AllergyWatch®

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

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No House Without Dog or Cat!

SENSITIZATION to cat or dog allergen is an important risk factor for asthma, and can occur at very low levels of allergen exposure. Data from the National Survey of Lead and Allergen in Housing (NSLAH) provide an opportunity to estimate indoor exposure to common allergens in U.S. homes.

Allergen levels were measured in dust samples obtained from the bed, bedroom floor, living room floor, and living room sofa in a nationally representative sample of 831 U.S. homes. At the time the samples were collected, 55% of the homes had had neither a cat nor a dog.

Nevertheless, nearly all homes had detectable levels of both cat and dog allergens. Fel d 1 was detected in 97% of beds, 97% of bedroom floors, 96% of living room floors, and 98% of sofas. Percentages of homes with detectable Can f 1 in the same locations were 94%, 95%, 98%, and 100%, respectively. Levels of Fel d 1 exceeded the provisional threshold for sensitization in 66% of homes and for asthma symptoms in 35%. Percentages of homes exceeding threshold levels of Can f 1 were 56% and 35%, respectively.

For all homes, geometric mean allergen concentrations were 4.73 µg/g for Fel d 1 and 4.69 µg/g for Can f 1. For homes with an indoor cat or dog, these values increased to 200 and 69 µg/g, respectively. The independent predictors of high allergen levels in homes without pets were the same as the demographic variables associated with owning pets, including white race and non-Hispanic ethnicity.

Nearly all U.S. homes have detectable levels of dog and cat allergen. In addition, most homes have allergen levels above the provisional thresholds for sensitization, while about one-third have levels above the provisional thresholds for asthma symptoms. Nearly all patients with asthma or allergy have at least some exposure to dog or cat allergen at home, whether or not they have pets.

COMMENT: *Data from the NSLAH have previously demonstrated that dust mite and mouse antigens are present in a surprising number of U.S. homes. This* ➤➤

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The American College of Allergy, Asthma & Immunology expresses its appreciation to Aventis Pharmaceuticals Inc.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

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report presents data regarding dog or cat allergen in a sampling of 831 homes. The important points include the fact that the critical level of cat antigen required for sensitization was exceeded in 15.7% of homes even without a cat present. For dog antigen the number was 9.3%, which is still remarkable. Clearly, animal allergens are ubiquitous in our homes. The clinical implication is that that animal sensitization should be considered even when there is no pet in the home. We frequently have patients ask permission to acquire furry pets. This study suggests that the dander may already be in their home.
S. M. F.
Arbes SJ Jr, Cohn RD, Yin M,et al: Dog allergen (Can f 1) and cat allergen (Fel d 1) in US homes: results from the National Survey of Lead and Allergens in Housing. **J Allergy Clin Immunol**. 2004;114:111-117. ♦♦

Above All, Do No Harm!

ALLERGEN immunotherapy (IT) is an effective treatment for allergic rhinitis and asthma. Although IT is safe, fatal reactions to allergen injections do occur. American Academy of Allergy, Asthma, and Immunology (AAAAI) members were surveyed regarding fatal reactions to allergen injections and skin tests occurring from 1990 through 2001.

A 6-question survey was sent to all 2,404 physician members of the AAAAI. Of these, 646 responded, a rate of 25%. The respondents directly reported 20 deaths resulting from immunotherapy reactions, while another 21 fatal reactions were reported by local physicians.

Near-fatal reactions were reported by 42% of respondents. The rate of fatal reactions to allergen IT was estimated at 1 death per 2.5 million injections, with an annual average of 3.4 deaths. One death occurred after skin-prick testing with food allergens.

A detailed questionnaire was sent to all physicians reporting deaths related to IT. Of 17 deaths for which detailed information was provided, 15 were in patients with asthma, usually poorly controlled. Three deaths occurred in settings without medical supervision. None of the patients were taking β-blockers, while one was taking an angiotensin-converting enzyme inhibitor. Fifty-nine percent of the fatal reactions occurred after maintenance IT injections. Three of the fatal reactions did not begin until more than 30 minutes after allergen injection, associated with delays to epinephrine treatment. Another 3 patients never received epinephrine.

The findings confirm the low rate of fatal reactions to allergen IT. Few deaths result from errors in allergen dosing, but some occur in settings without adequate facilities for management of anaphylaxis. Carefully following clinical guidelines for allergen IT may help to lower the risk of deaths related to allergen injections.

ALTHOUGH allergen IT is generally considered safe, fatal reactions can occur. One potential cause is incorrect allergen doses. Allergists were surveyed regarding their experiences with incorrect allergen injections.

In an e-mail survey, 1,717 allergists were asked about any incorrect allergy injections given in their office over the past 5 years. The response rate was 28%. Of the respondents, 58% reported on patients receiving injections intended for other patients while 74% reported administration of incorrect doses of vaccine. Most of the errors led to local reactions only, although one resulted in death.

Some of the errors involved patients receiving an injection intended for another patient with a similar name. Incorrect doses sometimes resulted from nursing errors.

Incorrect injections are common in allergy practice. The authors make recommendations for preventing such problems, based mainly on the recent Practice Parameter for allergen IT. Specific steps include the use of➤➤

patient-specific vials, standardized dosage sheets, and triple-checks of patients' identity.

COMMENT: *These two reports review surveys of allergists and their experiences with fatal and systemic reactions to allergen IT. The AAAAI survey polled 2,404 members and had a 25% response rate, which is accurate for this type of instrument. There were 41 fatalities over the 12-year period. This translates to a fatality rate of 1 per 2.5 million injections, which is similar to the previous report from the 1987 AAAAI survey. Although this report suggested that dosing errors and β-blockers were not major contributing factors, the paper by Aaronson and Gandhi did suggest that dosing errors are important. They report a survey of allergists' experiences with dosing errors and systemic reactions. Fifty-seven percent reported at least one wrong injection in the past 5 years, while 74% reported administering incorrect dosages. Although both papers recommend compliance with the recently published Practice Parameters for Allergen Immunotherapy, Aaronson and Gandhi also suggest continual nursing staff education, standardized forms, patient-specific vials, at least three patient identity checks, and other procedures to reduce the risk of error. All physicians are concerned about medical mistakes. Reducing the risk of errors that result in reactions to IT is critical.*
S. M. F.

Bernstein DI, Wanner M, Borish L, et al: Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001.
J Allergy Clin Immunol. 2004;113:1129-1136

Aaronson D, Gandhi T: Incorrect allergy injections: allergists' experiences and recommendations for prevention.
J Allergy Clin Immunol. 2004;113:1117-1121. ♦♦

The Role of Staphylococcal Toxins in AD

THE strains of *Staphylococcus aureus* colonizing the skin of patients with atopic dermatitis (AD) are generally capable of producing superantigenic toxins. These toxins, such as staphylococcal enterotoxin A and B (SEA and SEB), may contribute to AD via humoral immunity. Less is known about the role of exfoliative toxin x (ETx).

This study used polymerase chain reaction to detect genes for toxins produced by *S. aureus* isolated from the skin of 100 patients with AD. The patients ranged from infants to young adults, with AD ranging from mild to severe. In addition, enzyme-linked immunosorbent assay was used to measure SEB, staphylococcal exfoliative toxin A (ETA), total and specific IgE, and specific IgG in serum samples from 21 patients with mild to moderate AD.

The staphylococcal toxin most commonly detected from the skin strains was SEB, followed by ETx. Nearly all of the serum specimens had detectable ETA, but not SEB. Levels of ETA in sera from AD patients were higher than in controls, especially in infants. However, the AD sera did not have detectable ETA-specific IgE. Although ETA-IgG was more than twice as prevalent in AD patients as in controls, levels of ETA-IgG were not significantly different between groups.

Many patients with AD have been exposed to the staphylococcal toxin ETx. This toxin may play a role in AD exacerbations, particularly among infants. However, in contrast to SEB, these reactions do not seem to take place via production of specific IgE.

COMMENT: *The importance of* S. aureus *colonization of affected skin and the potential for staphylococcal enterotoxin to act as a superantigen to stimulate Th-2 inflammation are familiar concepts when we think of AD. Staphylococcal exfoliative toxins play an important role in "scalded skin syndrome," but the role of exfoliative toxins in AD is less familiar. These authors found that staphylococcal exfoliative toxins can frequently be detected in the serum of patients with AD, and levels were particularly high in infants. Perhaps we should be using antimicrobial therapy more aggressively in infantile eczema.*
S. A. T.

Yagi S, Wakaki N, Ikeda N, et al: Presence of staphylococcal exfoliative toxin A in sera of patients with atopic dermatitis. **Clin Exp Allergy**. 2004;34:984-993. ♦♦

The March of Science Is Slow!

THE rate of cephalosporin sensitization among patients with confirmed IgE-mediated hypersensitivity to penicillins remains unclear. Because of the risk of cross-reactivity, indicated cephalosporin treatment is sometimes deferred in penicillin-allergic patients. Cephalosporin cross-reactivity was assessed in a large group of patients with penicillin allergy.

The prospective study included 128 consecutive patients with documented penicillin allergy, without indications for cephalosporin treatment. All had a history of immediate reactions to penicillins, anaphylaxis in 81 patients and urticaria in 47; and positive skin test results to at least one penicillin reagent or semisynthetic penicillin. The patients underwent skin testing with cephalosporins, including cephalothin, cefamandole, cefuroxime, ceftazidime, ceftriaxone, and cefotaxime. If there was no reaction to any of the latter four drugs, challenge with cefuroxime axetil and ceftriaxone was carried out.

Skin testing for cephalosporins was positive in 14 patients, a range of 11%. Most of the positive reactions were to cephalothin or cefamandole. Seventy-one percent of patients who reacted to cephalosporins had a previous positive skin test result to the minor determinant mixture, compared to 39% of those without cephalosporin cross-reactivity: odds ratio 3.90. All patients with negative skin tests to the initial cephalosporins also tolerated cefuroxime axetil and ceftriaxone.

This study finds an 11% rate of cross-reactivity to cephalosporins among patients with documented penicillin allergy. Patients who react to the minor determinant mixture seem more likely to react to cephalosporins. When penicillin-allergic patients ➤➤

require cephalosporin treatment, the authors recommend initial skin testing, followed by graded challenge with the cephalosporin.

COMMENT: *This paper provides a working strategy to approach subjects referred with penicillin allergy with the hope of using parenteral or oral cephalosporins. We have a wide range of antibiotic choices, but bacterial resistance, costs, and potential side effects limit those choices. A reasonable, safe approach to testing and challenging with cephalosporins is provided in this report, recognizing the limited data we have about the predictive value of cephalosporin skin testing. How ironic that we have useful information to help with cephalosporin testing at a time when we cannot obtain the proven, evidence-based testing reagents: penicilloyl-polylysine (major determinant) or minor determinant mixture. I guess we are making progress but sometimes I wonder.*
D. K. L.
Romano A, Guéant-Rodriguez R-M, Viola M, et al: Cross-reactivity and tolerability of cephalosporins in patients with immediate hypersensitivity to penicillins.
Ann Intern Med. 2004;141:16-22. ♦♦

More on Drug Allergy

DRUG hypersensitivity reactions are common in hospital patients. These events call for rigorous diagnostic confirmation, including skin tests and drug provocation tests if indicated. The results of a large series of drug provocation tests in patients with a clinical history of immediate drug hypersensitivity reactions are reported.

The retrospective analysis included 1,128 consecutive patients referred over 5 years for evaluation of suspected immediate drug hypersensitivity reactions. Exclusion criteria included chronic urticaria; latex and food allergies; severe life-threatening skin reactions, such as vasculitis, exfoliative dermatitis, and toxic epidermal necrolysis or Stevens-Johnson syndrome; drug-induced autoimmune diseases; and specific organ hypersensitivity reactions. The remaining 898 patients underwent a total of 1,372 drug provocation tests. A positive result was defined as signs or symptoms of an immediate drug reaction, occurring up to 2 hours after the last administered dose (3 hours for aspirin and nonsteroidal anti-inflammatory drugs).

Just 17.6% of the drug provocation tests yielded positive results. In most of the positive tests, the hypersensitivity reaction was the same as the initial clinical event prompting referral, although usually milder and of shorter duration. All reactions were successfully managed.

Less than one-fourth of patients with suspected drug hypersensitivity reactions have a positive result on drug provocation testing. With appropriate controls, drug provocation testing offers a safe approach to confirming or rejecting the possibility of drug allergy. The authors note the possibility of false-negative results related to loss of sensitization, rare cofactors, and induction of tolerance.

COMMENT: *These authors retrospectively studied more than 1,300 drug provocation tests on more than 800 patients with histories suggesting immediate drug allergy. They confirmed drug reactions in less than 25% of patients. The provocation tests were considered effective and safe, provided that patients with severe comorbid illness--as well as those with documented, life-threatening reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and eosinophilic reactions with systemic symptoms and organ involvement--were excluded. The protocol is certainly worth considering when evaluating such patients in clinical practice.*
E. J. B.
Messaad, D, Sahia H, Benahmed S, et al: Drug provocation tests in patients with a history suggesting an immediate drug hypersensitivity reaction.
Ann Intern Med. 2004;140:1001-1006. ♦♦

"Wheezy Sneezers" Are Different

ALLERGIC rhinitis and asthma commonly occur together, suggesting a "continuum of airway disease." Few previous studies examined possible differences between asthma with seasonal rhinitis vs persistent asthma. Data from previous clinical trials were used compare these two groups of asthma patients.

The retrospective study used data from nine placebo-controlled clinical trials: six trials including 958 patients with coexisting seasonal allergic rhinitis and asthma and three trials including 607 patients with persistent asthma. For all trials, enrollment criteria included no oral corticosteroids for at least 3 months and no inhaled corticosteroids for at least 1 month. All patients had reversible airflow obstruction, with at least a 12% increase in FEV_1 over baseline.

The patients with seasonal rhinitis and asthma were more likely to be female. Total asthma symptom score was higher in the patients with seasonal rhinitis and asthma vs those with persistent asthma, including a 3-fold increase in the severity of cough. There was no significant difference in the use of rescue β_2-agonists or in the ratio of FEV_1 to forced vital capacity (FVC). However, the ratio of forced expiratory fraction 25%-75% to FVC was significantly lower in the patients with persistent asthma. In the seasonal rhinitis group, scores for asthma severity were significantly correlated with scores for nasal symptom severity.

The findings document significant clinical differences between patients with seasonal allergic rhinitis and asthma vs those with persistent asthma. Asthma with seasonal rhinitis is associated with increased chest symptoms, especially cough, that are out of proportion to the level of pulmonary function impairment. Although more study is needed, the characteristics of patients with seasonal rhinitis and asthma may warrant a new diagnostic classification, "allergic airway disease."

COMMENT: *It has become clear that defining asthma in terms of "mild," "moderate," and "severe" misses the mark when it comes to categorizing individual* ➤➤

patients. This landmark study identifies important clinical differences between perennial asthma and asthma associated with seasonal allergic rhinitis. The authors propose that the anatomic source of wheezing and cough may differ between these phenotypes, and that concurrent flaring of rhinitis may be responsible for more severe asthma symptoms without more severe impairment in lung function. If replicated in a prospective study, these findings may have important treatment implications, especially if they establish criteria for defining patients with "allergic airway disease" that emphasize the importance of rhinitis symptoms.
S. A. T.
Bosquet J, Boushey HA, Busse WW, et al: Characteristics of patients with seasonal allergic rhinitis and concomitant asthma.
Clin Exp Allergy. 2004;34:897-903. ♦♦

Most Children Don't "Outgrow" Asthma After Puberty

CHILDHOOD asthma is associated with an increased risk of asthma symptoms and nonreversible airway obstruction in adulthood. It is widely believed that children with asthma are likely to "outgrow" their disease after puberty. This clinical impression was tested using long-term follow-up data from children in the Tucson Children's Respiratory Study.

The analysis included 781 children enrolled at birth with follow-up assessments at intervals from 6 to 16 years. Based on the presence of frequent wheezing or a physician diagnosis of asthma plus any wheezing, 166 children were classified as having asthma on at least one prepubertal assessment. Rates of asthma persistence and remission after puberty were assessed, along with factors associated with these outcomes.

Of the children with prepubertal asthma, 58% had unremitting asthma, defined as persistent wheezing after puberty. In contrast, just 30% of children who had infrequent wheezing before puberty had unremitting wheezing, defined as any wheezing after puberty.

Frequent wheezing before was an independent risk factor for unremitting asthma. Other risk factors included obesity, early onset of puberty, active sinusitis, and positive skin-test results.

Most children with asthma before puberty have unremitting asthma after puberty. This is in direct contrast to the conventional wisdom that children with asthma "outgrow" their disease. Obesity appears to be an important and potentially remediable risk factor for asthma persistence after puberty.

COMMENT: *In the well-characterized cohort from the Tucson Children's Respiratory Study, the premise that childhood asthma typically remits during adolescence was examined. A lower percentage (30%) of children developed persistent asthma after puberty if they had only infrequent prepubertal wheezing. In contrast, 58% of prepubertal sustained asthmatics continued having chronic symptoms during adolescence. This should give pause to the practice of telling parents to expect their child's asthma to remit with the onset of puberty.*
G. D. M.
Guerra S, Wright AL, Morgan WJ, et al: Persistence of asthma symptoms during adolescence: role of obesity and age at the onset of puberty.
Am J Respir Crit Care Med. 2004;170:78-85. ♦♦

Study Doesn't Support Link Between Asthma and ADAM33 Gene

IDENTIFICATION of genes associated with susceptibility to asthma could have important implications for research and treatment. A previous study identified a disintegrin and metalloproteinase 33 (ADAM33) on chromosome 20p13 as a possible asthma susceptibility gene. The association between asthma and ADAM33 was evaluated in subjects from the Childhood Asthma Management Program (CAMP).

The family-based association study included 652 nuclear families with an asthmatic child enrolled in the CAMP. The families underwent genotyping studies for 17 different ADAM33 single nucleotide polymorphisms (SNPs), 9 of which had suggested associations with asthma in the previous report.

No specific SNP was associated with asthma among either white or African-American families. One common16-SNP haplotype, found in nearly 15% of white subjects, was associated with asthma. Although the findings provided marginal evidence of an asthma locus in the region in which ADAM33 was located, the associations were modest and did not agree with the previous study.

Polymorphisms of ADAM33 do not appear to be strongly related to asthmatic phenotypes. The failure to confirm the findings of the previous study may reflect differences between the study cohorts, or the effects may be important only in populations with some unknown characteristics.

COMMENT: *The genetic basis for susceptibility to asthma is unknown, but a 2002 report found a high association with the gene for the enzyme ADAM33. This study looked at 587 nuclear families of children in the CAMP study, and did not confirm a strong association with ADAM33. Darn!*
R. J. M.
Raby BA, Silverman EK, Kwiatkowski DJ, et al: ADAM33 polymorphisms and phenotype associations in childhood asthma.
J Allergy Clin Immunol. 2004;113:1071-1078. ♦♦

Nasal Amphotericin B Is Ineffective for Chronic Rhinosinusitis

RECENT reports have suggested that fungi play a primary role in causing chronic rhinosinusitis (CRS). Observational studies of nasal antifungal ➤➤

treatment with amphotericin B have yielded promising results. A randomized clinical trial of nasal amphotericin B for the treatment of CRS with nasal polyps is reported.

Seventy-eight patients referred for paranasal sinus surgery to remove nasal polyps were included in the trial. In blinded fashion, they were randomized to receive amphotericin B, 3 mg/mL, or saline nasal spray, 200 µL per nostril four times daily for 8 weeks. The study definition of response was a 50% reduction in the patient's baseline CT score.

Sixty patients completed the trial. Pretreatment nasal lavage specimens showed fungal organisms--mainly *Aspergillus* and *Penicillum* spp.--in 38 patients. Treatment with amphotericin B had no effect on the primary outcome measure: median CT scores were similar before and after treatment in both groups. Treatment response rate was 7% with amphotericin B vs zero in the placebo group. Median symptom score was worse after amphotericin B treatment than with placebo.

At least as used in this trial, nasal amphotericin B does not improve the outcomes of CRS with nasal polyposis, compared with placebo. Symptoms actually appear to worsen on amphotericin B. The findings are consistent with the view that fungi are "innocent bystanders" in the sinuses of immunocompetent hosts.

COMMENT: *Chronic hypertrophic sinusitis, usually accompanying polyposis, can be a severe chronic disease, the pathophysiology of which is hotly debated. Some believe that fungi cause the inflammatory response, and unblinded/uncontrolled treatment with nasal amphotericin lavage has been reported to be beneficial. This study used a blinded placebo-controlled design and failed to show any objective benefit after 8 weeks. Patients' symptoms actually worsened significantly. Let the debate continue.*
R. J. M.
Weschta M, Rimek D, Formanek M, et al: Topical antifungal treatment of chronic rhinosinusitis with nasal polyps: a randomized, double blind clinical trial.
J Allergy Clin Immunol. 2004;113:1122-1128. ♦♦

Doubling ICS Dose Is Ineffective for Asthma Flares

ASTHMA exacerbations are common even in patients with mild disease and are an important source of morbidity. Previous guidelines have recommended doubling the dose of inhaled corticosteroids (ICS) at the time of exacerbations. However, there are no randomized controlled trial data to support this recommendation. This randomized trial compared two approaches to managing asthma exacerbations: doubling the dose (DD) or continuing the maintenance dose (MD) of ICS.

The 6-month, prospective study included 290 patients taking a stable dose of ICS for asthma. Patients were randomized to either the DD or MD strategy, in case an exacerbation occurred. The two groups were comparable at baseline: mean age 33.5 years, FEV_1 2.8 L, and peak expiratory flow 422.9 L/min. The main outcome of interest was failure to regain disease control after the assigned treatment, as evidenced by the need for an oral steroid or an unscheduled medical visit.

Forty-six patients had asthma exacerbations during the study. The treatment failure rate was 41% in the DD group and 40% in the MD group. Most treatment failures in the DD group resulted from the need for systemic steroids; in the MD group, failure of asthma to return to baseline was the most frequent reason. Patient compliance was high in both groups.

For patients who experience asthma exacerbations while on maintenance ICS, doubling the dose seems to have little effect on the outcome of the exacerbations. Most such exacerbations seem to be of relatively short duration, even while continuing the maintenance dose.

COMMENT: *Asthma guidelines have recommended doubling the dose of maintenance ICS to treat or prevent progression of asthma flares. This Canadian group performed a prospective, randomized, double-blind trial comparing continued maintenance dose (MD) or doubling the dose (DD) at the point of exacerbation. Treatment failure was equivalent in both groups with the major component of treatment failure being asthma instability (23 on MD; 13 on DD). These observations agree with a prior study by Harrison et al.* Lancet. *2004;363:271-275). An excellent editorial by Busse and Lemanske outlines the reasons that may explain the ineffectiveness of this maneuver. For the moment, a prednisone burst appears to be a better alternative.*
E. J. B.
Fitzgerald JM, Becker A, Sears MR, et al: Doubling the dose of budesonide versus maintenance treatment in asthma exacerbations. **Thorax**. 2004;59:550-556. ♦♦

ICS Before Age 2 Improves Outcomes of Recurrent Bronchial Obstruction

THERE are few data to guide the use of inhaled corticosteroids (ICS) for recurrent wheezing in children under 2 years old. One large, randomized trial found that starting ICS in before age 2 in children with asthma led to improvements in lung function. Data from a Norwegian birth cohort study were used to examine the frequency of ICS treatment for recurrent bronchial obstruction in the first 2 years of life, and the possible effects on pulmonary function.

The study included 3,745 healthy newborns enrolled in the Environment and Childhood Asthma study in Oslo. By 2 years of age, 306 of the children had had at least two episodes of bronchial obstruction, or a persistent episode lasting longer than 4 weeks. These cases were matched to the same number of controls without bronchial obstruction. Tidal flow/volume measurements were performed at presentation and at age 2 in 21 cases who were treated with ICS, mean duration 10.3 months; and in another 33 cases who did not receive ICS. Fifteen controls also underwent lung function measurements.

In the entire birth cohort, 77 children received inhaled corticosteroids during the first 2 years of life, a rate of 2.1%. Among the children with recurrent ➤➤

bronchial obstruction, the rate of ICS treatment was 21%. Children with recurrent bronchial obstruction were similar to controls in most characteristics, including skin prick test results, maternal smoking, parental atopy, and total IgE, although they were more likely to have atopic dermatitis.

At presentation, the ratio of time to peak expiratory flow/total expiratory time (tPTEF/tE) was significantly lower in the ICS-treated children with recurrent bronchial obstruction than in untreated cases. In both case groups, tPTEF/tE was significantly lower than in controls. The ICS-treated cases showed a modest, borderline significant increase in tPTEF/tE from presentation to age 2. This change was significantly correlated with the duration of ICS treatment. By follow-up, the reduction in lung function among ICS-treated cases had disappeared.

Less than one-fourth of children with recurrent bronchial obstruction before age 2 are treated with ICS. Those children who receive ICS have reduced lung function, even compared to non-ICS-treated children with recurrent bronchial obstruction. This difference disappears by age 2, with the magnitude of improvement depending on the duration of ICS therapy.

COMMENT: *It has been demonstrated that delay in instituting ICS in children with asthma results in sustained loss of lung function. However, this has not been verified in infants and small children less than 2 years of age. Given the availability of nebulized ICS and persistent concern about growth effects of ICS use, particularly in infants and small children, objective evidence of efficacy is needed. This study demonstrates that only a small percentage of young children with asthma receive ICS. However, it appears that lung function is marginally improved in these children, compared to those who do not receive ICS. This suggests a good risk-benefit ratio for the judicious use of ICS in infants and small children who wheeze.*

G. D. M.

Devulapalli CS, Haaland G, Pettersen M, et al: Effect of inhaled steroids on lung function in young children: a cohort study.

Eur Resp J. 2004;23:869-875. ♦♦

In Occupational Asthma, Improvement Continues for Years After Exposure Ends

IN patients with occupational asthma (OA), removal of the offending exposure often results in improvement of the asthma, though usually not in complete cure. The authors performed a detailed analysis of long-term recovery in the methacholine responsiveness curve among workers with OA in the years after cessation of exposure.

The study included 80 workers with OA for whom the causative exposure had been removed. Most were men; average time of exposure with symptoms was over 3 years. All underwent at least two assessments of the provocative concentration of histamine causing a 20% reduction in FEV_1, and were followed up for at least 2 years after removal of the exposure. The "Carma" software program was used to analyze the shape of the PC_{20} recovery curve. The slope of recovery was analyzed over the first 2.5 years in 55 patients, and from 2.5 years to the end of follow-up in 56 patients

Expressed as the natural logarithm of PC_{20} per year, the slope of recovery was 0.27 during the first 2.5 years of follow-up and 0.09 from 2.5 years onward. Although both slopes were significantly different from zero, the slope was significantly steeper during the first 2.5 years. Factors affecting the recovery curve included time since removal of the exposure, patient sex, and baseline PC_{20} and FEV_1.

For workers with OA, the rate of improvement in PC_{20} is greatest in the first 2.5 years after cessation of occupational exposure. However, improvement continues at a slower rate for years afterward. The findings may have important implications for disability assessment in workers with OA.

COMMENT: *This study is important because it documents that avoidance of agents causing OA results in a rapid and sustained improvement in lung function evidenced by decreased methacholine sensitivity--a harbinger of airway inflammation. The authors followed 56 patients and demonstrated a sustained improvement in PC_{20} after removal from the occupational exposure. The improvement was most rapid over the first 2.5 years of observation. This suggests that altering work environments to include avoidance of the offending occupational agent can have a rapid and sustained therapeutic effect.*

G. D. M.

Malo J-L, Ghezzo H: Recovery of methacholine responsiveness after end of exposure in occupational asthma.

Am J Respir Crit Care Med. 2004;169:1304-1307. ♦♦

Reduced Lung Function Linked to Measures of Low SES

RELATIVELY few studies have examined the relationship between socioeconomic status (SES) and respiratory diseases. The data that do exist have included mainly individual-level measures of SES. Data from a large, population-based cohort were used to examine the relationship between pulmonary function and SES, including both individual and regional measures of SES.

The analysis included nearly 23,000 men and women aged 39 to 79 years, identified from Norfolk, U.K., general practices. The subjects were recruited between 1993 to 1997 as part of the European Prospective Investigation into Cancer. In addition to individual educational status and occupational social class, the Townsend Deprivation Index was used to assess deprivation in the areas in which subjects lived. The effects of SES measures on FEV_1 were assessed in regression models.

Current smoking was similarly prevalent in women and men, although women were more likely to be never-smokers. For all three measures, being of lower SES was associated with lower pulmonary function: doing ➤➤

manual labor, having low educational attainment, and living in a deprived area. All three were independent predictors of low pulmonary function, even after controlling for smoking.

In addition to social class and education, living in a socioeconomically deprived area is associated with reduced pulmonary function. Several factors could account for the effects of deprivation, including poor housing conditions, overcrowding, exposure to environmental tobacco smoke, low lung function at birth or during childhood, and diet and physical activity. The effects of SES on pulmonary function are modest, especially compared to smoking.

COMMENT: *Socioeconomic status has been suggested as a risk factor for asthma activity. Environmental determinants such as cigarette smoking (including secondhand smoke exposure) and allergen exposure have been advanced as reasons for the SES-asthma link. This study demonstrated that being of working-class, low-educational status and living in a socially deprived area were all associated with decreased lung function. These data may be useful in further identifying at-risk individuals for early intervention. Examining environmental factors in deprived areas may also provide potential prophylactic measures against developing asthma.*
G. D. M.
Shohaimi S, Welch A, Bingham S, et al: Area deprivation predicts lung function independently of education and social class.
Eur Resp J. 2004;24:157-161. ♦♦

Does a 3 mm Wheal Accurately Reflect Cat Allergy?

THE standard for diagnosis of immediate hypersensitivity is a 3 mm diameter wheal in response to skin prick testing. Nevertheless, there are sparse scientific data to validate this assumption. The ability to measure specific IgE levels provides a new approach to interpreting the results of skin prick tests. Skin prick testing and specific IgE measurement were performed to assess the optimal wheal size for diagnosing cat allergy.

The study included 45 patients referred for clinical evaluation of rhinoconjunctivitis, with or without mild intermittent asthma. All underwent skin prick testing using the Greer Dermapik device. Other evaluations included measurement of allergen-specific IgE level using the Pharmacia CAP FEIA method and nasal challenge with a standardized cat pelt extract, 10,000 BAU/mL.

Of 24 patients with no history of cat sensitivity, all had negative results on specific IgE measurement. Most had a completely negative response to nasal challenge, including symptom score, prostaglandin D_2, and tryptase. All but 3 had skin wheals of less than 3 mm diameter.

The remaining 21 patients did have a history of cat allergy. Of these, 16 had wheal diameters of 6 mm or larger on skin prick testing. Eleven tested positive for cat-specific IgE and had a completely positive response to nasal challenge. The traditional 3 mm wheal criterion had high sensitivity for cat allergy, but relatively low specificity. The optimal skin prick response to distinguish patients with true cat allergy was a 6 mm wheal.

In patients referred for evaluation of possible allergy, using the traditional criterion of a 3 mm wheal in response to skin prick testing seems to overestimate the percentage of patients with cat allergy. The criterion of a 6 mm wheal appears "more realistic" for diagnosis or exclusion of clinically relevant cat allergy, the investigators conclude.

COMMENT: *Much of our clinical information on the interpretation of skin tests was derived before the availability of more sophisticated immunologic measurement of IgE-mediated reactions. This carefully done study correlates skin test reactivity with important objective clinical and immunologic findings, which further improves our understanding on the importance of skin test reaction size and the potential variability among antigens. Further study on other antigens are needed to enhance our diagnostic acumen.*
A. M.
Zarei M, Remer CF, Kaplan MS, et al: Optimal skin prick wheal size for diagnosis of cat allergy.
Ann Allergy Asthma Immunol. 2004;92:604-610. ♦♦

Cetirizine Has Greater Antihistamine Activity Than Desloratadine

CETIRIZINE and desloratadine are both potent antihistamines with confirmed efficacy in the treatment of seasonal allergic rhinitis and chronic urticaria. The two drugs were compared for their ability to suppress wheal-and-flare responses to histamine in healthy volunteers.

The study included 18 healthy men and women with no evidence of clinical disease or allergies. In a randomized, three-way crossover design, the subjects were studied after receiving a single oral dose of cetirizine, 10 mg; desloratadine, 5 mg; and placebo. On each study day, histamine skin prick tests were performed at intervals to from 30 minutes to 24 hours after dosing, and the areas of the wheal-and-flare responses were measured.

For both antihistamines, the curves for inhibition of wheal and flare responses were well below those for placebo from 1 to 24 hours. Cetirizine had the lowest mean area under the curve (AUC) for inhibition of flare area. For desloratadine, the mean AUC was between those of cetirizine and placebo. On pairwise comparison, cetirizine's activity was significantly greater than desloratadine's. For all subjects, cetirizine produced at least 70% wheal inhibition within 3 hours.

In healthy volunteers, cetirizine is more effective in suppressing histamine-induced skin responses than desloratadine. Cetirizine also offers a short onset of action, with less interindividual variability than desloratadine.

COMMENT: *As managed care formularies continue to inform our patients that all the antihistamines "are the same," this type of relevant comparison is use-* ➤➤

ful. It is important to recognize that suppression of skin test wheal and flare may not correlate with control of airway inflammation in all allergic patients.
A. M.
Purohit A, Melac M, Pauli G, Frossard N: Comparative activity of cetirizine and desloratadine on histamine-induced wheal-and-flare responses during 24 hours. **Ann Allergy Asthma Immunol**. 2004;92:635-640. ♦♦

Long-Term Budesonide Doesn't Affect HPA Axis Function in Children

THE potential for effects on the hypothalamic-pituitary axis (HPA) is a key concern with the use of inhaled corticosteroids in children. Studies of the HPA axis in children commonly rely on noninvasive measurements of 24-hour urinary free cortisol excretion. However, responses to cortisol stimulation may provide a better indicator of the clinical significance of HPA suppression. Both types of tests were used to assess HPA function in children receiving long-term inhaled corticosteroids.

The study included 63 children with mild to moderate asthma enrolled in the Childhood Asthma Management Program (CAMP). The children received 3 years' treatment with inhaled budesonide 400 µg/d, nedocromil 16 mg/d, or placebo. Before treatment and after 1 and 3 years, the children underwent studies of HPA axis function: assessment of serum cortisol responses to adrenocorticotrophic hormone (ACTH) and measurement of 24-hour urinary free cortisol excretion.

At all times, serum cortisol responses to ACTH stimulation were similar among treatment groups. The groups were also similar in terms of urinary cortisol excretion per body surface area, after adjustment for age, race, sex, and treatment center. Measures of HPA axis function were unaffected by cumulative inhaled corticosteroid dose. Children receiving budesonide were less likely to need supplemental inhaled corticosteroids and used less oral corticosteroid than patients in the nedocromil and placebo groups.

Asthmatic children taking budesonide 400 µg/d show no alteration in HPA axis function at up to 3 years' follow-up. The findings of 24-hour urinary free cortisol measurement are consistent with responses to cortisol stimulation.

COMMENT: *Research studies that result in "negative" (normal) information are usually not that interesting to read. However, they often provide very important safety information, when relating to long-term effects of a chronic therapy. Such is the case with this outcome measurement of the CAMP, which demonstrates no effects of chronic budesonide inhalation on HPA axis function in children over a 3-year treatment period.*
J. A. A.
Bacharier LB, Raissy HH, Wilson L, et al: Long-term effect of budesonide on hypothalamic-pituitary-adrenal axis function in children with mild to moderate asthma. **Pediatrics**. 2004:113;1693-1699. ♦♦

High Endotoxin Levels Protect Against Eczema in At-Risk Infants

EXPOSURE to endotoxin in early childhood has been suggested as a protective factor against allergic diseases, including asthma and eczema. As part of the Home Allergens and Asthma Study, the relationship between endotoxin exposure and eczema during the first year of life was assessed in children at risk for allergy.

The prospective birth cohort study included 498 children born in the Boston area and having at least one parent with a history of asthma or allergies. In 401 homes, samples of living room dust were obtained for endotoxin measurement. This and other variables were evaluated as predictors of physician-diagnosed eczema during the first year of life.

Twenty-eight percent of the children were diagnosed with eczema before 1 year old. Paternal but not maternal history of eczema was significantly associated with eczema in the child; parental history of other atopic diseases did not affect the infants' risk of eczema. Babies born in the fall were more likely to develop eczema than those born in other seasons. Other factors--including levels of allergens in the home, birth weight, dietary factors, and exposure to older children--were not significantly associated with eczema.

On multivariate analysis, home endotoxin levels were significantly and inversely associated with the development of eczema during the first year of life. The accompanying odds ratio (OR) was 0.76 per quartile increase in endotoxin level. Having a dog at home was also inversely related to endotoxin level, although this factor was nonsignificant when endotoxin was added to the multivariate model. Paternal history of eczema was an independent predictor of eczema in the child, OR 1.91; as was maternal positivity for specific IgE to one or more allergens, OR 1.61.

For infants with a parental history of asthma or allergy, high levels of endotoxin in home dust samples are associated with a reduced risk of physician-diagnosed eczema during the first year of life. Other risk factors include paternal, but not maternal, history of eczema; and maternal allergic sensitization. The effects of exposure to dogs, and the potential relationship between dogs and endotoxin levels in the home, are unclear.

COMMENT: *The "allergic" molecule of the decade may be the endotoxin. Endotoxins have been identified as a possible preventative nonallergic mechanism, switching Th2 to Th1, in the onset of asthma. In this study, investigators shift focus to elevate the role of the endotoxin in the prevention of eczema. Levels of household endotoxins correlated inversely with the risk of infantile eczema in children with a parental history of asthma, eczema, or allergies. Maternal sensitization to a single allergen increased the chances of eczema in the first year. There were no clear associations between allergen levels and endotoxin, including dog allergen. This is the first report of the protective effects of endotoxin in early infancy and the onset of infantile eczema. Wonder what the future holds--I can't wait to see more on this subject.*
A. L. L.

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Phipatanakul W, Celedón JC, Raby BA, et al: Endotoxin exposure and eczema in the first year of life. **Pediatrics**. 2004; 114:13-18. ♦♦

For Obese Asthmatics, Losing Weight Improves Lung Function But Not Airway Reactivity

DATA from population-based studies suggest that obese women have an increased prevalence of asthma. A randomized trial found that weight loss improved pulmonary function and quality of life in obese asthma patients, although the study did address airway reactivity. The effects of weight loss on bronchial reactivity, pulmonary function, and disease-specific health status were evaluated in obese women with asthma.

The prospective study included 58 obese women, body mass index greater than 30 kg/m^2, enrolled in a 6-month intensive weight loss program. Twenty-four of the women had asthma. Fifty women who completed the study lost an average of 20 kg, or 17.4% of baseline body weight. Mean weight loss was 8.0% for women in the lowest quartile of weight loss vs 18.8% for those in the upper three quartiles.

On pulmonary function testing, each 10% reduction in body weight was associated with a 92 mL improvement in forced vital capacity and a 73 mL improvement in FEV_1. However, there was no association between weight loss and bronchial reactivity. Women who lost more than 13% of baseline body weight had improvements in pulmonary function measures, whereas those with lower levels of weight loss did not. Regardless of amount of weight lost, women who completed the 6-month program had improved respiratory health status.

For obese women with asthma, losing weight leads to improvements in pulmonary function measures. The greater the weight loss, the greater the improvement in pulmonary function. However, airway reactivity is unaffected by weight loss. Thus the benefits of weight loss appear to reflect reductions in mass loading on the respiratory symptoms, rather than improvements in the asthma itself.

COMMENT: *Many recent studies have focused on quality-of-life issues and disease management of asthma. The prevalence of obesity continues to rise in the United States and in developed countries worldwide. A study of sedentary U.S. women found that certain polymorphic changes on the β receptor significantly increased the chances of developing adult-onset asthma. A second study from Magid and colleagues (*Ann Emerg Med. *2004;43:551-557) identified an association between poor quality of life with decreased physical activity and asthma-related ED visits. The current study also found adverse effects on pulmonary function in overweight asthmatics. Even a decrease in weight of 10% translated into improvement in FEV_1 and FVC. Although these changes do not alter bronchial hyperreactivity, improved lung function provides a greater "cushion" during asthma flares.*
A. L. L.

Aaron SD, Fergusson D, Dent R, et al: Effect of weight reduction on respiratory function and airway reactivity in obese women. **Chest**. 2004;125:2046-2052. ♦♦

High Rate of Allergic Rhinitis in Children With ADHD

ATTENTION deficit-hyperactivity disorder (ADHD) is a common pediatric diagnosis, affecting up to 9% of school-aged boys and 3% of girls. Like allergic rhinitis, ADHD is associated with problems related to sleep and cognitive functioning. Rates of allergic rhinitis and atopy were evaluated in children with diagnosed ADHD.

The study included 30 children and adolescents with physician-diagnosed ADHD, based on DSM-IV criteria, seen in an outpatient child psychiatry clinic. Twenty-three patients underwent screening for allergic rhinitis, including history, physical examination, and skin prick testing. The study focused on symptoms of stuffy or runny nose, itchy or watery eyes, sneezing, snoring or mouth-breathing, drainage in the throat, and yellow or green nasal discharge.

In the total group of 30 children with ADHD, 80% had two or more symptoms of allergic rhinitis. Of this group, 53% had other atopic disorders, including asthma in 42% and atopic dermatitis in 10%. None had been diagnosed or treated for allergic rhinitis. Of the 23 children undergoing skin prick testing, 61% had at least one positive result.

Clinical screening and skin prick testing of children with ADHD suggest a high rate of allergic rhinitis. Other atopic disorders and a family history of atopy are common as well. The sleep problems and learning impairments associated with allergic rhinitis might contribute to the cognitive and behavioral symptoms of ADHD. Some children with ADHD might benefit from evaluation and treatment of allergic rhinitis.

COMMENT: *This very interesting report raises many important issues for the clinical allergist. While not proving a cause-and-effect relationship between ADHD and allergic rhinitis, the two conditions frequently coexist. We all recognize that a child with uncontrolled allergic rhinitis will have trouble concentrating and learning. It is hoped the primary care community will use this information to further recognize the importance of allergic disease in children. I wouldn't be surprised if adults with ADHD had similar findings.*
A. M.

Brawley A, Silverman B, Kearney S, et al: Allergic rhinitis in children with attention-deficit/hyperactivity disorder.
Ann Allergy Asthma Immunol. 2004;92:663-667. ♦♦

PGD_2 Metabolite Shows Early Increase After Allergen Challenge

THE cyclo-oxygenase metabolite and bronchoconstrictor prostaglandin D_2 (PGD_2), generated by activated mast cells during allergic responses, may ➤➤

play a role in asthma. Previous studies of PGD_2 and its metabolites have focused on measurements in urine, bronchoalveolar lavage fluid, and sputum, not plasma. The primary PGD_2 metabolite 9α,11β-PGF_2 was evaluated as a plasma marker of mast cell activation in asthma.

The study included 32 patients with allergic asthma and 50 nonallergic controls. Gas chromatography/mass spectrometry was performed to measure baseline plasma and urinary levels of 9α,11β-PGF_2 in both groups. Other measurements included serum tryptase levels and urinary leukotriene E_4 (LTE_4). In addition, 10 randomly selected asthma patients were studied before and after specific bronchial allergen challenge.

At baseline, the asthma patients and controls had similar mean plasma and urinary levels of 9α,11β-PGF_2. Serum tryptase levels were comparable as well, although urinary LTE_4 was higher in the asthmatic group. After allergen challenge, the asthma patients had an early 5-fold increase in mean plasma 9α,11β-PGF_2: from 3.38 to 16.98 pg/mL. Levels of 9α,11β-PGF_2 returned to baseline within 2 hours. There was also a borderline significant increase in urinary 9α,11β-PGF_2 within 2 hours after allergen challenge. Serum tryptase was unchanged, but urinary LTE_4 increased 2.5-fold within 2 hours.

In patients with allergic asthma, the PGD_2 metabolite 9α,11β-PGF_2 increases sharply in response to bronchial allergen challenge. This plasma marker decreases to baseline within 2 hours after allergen challenge, at which time a modest increase in urinary 9α,11β-PGF_2 is observed. Plasma 9α,11β- PGF_2 appears to be a useful indicator marker of PGD_2 synthesis in asthma, and PGD_2 to play an active role in the early asthmatic response.

COMMENT: *Prostaglandin $D_2$2 is a major cyclo-oxygenase metabolite almost entirely generated by activated mast cells. It is a potent bronchoconstrictor in humans. Although debate continues as to the role of eosinophilic granulocytes in asthma, there is increasing evidence that mast cells play a key role in its pathophysiology. It is hypothesized that PGD_2 mediates the component of allergen-induced bronchoconstriction that remains resistant to antihistamines and antileukotrienes. Our ability to measure PGD_2 in plasma may open new doors to more precisely define the role of PGD_2 and the mast cell in the airway.*
E. J. B.

Bochenek G, Nizankowska E, Gielicz A, et al: Plasma 9α,11β-PGF_2 metabolite, as a sensitive marker of mast cell activation by allergen in bronchial asthma.
Thorax. 2004;59:459-464. ♦♦

"Add-On" Omalizumab Helps in Poorly Controlled Asthma

POORLY controlled, moderate to severe asthma carries high morbidity and mortality. Previous trials suggest that "add-on" anti-IgE therapy with omalizumab reduces exacerbations in patients with allergic asthma of varying severity. This open-label trial evaluated the use of omalizumab in patients with poorly controlled asthma, added to best standard care.

The randomized, multicenter European trial included 312 adolescent to adult patients with poorly controlled, moderate to severe allergic asthma. All were receiving inhaled corticosteroids: at least 400 µg/d of inhaled beclomethasone (or equivalent) for adolescents and 800 µg/d for adults. All patients were placed on best standard care, based on National Heart, Lung and Blood Institute guidelines. This consisted of daily treatment with moderate to high doses of inhaled corticosteroids, sometimes with a long-acting bronchodilator. In addition, patients were randomized in a 2-to-1 ratio to receive 12 months of omalizumab, at least 0.016 mg/kg/IgE sc every 4 weeks; or no further treatment.

The main outcome measure, mean annualized number of asthma deterioration-related incidents, was 9.76 per patient-year with best standard care vs 4.92 per patient-year with add-on omalizumab. Thirty-six percent of patients in the omalizumab group were completely free of such event during the study year, compared with 20% of controls. Anti-IgE therapy was also associated with a lower mean rate of clinically significant asthma exacerbations: 2.86 vs 1.12 per patient-year, respectively. Patients in the omalizumab group were also less likely to require rescue medication, with a higher absolute FEV_1 and lower symptom scores.

For patients with poorly controlled, moderate to severe allergic asthma, adding anti-IgE therapy to best standard care has significant clinical benefits, including a one-half reduction in asthma deterioration-related incidents. Other benefits include fewer exacerbations, reduced symptom scores, and reduced resource utilization. Add-on therapy with omalizumab has the potential to improve disease control and everyday functioning in patients with poorly controlled asthma.

COMMENT: *The introduction of inhaled steroids was a major advance in the treatment of asthma. Nevertheless, a significant number of asthmatic patients are unable to achieve complete control of their disease. These authors performed an open-label, parallel-group study to determine the effect of omalizumab on disease control in patients with severe asthma receiving the best standard care. This therapy reduced asthma deterioration-related incidents by 50%. Anti-IgE was complementary to long-acting β-agonists or leukotriene receptor antagonist add-on therapy. The mechanism by which anti-IgE improves asthma remains uncertain, and thus it remains to be determined whether anti-IgE might be beneficial to patients with nonallergic asthma.*
E. J. B.

Ayres JG, Higgins B, Chilvers ER, et al: Efficacy and tolerability of anti-immunoglobulin E therapy with omalizumab in patients with poorly controlled (moderate to severe) allergic asthma.
Allergy. 2004;59:701-708. ♦♦

REVIEWS OF NOTE

COMMENT: *Several times over the past four decades, Dr. Norman has published reviews of progress in allergy immunotherapy. His latest review covers 1999 to 2004, describing recently elucidated mechanisms, clinical results, altered antigen strategies, and sublingual administration possibilities. Since immunotherapy is what distinguishes our specialty more than anything else, this review--and the companion article on mechanisms--is bedrock stuff for every allergist.*
R. J. M.
Norman PS: Immunotherapy: 1999-2004.
J Allergy Clin Immunol. 2004;113:1013-1023. ♦♦

COMMENT: *If you suffer from cytokinophobia and your brain freezes at the mere mention of CD4+CD25+ T cells, this review of immunotherapy mechanisms is for you. Specific allergen immunotherapy acts through these Treg cells to produce IL-10 and TGFβ and thereby alter Th1/Th2 balance, and to produce IgG4. (There, that wasn't so painful.) Of course, you'll want to see the pretty pictures too.*
R. J. M.
Till SJ, Francis JN, Nouri-Aria K, Durham SR: Mechanisms of immunotherapy.
J Allergy Clin Immunol. 2004;113:1025-1034. ♦♦

COMMENT: *This excellent review examines the present level of knowledge for performing double-blind, placebo-controlled challenges in patients with suspected food allergy. The guidelines are especially focused on safety and feasibility of conducting such studies and on enabling future comparison of results from different centers.*
E. J. B.
Bindslev-Jensen C, Ballmer-Weber BK, Bengtsson U, et al: Standardization of food challenges in patients with immediate reactions to foods - position paper from the European Academy of Allergology and Clinical Immunology. **Allergy**. 2004;59:690-697. ♦♦

COMMENT: *Hospital consultation for drug allergy or anaphylaxis is the most common reason I am asked to see a patient in the hospital. This review provides a comprehensive summary of the potential causes of anaphylaxis associated with general anesthesia. One its strengths is an extensive table with medications and concentrations suggested for skin testing. The article is well-referenced. A personal criticism is the amount of discussion devoted to local anesthetics, a problem of minimal importance in my opinion.*
D. K. L.
Thong BY-H, Yeow-Chan: Anaphylaxis during surgical and interventional procedures.
Ann Allergy Asthma Immunol. 2004;92:619-628. ♦♦

COMMENT: *While exceptionally rare, human seminal plasma allergy (HSPA) causes significant morbidity in affected patients and their partners. This very thorough review includes discussion of HSPA's presentation, diagnosis, natural history, pathophysiology, differential diagnosis (such as latex allergy), and management.*
S. A. T.
Shah A, Panjabi C: Human seminal plasma allergy: a review of a rare phenomenon.
Clin Exp Allergy. 2004;34:827-838. ♦♦

COMMENT: *This literature review from the decade of the 1990s again reminds us that there are many unanswered questions when treating mild intermittent asthma. Given the fact that our current classification schemes and measurements of airway inflammation are imperfect, it seems prudent to continue to use anti-inflammatory medications for most asthmatic patients. We will continue to await the definitive answer to this question.*
A. M.
Van den Toorn LM: Clinical implications of airway inflammation in mild intermittent asthma.
Ann Allergy Asthma Immunol. 2004;92:589-594. ♦♦

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