneous immunotherapy in children: complete and updated review from 2006 onward.
Ann Allergy Asthma Immunol. 2011;107:407-416. ♦♦

Is Fungal Immunotherapy for Allergic Fungal Sinusitis Safe?

ALLERGIC fungal sinusitis can be a chronic problem with a complex course, including multiple surgeries. Some studies have reported positive outcomes of allergen immunotherapy to functional allergens, including fewer recurrences after surgery. However, there are concerns that high-dose fungal immunotherapy could lead to systemic hypersensitivity.

The researchers analyzed safety outcomes in 14 patients receiving high-dose subcutaneous fungal immunotherapy for allergic fungal sinusitis. The patients were 8 women and 6 men; mean age was 37 years and mean time on immunotherapy 22 months. Compared to a matched group of patients receiving non-fungal immunotherapy, there was no increase in local reactions, large or late local reactions, or back titrations among the patients with allergic fungal sinusitis. There was one case of mild systemic urticarial reaction to immunotherapy in each group.

A literature search identified 8 previous studies of subcutaneous fungal immunotherapy, 7 of which used low-dose subcutaneous immunotherapy. None of these reports described more than minor local reactions.

Fungal immunotherapy for patients with allergic fungal sinusitis does not appear to cause a higher rate or severity of adverse reactions, compared to pollen immunotherapy. The results support the safety of proceeding with clinical trials of high-dose subcutaneous immunotherapy for this group of patients.

COMMENT: *There is no consensus on the indications, safety, and efficacy of fungal immunotherapy, which has been recommended for allergic fungal sinusitis. The authors demonstrate that subcutaneous fungal immunotherapy is not associated with any more adverse reactions than current pollen immunotherapy. Although the findings are reassuring, further large, controlled, prospective studies are needed to validate the safety and efficacy of this treatment. Fungal immunotherapy may prove a promising modality for difficult-to-treat allergic fungal sinusitis.*
C.C.R.
Greenhaw B, deShazo RD, Arnold J, Wright L: Fungal immunotherapy in patients with allergic fungal sinusitis.
Ann Allergy Asthma Immunol. 2011;107:432-436. ♦♦

CLINICAL TIDBITS

SCIT + SLIT in the Same Patient--Perhaps More Efficacious and Safer than SCIT Alone!

BECAUSE of side effects and the need for repeated injections, subcutaneous immunotherapy (SCIT) is relatively little used in children. Sublingual immunotherapy (SLIT) offers an improved safety profile, but a later onset of action. This study evaluated a combined SCIT and SLIT protocol for children with allergic asthma.

The randomized trial included 51 children with allergy to house dust mite and mild to moderate asthma. One group received a combination of SCIT in the buildup phase and SLIT in the maintenance phase. The other groups received SCIT, SLIT, or medications alone.

Children receiving SCIT alone or SCIT plus SLIT had a better response in terms of asthma attacks and inhaled corticosteroid dose. Rhinitis symptom scores improved only in the SCIT plus SLIT group. Both the SCIT and SLIT groups showed increased levels of regulatory and Th1 cytokines. The two SCIT groups had increased antigen-specific IgG4 levels, which the SLIT-only group did not.

This study shows promising results with a combination of SCIT and SLIT for mite-allergic children with asthma. This approach may combine the rapid onset and potency of SCIT with the improved safety and comfort of SLIT.

COMMENT: *This unique study design compared treatment of dust mite-allergic asthmatic children with either or both SLIT and SCIT. Children receiving SCIT, with or without SLIT, had more rapid improvement in symptoms as well as induction of mite-specific IgG4 antibodies. The combination of SCIT plus SLIT was more effective than SLIT or pharmacotherapy alone. Interestingly, the use of SCIT plus SLIT was safer compared to SCIT alone. There may be therapeutic, immunologic, and safety benefits to the use of combined SCIT and SLIT in children with allergic asthma.*
S.M.F.

Keles S, Karakoc-Aydiner E, Ozen A, et al: A novel approach in allergen-specific immunotherapy: combination of sublingual and subcutaneous routes.
J Allergy Clin Immunol. 2011;128:808-815. ♦♦

T Regulatory Cells in Specific Immunotherapy--More to Come

THERE is a growing body of knowledge regarding T regulatory (Treg) cells and their role in the response to allergen specific immunotherapy (SIT). The authors review and synthesize recent evidence on Treg functions in allergic immune responses and SIT.

The goal of SIT is to induce peripheral T-cell tolerance, characterized by reduced proliferation of allergen-specific T cells and reduced secretion of Th1 and Th2 cytokines. Immunotherapy leads to the generation of allergen-specific Treg cells with production of the suppressive cytokines interleukin-10 and transforming growth factor-β. In addition to inhibiting allergen-specific Th1 and Th2 responses, Treg cells act to suppress production of IgE. They also influence the priming, survival, and activity of the effector cells of allergic inflammation, including eosinophils, basophils, and mast cells.

Recent studies have helped to clarify the interactions regulating different subsets of T cells, suggesting possible new pathways of immunotherapy. Vaccines may be developed to induce or expand Treg cell responses or numbers, thus leading to new approaches to preventing sensitization. Further studies of Treg cells and their function are needed to better understand the mechanisms of peripheral allergen tolerance and a well-balanced immune response.

COMMENT: *There is increasing interest in the function and importance of Treg cells in different atopic diseases. With regards to specific immunotherapy, the cells are essential in the immune response that leads to tolerance. As we learn more about Treg cells and the cytokines that suppress allergic responses, the importance of their key role is slowly being elucidated.*
V.H.-T.
Ozdemir C, Kucuksezer UC, Akdis M, Akdis CA: Specific immunotherapy and turning off the T cell: how does it work?
Ann Allergy Asthma Immunol. 2011;107:381-392. ♦♦

Will Immunotherapy Become the Treatment for Food Allergy and AD?

SPECIFIC immunotherapy (SIT) has well-documented efficacy in the treatment of allergic rhinoconjunctivitis and allergic asthma. The authors review research evidence on the uses of SIT for nonrespiratory allergic diseases, specifically atopic dermatitis (AD) and food allergies.

The review identified four randomized trials of oral food desensitization for IgE-mediated food allergies; all studies involved cow's milk, while one involved cow's milk and egg. Success rates in achieving tolerance of the target allergen ranged from 36% to 92%. Responses were achieved even in some patients with a history of severe clinical reactions to foods.

Studies of SIT for AD were highly heterogeneous, with only two placebo-controlled trials: one of subcutaneous and one of sublingual immunotherapy. Both involved patients with dust mite allergy. Significant improvement in AD activity was noted in 72% of patients receiving subcutaneous immunotherapy and 54% receiving sublingual immunotherapy.

Based on a few randomized trials, oral immunotherapy can induce at least partial tolerance in most patients with IgE-mediated food allergies. Two studies provide evidence that SIT may be a useful option for selected patients with AD. Further study is needed to explore the potential of SIT as "active" therapy for these nonrespiratory allergic diseases.

COMMENT: *This review looked at recent studies investigating SIT as an additional therapeutic option for patients with nonrespiratory allergic diseases for which avoidance of a food allergen or treatment of a reaction are the current options. A prolonged protocol was well tolerated and effective in patients with peanut oral immunotherapy. In a study of oral immunotherapy for milk allergy, patients in the active immunotherapy group tolerated higher amounts of milk than the placebo group. Patients with AD have also benefited with treatment for subcutaneous or sublingual immunotherapy for dust mite allergy. These are promising options for the treatment of diseases currently without "cure."*
V.H.-T.
Pajno GB, Finegold I: SIT beyond respiratory diseases.
Ann Allergy Asthma Immunol. 2011;107: 395-400. ♦♦

Magnetic Fields: A Risk Factor for Asthma?

INCREASING exposure to magnetic fields (MFs) is a possible environmental contributor to the increase in childhood asthma. The association between MF exposure in utero and the development of childhood asthma was investigated in a prospective cohort study.

Exposure was assessed by having pregnant women carry MF meters during pregnancy. Six hundred twenty-six offspring were followed up for as long as 13 years for the clinical diagnosis of asthma. On adjusted analysis, each 1 mG increase in maternal MF exposure was associated with a 15% increase in the risk of asthma in offspring. Compared to the group with low exposure, adjusted hazard ratios were 1.74 in the medium-exposure group and 3.52 in the high-exposure group. There was evidence of a synergistic interaction between MF exposure, maternal history of asthma, and being first in birth order.

These prospective data suggest that in utero MF exposure could be a contributor to childhood asthma risk. Although replication is needed, the findings point to a possible increase in asthma associated with a ubiquitous environmental exposure. ➤➤

COMMENT: *Environmental exposure to MF has been implicated in a variety of childhood disorders, including leukemia in children exposed to higher than 4 milligauss (mG). In this prospective cohort study, MF was measured during pregnancy and the offspring were followed for up to 13 years for the development of asthma. When the children had more than 2 mG exposure in utero, there was a 3.5-fold increased risk of developing asthma. Interestingly there was a synergistic effect between exposure to MF and maternal history of asthma, with more than 6-fold increased rate of asthma for each 1 mG increase in MF level during pregnancy in mothers with asthma. The potential mechanism for this interaction is not clear. However, the authors suggest that the increasing prevalence of pediatric asthma may be at least partly related to increasing exposure to environmental MF.*
S.M.F.
Li D-K, Chen H, Odouli R: Maternal exposure to magnetic fields during pregnancy in relation to the risk of asthma in offspring.
Arch Pediatr Adolesc Med. 2011;165:956-950. ♦♦

A Smoking Gun: Parents Underestimate Prenatal Tobacco Exposure

THE best measure of prenatal exposure to tobacco smoke--including both active and passive smoking--is unknown. This study compared parent reports with biomarkers of prenatal exposure to tobacco smoke as predictors of wheezing during early life.

A birth cohort study included 398 mother-infant pairs enrolled during pregnancy with follow-up to age 2. Tobacco exposure was assessed by maternal report, maternal serum cotinine level, and meconium cotinine level. Wheezing was assessed every 6 months by parent report.

Cotinine was detected in serum samples from 61% of mothers, compared to a 26% rate of parent-reported active or passive tobacco exposure. Adjusted odds ratios of wheezing for subjects in the 95th vs the 5th percentile were 2.6 for maternal serum cotinine, 2.0 for meconium cotinine, and 1.7 for parent-reported smoking.

Parents appear to underreport exposure to active or passive smoking during pregnancy. Maternal serum cotinine is more closely associated with wheezing in early life, compared to parent-reported exposure.

COMMENT: *Mothers in particular may underreport their own smoking versus not considering other exposures to environmental tobacco smoke during their pregnancies. This finding, while disappointing, is not terribly surprising. What remains unclouded: the risk of wheeze in children up to age 2 is proportionate to prenatal maternal serum cotinine levels!*
K.R.M.
Spanier AJ, Kahn RS, Xu Y, et al: Comparison of biomarkers and parent report of tobacco exposure to predict wheeze.
J Pediatr. 2011;159:776-782. ♦♦

Ancestral Effects on Food Sensitization?

PREVIOUS studies have suggested racial variations in the prevalence of food sensitization. These studies are limited by the use of self-reported race. The current study used data on genetic ancestry in assessing racial disparities in food sensitization.

An urban, multiethnic birth cohort of 1,104 children underwent measurement of specific IgE for 8 common food allergens. Sensitization was defined as a specific IgE level of 0.35 kUA/L. Associations of sensitization with self-identified race and genetic ancestry were analyzed.

The overall rate of food sensitizations was 35.5%. On multivariate analysis, food sensitization was associated with self-reported black race, odds ratio (OR) 2.34; and with African ancestry, OR 1.07 per 10% increment. The presence of 3 or more food sensitizations was also associated with self-reported black race, OR 3.76; and African ancestry, OR 1.19. African ancestry was significantly associated with sensitization to peanut and egg, but not milk.

Food sensitization is associated not only with self-reported black race but also with genetic African ancestry. African ancestry appears to be specifically associated with peanut sensitization at levels associated with clinical allergy.

COMMENT: *Genetic studies have found that people of African ancestry have an increased risk of asthma, compared to those of European ancestry. Thus it is not far-fetched to imagine other allergic comorbidities in those sharing African descent. Most interesting in this study is the variability of sensitivity, by particular food allergen.*
K.R.M.
Kumar R, Tsai H-J, Hong X, et al: Race, ancestry, and development of food-allergen sensitization in early childhood.
Pediatrics. 2011;128:e821-e829. ♦♦

Late Preterm Birth Associated with Childhood Asthma

LATE preterm birth--34 to 36 weeks--has been linked to an increased risk of respiratory disease during the neonatal period. This study evaluated late preterm birth as a possible risk factor for childhood asthma.

The retrospective study included data on 7,925 infants born after 24 to 42 weeks' gestation and followed up to age 18 months. Seven percent had late preterm birth, while 21% had low-normal gestation--37 to 38 weeks. Associations between these categories and the presence and severity of asthma were assessed.

By age 18 months, 8.3% of the children had been diagnosed with asthma. Infants with late preterm gestation were more likely to be diagnosed with persistent asthma, adjusted odds ratio (OR) 1.68. They were also more likely to be using inhaled corticosteroids, OR 1.66; and had more acute respiratory visits, rate ratio 1.44.

Low-normal gestation was also associated with increases in asthma diagnosis and inhaled corticosteroid use: OR 1.34 and 1.39, respectively.

Late-preterm birth and low-normal gestation may be associated with increased rates of certain early childhood asthma outcomes. The study provides evidence that the health impact of late preterm delivery extends into the second year of life.

COMMENT: *Gestational age at birth has been trending downward over time, to the extent that 39 weeks' gestation might now be the average for U.S. births! The implications of this study are considerable and could help explain some of the increase in childhood asthma.*

The retrospective cohort study reviewed mode of birth as a confounding variable; the C-section rate here progressively decreases by week of gestation. Therefore, birth method itself might explain some of the observed association between gestational age and asthma, as C-section births are also positively associated with risk of asthma in children.

K.R.M.

Goyal NK, Fiks AG, Lorch SA: Association of late-preterm birth with asthma in young children: practice-based study.

Pediatrics. 2011;128:e830-e838. ♦♦

Reversible Airflow Limitation in COPD: Review and Update

AIRFLOW limitation that is not fully reversible is part of the definition of chronic obstructive pulmonary disease (COPD), based on American Thoracic Society/European Respiratory Society (ATA/ERS) guidelines. However, some COPD patients may have significant reversibility. The authors review recent data on the concept of reversibility in COPD.

Recent studies have reported clinically significant reversibility of airflow limitation in some patients with COPD. The confusion surrounding this issue reflects the complexity and variability of acute response to bronchodilator and the lack of a standard technique of assessing reversibility. In contrast to the commonly used FEV_1-based definitions of reversibility, measures based on lung volume may be more relevant to patients with severe COPD.

The value of acute reversibility in predicting long-term response to maintenance therapy is uncertain. However, reports suggest that patients without an acute response to short-acting bronchodilators may still derive long-term benefit from maintenance bronchodilators. Factors affecting reversibility may include disease severity, reversibility criteria, and the drug and test methods used.

An update and review on the concept of reversible airflow limitation in COPD is presented. More research is needed to determine how reversibility is related to important clinical outcomes, such as quality of life and exercise capacity, across different levels of COPD severity.

COMMENT: *The "take-home" for this article is that reversibility occurs in COPD and clearly there may be overlap in clinical presentations of COPD and asthma. According to ATS/ERS recommendations, COPD may at times be treated as asthma. There are clear pathogenic differences. When reviewing clinical trials of COPD or asthma, careful attention should be given to the subject selection to ensure, as best as possible, a homogeneous population.*

S.F.W.

Hanania NA. Celli BR, Donohue JF, Martin UJ: Bronchodilator reversibility in COPD.

Chest. 2011;140:1055-1063. ♦♦

Can We Predict Whether Cyclosporine Will Help Adults with Chronic Urticaria?

CHRONIC urticaria (CU) is a difficult-to-treat condition, with no clear choice for patients in whom initial treatment is unsuccessful. The outcomes of low-dose cyclosporine therapy for CU were analyzed, including factors associated with response.

The retrospective study included 68 adults with CU who completed a course of treatment with cyclosporine. All had urticaria more than 3 days per week for 6 consecutive weeks with failure of firstline therapy. The average cyclosporine dose was 1.8 mg/kg.

The complete remission rate, defined as no more than 1 day of hives per month, was 78%. Seven patients experienced recurrence; all responded to resumption of cyclosporine therapy. Factors associated with a good response to cyclosporine included a history of hives, shorter duration of urticaria, and a positive CU index. Side effects were generally mild and resolved with dose reduction.

This study reports a high rate of complete remission with cyclosporine among patients with CU who do not respond to initial therapy. Further studies will be needed to confirm these good results and the predictors of successful response.

COMMENT: *I have always wondered what patients will benefit from one treatment option over another, especially for CU. Antihistamines were used to treat all patients in this cohort initially. The authors describe greater than 75% complete remission with low doses of cyclosporine. Favorable response to treatment was predicted by history of hives, shorter duration of urticaria, and CU index of 10 or higher. I am looking forward to prospective studies to confirm the results, especially for this disease that can be so difficult to treat.*

V.H.-T.

Hollander SM, Joo SS, Wedner HJ: Factors that predict the success of cyclosporine treatment for chronic urticaria.

Ann Allergy Asthma Immunol. 2011;107:523-528. ♦♦

How Do Asthma Treatments Affect the Risk of Exacerbations during Colds?

COLDS are a major cause of asthma exacerbations. This study looked at how various asthma treatments affect the risk and severity of cold-related asthma exacerbations.

The researchers analyzed data on 12,507 asthma patients receiving 6 to 12 months of double-blind treatment with various regimens of asthma medications. The patients, drawn from five clinical trials conducted worldwide, had poorly controlled asthma at baseline.

Exaerbations were defined in terms of oral corticosteroid use, hospitalization or emergency department visit, or both. The analysis included exacerbations occurring within 14 days of a reported cold.

There was no difference in the incidence of colds among patients receiving different treatments. When colds occurred, asthma symptoms and use of reliever medications increased. In patients taking budesonide/formoterol maintenance and reliever therapy, the rate of severe exacerbations was significantly lower compared with pooled and individual fixed-dose maintenance treatments plus as-needed short-acting β_2-agonist (SABA): relative risk (RR) 0.64.

On analysis of individual treatments, the greatest reduction was seen with budesonide/formoterol maintenance and reliever therapy, compared to the same maintenance dose of inhaled corticosteroid (ICS)/long-acting β_2-agonist (LABA): RR 0.48. The risk of cold-related exacerbations was not significantly reduced on comparison with higher maintenance doses of ICS or ICS/LABA. There was also no reduction with as-needed LABA versus as-needed SABA.

Budesonide/formoterol maintenance and reliever therapy appears to reduce the risk of severe asthma exacerbations related to cold, compared to ICS with or without LABA and with as-needed SABA. Inhaled corticosteroid appears to be the key treatment factor lowering cold-related exacerbation risk.

COMMENT: *These data continue to support a notion that has been previously stated in multiple publications. The use of either short- or long-acting bronchodilator with inhaled corticosteroid at the onset of exacerbations is a significant adjunct in decreasing the chance of more severe exacerbations.*
B.E.C.
Reddel HK, Jenkins C, Quirce S, et al: Effect of different asthma treatments on risk of cold-related exacerbations.
Eur Respir J. 2011;38:584-593. ♦♦

REVIEWS OF NOTE

COMMENT: *This is an excellent review regarding the spectrum of pulmonary involvement with* Aspergillus *and the implications for therapy.*
B.E.C.
Kousha M, Tadi R, Soubani AO: Pulmonary aspergillosis: a clinical review.
Eur Respir Rev. 2011;20:121:156-174. ♦♦

COMMENT: *Transient receptor potential cation channel, subfamily A, member 1 (TRPA1) channels are nonselective cation channels that are activated by a range of natural products (eg, allyl isothiocyanate), a multitude of environmental irritants (eg, acrolein, which is present in air pollution, vehicle exhaust, and cigarette smoke), and inflammatory mediators (eg, cyclopentenone prostaglandins). TRPA1 activation on afferent neurons (eg, vagal) may contribute to cough. TRPA1 has been implicated in animal models of asthma. Antagonists have been developed but appropriate human studies in asthma have not been carried out.*
S.F.W.
Belvisi MG, Dubuis E, Birrell MA: Transient receptor potential A1 channels: insights into cough and airway inflammatory disease.
Chest. 2011;140:1040-1047. ♦♦

COMMENT: *This is an excellent review of drug desensitization ("induction of tolerance") and adds to the information contained in the recently published Drug Allergy Practice Parameter.*
S.A.T.
Liu A, Fanning L, Chong H, et al: Desensitization regimens for drug allergy: state of the art in the 21st century.
Clin Exp Allergy. 2011;41:1679-1689. ♦♦