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 Mouse!; or, Hickory-Dickory-Dock....

A recent study of inner-city children with asthma found mouse allergen in the homes of nearly all children. Many of the children were sensitized to mouse, and this risk increased with level of mouse allergen exposure at home. This study examined mouse allergen exposure and sensitization among middle-class, suburban children with asthma.

A total of 335 asthmatic children, aged 6 to 17 years, were recruited from three pediatric practices in suburban Baltimore and one city practice. Each child's home underwent a standard environmental assessment, including collection of dust samples for measurement of mouse allergen (Mus m 1) and other common allergens. The children underwent allergen skin testing; sociodemographic data were collected by parental questionnaire.

Seventy-seven percent of the children lived in the suburbs. Most of the families had annual incomes over $50,000; more than three-fourths of the mothers had been to college. Detectable levels of Mus m 1 were found in 75% of bedrooms, median level 22 ng/g; 80% of TV rooms, 28 ng/g; and 63% of kitchens, 17 ng/g. Skin tests were positive to mouse allergen in 13% of children overall, including 12% of suburban and 18% of city children. The prevalence of sensitization to mouse and other allergens was not significantly different between groups.

Predictors of high levels of mouse allergen in bedrooms included lower maternal education, living in the city, and higher levels of cockroach allergen in the bedroom. The higher the level of Mus m 1 exposure in the bedroom, the higher the risk of a positive skin test result to mouse. In addition, children sensitized to dog were 7 times more likely to have a positive reaction to mouse allergen.

As in inner-city children, middle-class suburban children with asthma have high rates of exposure to mouse allergen.Rates of sensitization to mouse are higher for children exposed to high levels of mouse allergen and those sensitized to dog. The effects of mouse allergen on asthma morbidity warrant further study. ➤➤

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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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COMMENT: *Suburban parents will certainly be surprised to learn that mouse allergen has been found in almost 70% of homes of asthmatic children living in suburban middle-class neighborhoods. Over 10% of children from those homes were sensitized to Mus m 1, the major mouse allergen. Although the association with bedroom cockroach allergen is plausible, the finding that sensitivity to dog dander carried a 7-fold increase in the risk of mouse allergy is perplexing. These Johns Hopkins researchers suggest that mouse allergen exposure may be more common than previously thought, even in suburban households. Is there really "a mouse in the house?"*
S. M. F.

Matsui EC, Wood RA, Rand C, et al: Mouse allergen exposure and mouse skin test sensitivity in suburban, middle-class children with asthma.
J Allergy Clin Immunol. 2004;113:910-915. ♦♦

Prevention Is Better Than Cure

ONE promising approach to primary asthma prevention is reduction of risk factors for families at high genetic risk. A multicomponent intervention for asthma prevention in high-risk infants was evaluated in a randomized, controlled trial.

The Canadian Asthma Primary Prevention study included 545 infants born to families with an "immediate" family history of asthma: a first-degree relative with asthma or two first-degree relatives with other IgE-mediated allergic diseases. Before birth, the infants were randomized to intervention and control groups. The multifaceted intervention comprised a range of allergen avoidance measures, including bed covers, applications of benzyl benzoate, avoidance of pets and smoking, encouragement of breast-feeding for at least 4 months, and avoidance of day care for the first year. Patients assigned to the control group received usual care. Outcomes assessment at age 2 included skin testing and evaluation by a pediatric asthma specialist.

At age 2, asthma was present in 19.5% of children overall: 16.3% in the intervention group vs 23.0% in the control group. Atopy was present in 14.5% of children overall, with no significant difference between the intervention and control groups. The study intervention was associated with a 60% reduction in persistent asthma and a 90% reduction in recurrent wheeze, compared with usual care.

Asthma was more likely for children exposed to maternal smoking, during either pregnancy or the first year of life. Infants with positive skin test results at age 1--particularly to foods--were more likely to have asthma by age 2. Children who went to day care were at lower risk of atopy.

Through age 2, a multicomponent intervention can reduce the risk of asthma for children at high genetic risk. The current analysis finds no significant effect on atopy risk. The authors plan to re-evaluate the study children when they reach school age.

COMMENT: *Current guidelines recommend the use of allergen avoidance measures, particularly in homes with infants of allergic families. These Canadian researchers analyzed preliminary data from an ongoing prospective study of infants followed for 2 years. The intervention group had lower levels of dust mite and pet allergens in the home. The study intervention also reduced exposure to tobacco smoke, encouraged breast-feeding, and delayed introduction of solid foods. These measures were effective in preventing asthma with a 60% reduced incidence of persistent bronchospasm. The authors will be following this cohort over the next 5 to 10 years. We look forward to their subsequent findings.*
S. M. F.

Becker A, Watson W, Ferguson A, et al: The Canadian asthma primary prevention study: outcomes at 2 years of age.
J Allergy Clin Immunol. 2004;113:650-656. ♦♦

U.S. Data Show Falling Rate of Asthma Death

PREVIOUS studies suggested that the rate of asthma mortality in the United States increased from the late 1970s through the late 1980s, leveling off during the 1990s. Recent trends in asthma death rates were analyzed, including correction for changes in the *International Classification of Diseases* (ICD).

The analysis used National Center for Health Statistics data on asthma deaths in the United States from 1977 through 2000. Per 100,000 population, the rate of deaths with asthma as the underlying cause increased from 0.8 in 1977 and 1978, to 2.0 in 1989, to 2.1 in 1994 through 1996. In 2000, the rate decreased to 1.6 per 100,000. This trend was only partially explained by classification changes introduced with ICD-10.

Rates of asthma death decreased for both sexes, but were consistently higher for women. With adjustment for age, asthma mortality was much higher for black patients than for whites.

The rate of deaths from asthma in the United States appears to have decreased since the late 1990s. This trend likely reflects improvements in asthma management and recent reductions in asthma prevalence.

COMMENT: *The author has extensive experience in reviewing and interpreting the epidemiology of asthma. This latest installment on the risk of death in asthma shows that asthma deaths have decreased since 1996. These data are complicated by a change in ICD-10, assigning deaths in subjects with both asthma and chronic obstructive pulmonary disease to "other chronic lower respiratory diseases." ICD-9 assigned such individuals to asthma. However, even after correction for this change, the mortality rate for asthma has improved significantly, decreasing from 2.0 per 100,000 population in 1998 to 1.6 in 2000. We have come a long way, but there is always room for improvement.*
D. K. L.
Sly MR: Continuing decreases in asthma mortality in the United States. **Ann Allergy Asthma Immunol.** 2004;92:313-318. ♦♦

Study Reports High Success Rate of Antibiotic Desensitization

INFECTIONS in patients with antibiotic allergy can pose a difficult challenge, especially when the organism is sensitive only to the antibiotic that the patient is allergic to. This problem is often seen in patients with cystic fibrosis (CF), who have high rates of antibiotic allergy. An experience with antibiotic desensitization is presented, focusing on newer antibiotics commonly used in CF patients.

The experience included 21 patients undergoing attempted antibiotic desensitizations at one children's hospital from 1996 to 2001. The patients were 15 females and 6 males, mean age 23 years; all but 2 had CF. Selection criteria included a history of IgE-mediated allergy to an antibiotic and/or a positive skin test result to that antibiotic or an antibiotic with known cross-reactivity. The desensitization protocol started at a dose of 2 µg or 1/1,000,000 of the therapeutic dose, given by 30-minute IV infusion. This was followed by 10-fold dose increases until the therapeutic dose was reached.

Desensitizations to 12 different antibiotics--most commonly piperacillin--were attempted. Of 57 attempted desensitizations, 43 were successful, a rate of 75%. Significant allergic reactions led to termination in 19% of attempts; in most of these cases, the reaction appeared to result from a non-IgE mechanism. None of the patients died or required other aggressive interventions. The remaining 5% of attempts were discontinued for other reasons.

Antibiotic desensitization provides an option for patients with serious infections that can only be treated by the antibiotic to which they are allergic. Using the patient selection and desensitization approaches described, the authors report a 75% success rate.

COMMENT: *This report provides very useful information for the clinical allergist. The authors provide their experience in successfully desensitizing 75% of 57 attempts in 21 pediatric and adult patients. They provide examples of protocols and orders which can be very helpful when attempting these challenging procedures. While the number of patients attempted with each drug is small, this experience from Boston Children's Hospital is a very important addition to the drug allergy literature.*
A. M.
Turvey SE, Cronin B, Arnold AD, Dioun AF: Antibiotic desensitization for the allergic patient: 5 years of experience and practice.
Ann Allergy Asthma Immunol. 2004;92:426-432. ♦♦

Severity Factors Predict Response to Omalizumab in Allergic Asthma

ANTI-IgE therapy with omalizumab can improve disease control for patients with allergic asthma who remain symptomatic despite inhaled corticosteroid therapy. Some patients respond better than others; information on which patients are most likely to benefit would aid clinical decision making. Factors associated with a good response to omalizumab for allergic asthma were analyzed.

The analysis included 1,070 allergic asthma patients from two randomized, placebo-controlled trials of omalizumab. All had persistent symptoms despite moderate- to high-dose inhaled beclomethasone dipropionate (BDP), mean dose 725 µg/d. Univariate and multivariate analyses were performed to identify baseline patient characteristics associated with clinical response.

On a composite measure of response, predictors of a higher likelihood of response to omalizumab were high BDP dose, history of emergency asthma treatment within the past year, and low FEV_1. For the 742 patients with at least one of these factors, the odds of response were 2.25-fold higher with omalizumab than placebo. ➤➤

For patients with all three severity indicators, the odds ratio increased to 4.20.

The percentage of patients responding to omalizumab increased from 38% at 4 weeks to 64% at 16 weeks. Of patients with a response to omalizumab at 16 weeks, 61% had responded by 4 weeks and 87% by 12 weeks.

For patients with allergic asthma, certain severity indicators predict a higher response rate to add-on therapy with omalizumab: high inhaled BDP dose, recent emergency treatment, and poor lung function. At least 12 weeks of treatment may be needed to ascertain response to omalizumab.

COMMENT: *While on the one hand the potential to eliminate circulating IgE is a "dream come true" for allergists, the availability of omalizumab has not been a panacea for our patients. Identifying patients who will benefit most from this drug is a critical issue, since the financial costs involved effectively prohibit the "let's give this a try" approach. The results of this pooled analysis suggest that improvement on omalizumab is independently related to markers of asthma severity (FEV_1 of 65% predicted or less; emergent treatment in the past year) and increasing doses of inhaled corticosteroid therapy (BDP dose over 800 µg/d).*
S. A. T.
Bousquet J, Wenzel S, Holgate S, et al: Predicting response to omalizumab, an anti-IgE antibody, in patients with allergic asthma.
Chest. 2004;125:1378-1386. ♦♦

Tacrolimus vs Cyclosporine for Atopic Dermatitis: Randomized Trial

THE immunosuppressant drugs cyclosporine and tacrolimus--with similar effects on T immune responses--have both been used to treat atopic dermatitis. No studies have directly compared these two treatments. This randomized trial compared topical tacrolimus with oral cyclosporine for treatment of AD in adolescents and adults.

Thirty patients with moderate to severe AD, mean age 27 years, were randomized to 0.1% tacrolimus ointment, applied twice daily; or oral cyclosporine, 3 mg/kg once daily. Outcome measures included the 0-to-103 SCORAD score, as well as symptom scores, sleep disturbance, and use of cetirizine rescue medication.

Both groups had significant reductions in SCORAD from baseline to the second week of treatment. However, the extent of improvement was greater with tacrolimus: from 69.0 to 54.7, compared to 73.7 to 67.3 in the cyclosporine group. The area under the curve for serial SCORAD over the 6-week study favored tacrolimus as well. Tacrolimus also yielded better results in terms of itching, erythema, sleep interference, and cetirizine use.

For adults with moderate to severe AD, topical tacrolimus and oral cyclosporine are both effective treatments. However, tacrolimus appears to offer a faster onset of action. Both immunosuppressants are safe, but cyclosporine has more potential for long-term side effects.

COMMENT: *Oral cyclosporine has been previously shown to be efficacious in difficult to manage children and adults with atopic dermatitis, although its potential for long-term side effects has limited its use. This small but well-controlled, head-to-head, 6-week trial compared the effects of oral cyclosporine (3 mg/kg/d) and topical tacrolimus (0.1% bid) in adolescents and adults with moderate to severe atopic dermatitis. Both treatments were efficacious. However, somewhat surprisingly, tacrolimus had a faster onset of action and produced greater improvements in symptom scores, sleep disturbance, and need for rescue antihistamine medication. These results add to the evidence supporting the use of topical calcineurin inhibitors as potent alternatives to topical corticosteroids for atopic dermatitis.*
S. A. T.
Pacor ML, Di Lorenzo G, Martinelli N, et al: Comparing tacrolimus ointment and oral cyclosporine in adult patients affected by atopic dermatitis: a randomized study.
Clin Exp Allergy. 2004;34:639-645. ♦♦

Genetics vs Early Exposures: How Do They Affect Asthma Onset and Remission?

MANY questions remain about the effects of early-life exposures on the risk and outcomes of asthma. A large body of questionnaire data was analyzed to assess congenital factors and childhood exposures affecting the onset and remission of asthma in childhood and adulthood.

The study included data on asthma history in over 18,000 participants in the clinical stage of the European Community Respiratory Health Survey (ECRHS). Asthma onset was defined as the patient's age at the first asthma attack; remission was defined as no asthma attacks or asthma treatment for 2 years.

Subjects with a family history of asthma or allergy were at higher risk of developing asthma, hazard ratio (HR) 1.89; with a lower chance of lifelong asthma remission, HR 0.79. Regardless of family history, subjects with acute respiratory infections in early life were at higher risk of asthma onset into adulthood: pooled HR 3.19.

Contact with older children early in life was associated with a reduced risk of asthma, HR 0.84; and an improved chance of childhood asthma remission, HR 1.50. Having pets reduced asthma risk in childhood only, HR 0.78. Exposure to mother's smoking had no effect on asthma in this study. Females were less likely to have asthma onset in childhood, HR 0.62; but more likely in adulthood, HR 2.01. The findings were consistent for patients with positive and negative results on specific IgE assays.

This large, retrospective study supports the importance of family history and early infectious exposures for subsequent asthma risk. Depending on the duration and type of exposure, infectious agents may increase or reduce the chances of a non-IgE, anti-inflammatory response. In this way, early environmental exposures may modify the genetic tendency to develop asthma. More study of these mechanisms is needed. ➤➤

COMMENT: *These researchers used data from the ECRHS to analyze retrospective questionnaires from 18,156 subjects. The interesting findings reaffirm that a family history of asthma and/or allergies as well as early, severe respiratory infections are associated with an increased risk of lifelong asthma. This study also reaffirms certain aspects of the hygiene hypothesis, particularly that contact with older children and pets has a protective effect against childhood asthma. Although the weakness of this report is the retrospective self-reporting, strengths include the large, multisite sample size. The bottom line is that this study adds fuel to the argument that it's not nature vs nurture, but an interaction of both.*
S. M. F.

de Marco R, Pattaro C, Locatelli F, et al: Influence of early life exposures on incidence and remission of asthma throughout life.
J Allergy Clin Immunol. 2004;113:845-852. ♦♦

Is Specific Immunotherapy Beneficial for Mite-Allergic Asthma Patients?

HOUSE dust mite (HDM) allergen is a leading cause of perennial asthma. Previous studies have suggested that specific immunotherapy may be of benefit for patients with asthma associated with HDM allergy. This study directly compared the efficacy of immunotherapy and standard drug treatment for patients with mild to moderate asthma and HDM allergy.

Ninety-five patients with mild to moderate asthma and a positive skin-prick response to HDM extract but no other perennial allergen were recruited for the study. About one-third were less than 18 years old. In a 1-year observational phase, the patients received standard therapy, consisting of guideline-adjusted drug treatment and allergen avoidance. They were then randomized to receive 3 years of active or placebo subcutaneous immunotherapy. Active immunotherapy consisted of a mixture of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* vaccine.

Seventy-two patients completed the study. Those receiving HDM immunotherapy had small but significant improvements in morning and evening peak expiratory flow. Active immunotherapy was also associated with reduced use of rescue bronchodilators and reduced skin sensitivity to HDM extract. There were no significant differences in asthma symptom scores, inhaled corticosteroid dosage, FEV_1, or bronchial responsiveness.

For patients with asthma and HDM allergy, specific immunotherapy has modest but significant benefits, when added to guideline-directed drug treatment. The results suggest that, for patients receiving optimal medical therapy, HDM sensitization may not be an important trigger for asthma exacerbations.

COMMENT: *These investigators studied the effect of HDM allergen immunotherapy in patients with allergic asthma. Although there was statistical significance for only marginal benefit with immunotherapy, there were several confounding factors. The problems with this investigation included the fact that a quarter of the patients were dropped before completing the study and that many patients may have been overtreated with inhaled corticosteroids. The sample size was relatively small, and all patients were monosensitized to HDM. In practice, we rarely use single-allergen immunotherapy. Although the statistical analysis suggested only marginal benefit with mite immunotherapy, in reality there is strong evidence documenting added benefit of specific immunotherapy for allergic asthma.*
S. M. F.

Maestrelli P, Zanolla L, Pozzan M, et al: Effect of specific immunotherapy added to pharmacologic treatment and allergen avoidance in asthmatic patients allergic to house dust mite
J Allergy Clin Immunol. 2004;13:643-649. ♦♦

In Preterm Infants, Perinatal Factors Affect Later Asthma Risk

THE rate of premature births among white patients has increased significantly over the last two decades. It is unclear whether preterm birth, and the associated in utero and perinatal exposures, contributes to later asthma risk. These questions were addressed in a follow-up study of former premature infants.

The analysis included a cohort of 404 children born prematurely at Cleveland-area hospitals between 1988 and 1993. Based on clinic visits at age 8 to 11 years, information on current asthma status was available for 251 former preterm infants: 97 were asthmatic and 154 were not. Various factors associated with prematurity were analyzed as risk factors for childhood asthma.

Compared to nonasthmatics, the children with asthma were more likely to be boys and African-American. The asthmatic children also had higher body weights and a higher rate of atopy. Maternal asthma was a significant risk factor, odds ratio (OR) 3.5. Children with asthma were more likely to have received perinatal respiratory support, including surfactant, mechanical ventilation, and postnatal corticosteroids. They were also more likely to have a history of chronic lung disease, OR 3.3.

Sepsis was actually associated with a lower rate of childhood asthma, OR 0.2. Girls who were small for gestational age were also at reduced asthma risk, OR 0.05.

For infants born prematurely, certain perinatal characteristics affect the subsequent risk of childhood asthma. Risk is particularly high, OR 14.2, for preterm infants requiring mechanical ventilation plus steroids. The protective effects of sepsis and of intrauterine growth retardation in girls warrant further study.

COMMENT: *Just because a child is born premature does not mean he or she will be more likely to become an asthmatic. However, this study of 251 former pre-term infants--now at age 8 to 11 years--would indicate that those infants who required both mechanical ventilation and postnatal systemic steroids are 14 times more likely to develop asthma! Other risk factors for asthma include African-American heritage (3 times), maternal history of asthma (3.5 times), and the development* ➤➤

of chronic lung disease (3 times). Interestingly, having neonatal sepsis decreased the risk (0.2 times) of developing asthma later in life!
J. A. A.
Grischkan J, Storker-Isser A, Rosen CL, et al: Variation in childhood asthma among former preterm infants.
J Pediatr. 2004;144:321-325. ♦♦

What Are Risk Factors for Recurrent Anaphylaxis in Children?

EVEN with accurate diagnosis and treatment, some allergic children have more than one episode of anaphylaxis. A previously reported cohort of children with anaphylaxis was followed up to determine rates of and risk factors for recurrent anaphylaxis.

In the previous study of 76 children referred for evaluation of anaphylaxis, nearly 80% had one or more positive skin-prick results to common inhalant or food allergens. Positive skin test results were less common in children with venom-induced allergy. Anaphylactic reactions to foods were more common in younger children and those with eczema, while exercise-induced anaphylaxis was associated with older age and urticaria-angioedema reactions.

The current analysis included 46 respondents to a follow-up telephone survey conducted by a pediatric allergist. During a mean 7-year follow-up, 30% of patients had recurrent anaphylaxis. Recurrences were two to three times more likely for patients with atopic dermatitis, either at the time of the initial study or at follow-up; and for those with urticaria-angioedema at follow-up. Over 90% of patients sensitized to one or more food allergens in the initial study had recurrent anaphylaxis.

At follow-up, 85% of patients were being treated with antihistamines, bronchodilators, and/or inhaled corticosteroids. Even though all of the children received self-injectable epinephrine at their first evaluation, only 39% still had an epinephrine kit at home.

For children with anaphylaxis, risk factors for recurrent episodes include atopic dermatitis, urticaria/anigoedema, and positive skin tests to food allergens. More effort is needed in education and monitoring of children with anaphylaxis and food allergies, including making sure they know how to use self-injectable epinephrine.

COMMENT: *There is very little information on the natural history of anaphylaxis in children. These Italian authors highlight risk factors for recurrence. Since inadvertent exposures to allergenic foods occur in childhood, greater efforts are needed to educate parents and care providers on the importance of readily available epinephrine for susceptible children.*
A. M.
Cianferoni A, Novembre E, Pucci N, et al: Anaphylaxis: a 7-year follow-up survey of 46 children.
Ann Allergy Asthma Immunol. 2004;92:464-468. ♦♦

Adverse Reactions Occur in Less Than 1% of SIT Injections

THE efficacy of specific immunotherapy (SIT) is now well-established, but there is continued concern about the risk of adverse--especially fatal--reactions. Despite controlled studies showing a low risk of systemic reactions (SRs), some countries have instituted regulations limiting the use of SIT. The safety of SIT for patients with allergic diseases was evaluated in a prospective monitoring study.

The study included 488 patients with allergic and/or asthma receiving SIT at 14 Spanish allergy departments. In all patients, SIT was given according to European guidelines using commercially available, biologically standardized dust mite or pollen extracts. The final analysis included 423 patients who completed SIT and had complete follow-up data.

In the experience of over 17,500 injections, local adverse reactions occurred in 11.9% of patients, or 0.6% of doses. Systemic reactions occurred in 3.7% of patients, or 0.3% of doses. All of the 53 SRs were rated as mild or non-life-threatening; there were no cases of anaphylaxis or life-threatening reaction.

No independent risk factors for SRs were identified. However, 5 patients had more than three SRs, for a total of 36. Stopping SIT in this group would have prevented 40% of all SRs.

This prospective study supports the safety of SIT for patients with rhinitis and/or asthma. Local and systemic adverse reactions occur in less than 1% of doses, with no life-threatening reactions in this series. The authors suggest a policy of discontinuing SIT in patients with three or more SRs.

COMMENT: *Immunotherapy is generally regarded in as a safe procedure in the United States. However, in the United Kingdom, safety concerns have led to guidelines that have virtually eliminated its availability to the average patient with allergic rhinitis and/or allergic asthma. The safety data on which U.S. satisfaction and U.K. concerns are based have been nearly exclusively retrospective. This prospective multicenter study from Spain involved 17,000 injections using pollens or mites (but not both) in nearly 500 patients. Systemic reactions occurred in 0.9% of injections. Although not powered to address fatality risk, the results support the conclusion that immunotherapy is generally safe. However, a small subset of patients account for a significant proportion of systemic reactions, suggesting that perhaps there should be a "three strikes and you're out" rule.*
S. A. T.
Moreno C, Cuseta-Herranz J, Fernández-Távora L, et al: Immunotherapy safety: a prospective multi-centric monitoring study of biologically standardized therapeutic vaccines for allergic diseases.
Clin Exp Allergy. 2004:34:527-531. ♦♦

Infants Exposed to Passive Smoking Have Reduced IL-10 Production

PREVIOUS studies have found reduced levels of dendritic cell interleukin-10 (IL-10) production in patients with asthma or atopy. This study evaluated the possible relationship between IL-10 and a key risk factor for childhood asthma: exposure to environmental tobacco smoke (ETS).

Production of IL-10 in stimulated dendritic cell cultures was measured by enzyme immunoassay for 37 healthy infants: 21 with and 16 without exposure to ETS. Cultures from blood samples obtained at 2 weeks and 3 months of age showed no difference in IL-10 production in the ETS-exposed and nonexposed infants.

However, by age 5 months, there was a significant difference. In the nonexposed group, the percentage of infants with detectable IL-10 increased from 25% at 2 weeks and 20% at 3 months to 36% at 5 months. In contrast, in the ETS-exposed group, the proportion with detectable IL-10 decreased from 33% at 2 weeks and 19% at 3 months to 7% at 5 months.

For infants exposed to ETS, production of IL-10 by dendritic cells decreases significantly during the first 5 months of life. The results raise the possibility that reduced IL-10 production could play a role in the relationship between ETS exposure and asthma/atopy risk in children.

COMMENT: *Interleukin-10 is an important cytokine with variable effects, including inhibition of cellular immunity and allergic inflammation and stimulation of humoral and cytotoxic immune responses. This small study provides support for an interesting hypothesis--infant exposure to ETS progressively decreases IL-10 production by peripheral blood dendritic cells. Thus, Th2 responses could be enhanced and viral infections become more severe with a decrease in IL-10 from tobacco smoke exposure. The net result would be increased childhood allergic symptoms and respiratory complications. This novel mechanism, if confirmed, might allow monitoring of at-risk children and, at the very least, provides more evidence to plead with parents not to light up.*
D. K. L.
Gentile D, Howe-Adams J, Trecki J, et al: Association between environmental tobacco
smoke and diminished dendritic cell interleukin 10 production during infancy.
Ann Allergy Asthma Immunol. 2004;92:433-437.

The Rush Is On!

SPECIFIC immunotherapy is the only effective treatment for patients with systemic reactions to Hymenoptera stings. Recent ultrarush immunotherapy protocols have reduced the time to reach the target maintenance dose from weeks to hours, but there are concerns about the safety of these approaches. An experience with a 1-day, ultrarush desensitization protocol for Hymenoptera allergy is reported.

Fifty-seven patients with IgE-mediated allergy to Hymenoptera venom went through the ultrarush protocol, which achieved a cumulative dose of 101.1 µg in 150 minutes. To reduce the chances of missing adverse effects, no antihistamines were allowed for 15 days before desensitization and during the protocol.

The ultrarush protocol was completed by all but 1 patient, who had a hypertensive crisis unrelated to attempted desensitization. Venom-specific IgE and other immunologic parameters were altered within 15 days. Skin prick test results became negative in 25% of patients and decreased significantly in another 25%. No adverse effects occurred in 64% of patients, while mild systemic reactions occurred in just 7%. Of 23 patients who were stung in the year after desensitization, none had more than a local reaction.

The authors' ultrarush protocol offers a safe and effective approach to Hymenoptera desensitization. Immunologic changes and clinical tolerance are quickly established, with no major adverse effects.
Schiavino D, Nucera E, Pollastrinni E, et al: Specific ultrarush desensitization in Hymenoptera venom-allergic patients.
Ann Allergy Asthma Immunol. 2004:92;409-413. ♦♦

RUSH immunotherapy can greatly reduce the time to reach a maintenance dose of allergen, at the risk of a higher rate of systemic reactions. Few studies have evaluated the safety of rapid immunotherapy to multiple allergens.

An experience of 65 patients receiving rush immunotherapy to multiple aeroallergens was reviewed. In a 1-day protocol, patients received a full course of immunotherapy extracts within 4 hours, followed by a 2-hour observation period. Patients were pretreated with prednisone, cetirizine, ranitidine, and zafirlukast or montelukast. Systemic reactions were graded from mild to severe.

Thirty-eight percent of patients had systemic reactions. All of these reactions occurred in response to the last 3 injections, and 72% after the final dose. About three fourths of reactions were rated mild and 20% moderate. There was just 1 severe reaction, a rate of 4%. This reaction, including a sharp drop in blood pressure, did not occur until 150 minutes after an injection. Patients with a higher degree of skin test sensitivity and those receiving extract with weed or dog allergen were more likely to have systemic reactions. Patient satisfaction was high.

This "fairly aggressive" protocol for rush immunotherapy with multiple aeroallergens has a systemic reaction rate higher than in conventional immunotherapy. However, most reactions are mild and manageable. A long observation period is needed, as reactions may be delayed.

COMMENT: *Allergists/immunologists should be aware of the growing data related to rush immunotherapy. Increasing co-pays for injections may eventually put traditional immunotherapy out of reach for many of our patients. Achieving maintenance in 1 day is an increasingly attractive option, even with the* ➤➤

higher systemic reaction rate. These two studies--from different continents and using different allergens--both conclude thatrush immunotherapy is practical. Venom rush immunotherapy results in less anaphylaxis, as shown by other studies. The rush is on!
D. K. L.
Harvey SM, Laurie S, Hilton K, Khan DA: Safety of rush immunotherapy to multiple aeroallergens in an adult population.
Ann Allergy Asthma Immunol. 2004;92:414-419. ♦♦

Do Antibodies to *S. aureus* Enterotoxins Affect Inflammation in Nasal Polyposis?

A previous study linked the presence of IgE antibodies to *Staphylococcus aureus* enterotoxins (SAEs) to eosinophilic inflammation in nasal polyp tissue. Relationships among SAE antibodies, aspirin sensitivity, and eosinophilic inflammation were assessed in patients with nasal polyps.

The study included 40 patients with nasal polyps undergoing sinus surgery. Based on responses to a bronchial aspirin challenge test, 13 patients were aspirin sensitive and 27 were aspirin tolerant. In surgical specimens, enzyme immunoassay was performed to measure interleukin-5 (IL-5) and eosinophil cationic protein (ECP), while the ImmunoCAP system was used to measure total IgE and specific IgE to a mix of three SAEs. Tissue samples from 12 healthy controls were studied for comparison.

Levels of IL-5, ECP, total IgE, and specific IgE to the SAE mix were significantly higher in patients with aspirin-sensitive nasal polyposis than in aspirin-tolerant patients or controls. On subgroup analysis of aspirin-tolerant patients, eosinophilic markers were significantly higher for patients who were SAE-positive than for those who were SAE-negative. In contrast, for aspirin-sensitive patients, SAE status was unrelated to inflammatory markers.

Among patients with nasal polyposis, those with aspirin sensitivity have increased IgE antibodies to SAEs in nasal polyp tissues, as well as increased levels of eosinophil-related mediators. For aspirin-tolerant patients, the presence of SAE antibodies is significantly related to markers of eosinophilic inflammation. The lack of such an association in aspirin-sensitive patients suggests that the immune response to SAEs is a disease-modifying factor distinct from aspirin sensitivity.

COMMENT: *Improving our current therapeutic strategies in asthma and chronic sinusitis depends in part on refining our understanding of the pathophysiologic differences between various disease phenotypes. The presence of specific IgE to* S. aureus *enterotoxins in nasal polyp tissue has generated interest. In this study,* S. aureus *enterotoxin-specific IgE levels were highest in aspirin-sensitive nasal polyp patients, although aspirin-tolerant nasal polyp patients had higher levels than controls. While the findings are exciting, additional studies are necessary to determine whether this enterotoxin is involved in the pathogenesis of NSAID sensitivity.*
S. A. T.
Pérez-Novo CA, Kowalski ML, Kuna P, et al: Aspirin sensitivity and IgE antibodies to Staphylococcus aureus *enterotoxins in nasal polyposis: studies on the relationship.*
Int Arch Allergy Immunol 2004; 133:255. ♦♦

Certainty Begins With Doubt

PREVIOUS trials have suggested that asthma patients using β_2-agonists on a regular basis may develop tolerance to these medications, with increased inflammation and increased asthma exacerbations. This meta-analysis examined the effects of regular β_2-agonist use on respiratory function and β_2 receptor function.

The analysis included 22 randomized, placebo-controlled trials, including 323 patients, of regular β_2-agonist use by asthma patients. In each study, patients assigned to regular β_2-agonists received at least 1 week of treatment; those in the placebo group were not permitted to use β_2 on an "as-needed" basis.

Patients taking regular β_2-agonists had no change in mean FEV_1 after treatment or in net FEV_1 treatment effect, compared with the placebo group. However, regular β_2-agonist use was associated with significant reductions in other measures, including an 18% decrease in peak FEV_1 response to later β_2-agonist treatment, a 35% reduction in FEV_1 dose response to β_2-agonists, and a 26% decrease in PC_{20} to bronchoconstrictor stimuli. Other findings included reduced leukocyte β_2-receptor density, binding affinity, and in vitro responsiveness to isoproterenol.

Asthma patients using β_2-agonists regularly for as little as 1 week develop tolerance to the effects of these medications. Regular β_2-agonist use may lead to increased airway inflammation and poorer disease control.

COMMENT: *Clinicians are faced with a variety guidelines recommending the use of regular, long-acting β-agonists in asthma. Investigative trials have shown no negative effect of regularly scheduled, short-acting β-agonists (*N Engl J Med. 1996;335:841-847.*) However, there is now a warning of potential fatality on salmeterol, and genetic evidence suggests that a sizable subgroup of patients may be at risk of negative outcomes if using regularly administered β-agonists. This meta-analysis included 22 studies: only one investigated severe asthma, while the majority were limited to mild or asymptomatic asthma. The conclusion is that regular use of either short- or long-acting β-agonists results in tolerance and may be associated with poorer disease control. A subgroup analysis showed no protective effect of inhaled corticosteroids. β-Agonists are a trusted ally in the war against asthma, but we should recall Shakespeare's advice, "Modest doubt is called the beacon of the wise."*
D. K. L.
Salpeter SR, Ormiston TM, Salpeter EE: Meta-analysis: Respiratory tolerance to regular β2-agonist use in patients with asthma.
Ann Intern Med. 2004;140:802-813. ♦♦

For HCV-Infected Asthma Patients, Response to Interferon Affects Response to Salbutamol

AMONG patients with chronic obstructive pulmonary disease, infection with hepatitis C virus (HCV) has been linked to an accelerated decline in lung function. This loss of lung function is unaffected by treatment with interferon. The current study looked at relationships among decline in lung function, and airway response to salbutamol in HCV-infected patients with asthma.

The study included 55 asthma patients positive for HCV. All patients received 6 months of treatment with interferon-α; 18 had a virologic response. From year 1 to years 3 and 6 after treatment, pre- and post-bronchodilator FEV_1 decreased only in the patients without a virologic response to interferon. Interferon nonresponders also had lower reversibility with salbutamol at 3 and 6 years. This was so on comparison with the interferon responders and with non-HCV-infected asthma patients. The rate of decline in salbutamol reversibility was also sharper in the interferon nonresponders.

However, interferon nonresponders had increased reversibility with oxitropium at both 3 and 6 years, compared to either comparison group. They also showed a sharp increase in oxitropium reversibility during follow-up. The rate of decline in carbon monoxide diffusing capacity was faster in interferon nonresponders, compared with interferon-responders or HCV-negative asthmatics.

For HCV-infected asthma patients who do not have a virologic response to interferon, pulmonary function decreases more rapidly than in interferon responders or non-HCV-infected asthma patients. Interferon nonresponse is also associated with reduced salbutamol reversibility.

COMMENT: *Prior studies have observed that selected patients with chronic viral infection fail to respond to anti-asthma therapy. These authors studied 55 HCV-positive asthmatics who were given interferon-α for 6 months. They observed a significant decrease in response to salbutamol at 3 and 6 years in those who failed to respond to interferon. In contrast, response to oxitropium at 3 and 6 years was significantly higher in interferon non-responders. Since chronic viral infection increases CD8+ T lymphocytes in the airways and parenchyma, the authors speculate that these cells cause asthma with COPD-like inflammation that responds poorly to salbutamol, but better to an anticholinergic agent. This study has many possible implications for how viral infections may alter the course of asthma and its response to therapy.*
E. J. B.

Kanazawa H, Yoshikawa J: Accelerated decline in lung function and impaired reversibility with salbutamol in asthmatic patients with chronic hepatitis C virus infection: a 6-year follow-up study.
Am J Med. 2004;116:749-752. ♦♦

Prospective Study Tracks Onset of Occupational Asthma in Bakers

BAKERS are a high-risk group for respiratory allergies related to occupational exposures. Apprentice bakers were prospectively studied to clarify the incidence, risk factors, and course of respiratory allergy in bakers.

The study included 287 apprentice bakers, first evaluated before starting a vocational training program. Assessments included a questionnaire, skin-prick testing to occupational and common allergens, and measurement of total and specific IgE levels.

Occupational chest symptoms occurred during the first year in 4.2% of subjects and the second year in 8.6%. Rates of hypersensitivity to occupational allergens were 4.6% and 8.2%, respectively. At 2 years, occupational allergic rhinitis was diagnosed in 12.5% of apprentice bakers and occupational asthma/cough-variant asthma in 8.7%.

Just 20% of bakers with occupational asthma had allergic rhinitis at their previous assessment. Of 25 affected workers, 84% had chronic cough as their only symptom. Independent risk factors for hypersensitivity to occupational allergens were positive skin-prick results to common allergens, odds ratio (OR) 10.6; occupational rhinitis, OR 3.9; and occupational asthma, OR 3.9. Subjects who had a positive skin-prick response to occupational allergens when entering the training program were at increased risk of occupational asthma, OR 6.9.

This study documents the high risk of occupational asthma and rhinitis among apprentice bakers. The main risk factor for occupational asthma in this group is positive skin-prick results to common and occupational allergens. Most bakers with occupational respiratory symptoms are sensitized to a specific allergen; in those with occupational asthma, rhinitis and chest symptoms usually develop around the same time.

COMMENT: *This study represents a rare, prospective look into the incidence, risk factors and natural history of occupational allergy in apprentice bakers in Poland. Sensitivity to work-related allergens, verified using specific challenge tests, developed in 8.2% of subjects after 2 years of exposure. Interestingly, sensitization to common allergens preceded work-related rhinitis in 69% of cases and asthma in 64%. Chronic cough developed at the same time as rhinitis and was often the sole manifestation of asthma.*
E. J. B.

Walusiak J, Henke W, Górski P, Palczynski C: Respiratory allergy in apprentice bakers: do occupational allergies follow the allergic march?
Allergy.2004;59:442-450. ♦♦

TLR Defect Causes Lack of Resistance to *S. pneumoniae*: case report

THE toll-like receptor (TLR) family appears to play a key role in controlling the innate immune system, but many questions remain about the how TLRs affect resistance to infection. The case of a young boy with a profound deficiency in TLR signaling are presented.

The child, first seen at age 9 months, had repeated episodes of *Streptococcus pneumoniae* bacteremia. In the absence of classic immunodeficiencies, NF-κB translocation and cytokine mRNA and protein expression studies were performed to assess TLR signaling responses to various TLR- and interleukin-1-receptor (IL-1R)-specific agonists. The results showed a severe deficiency of the TLR/IL-1R signaling pathway, leading to failed recognition of whole bacteria as well as various bacterial components. At the same time, the patient showed intact expression of interleukin receptor associated kinase-4 and translocation of NF-κB.

A child with a TLR-mediated defect of cytokine production but intact antibody responses is reported. The findings in this case highlight the importance of TLR signal--independent of NF-κB translocation--in defending against pyogenic infections.

COMMENT: *Early in our quest for knowledge about normal human humoral and cellular defense mechanisms, careful study of individual patients with severe infections gave valuable clues as to the nature of adaptive immunity. Now it is apparent that innate immunity with intact toll-like receptors (TLRs) is equally important for a normal immune response to infections. This report involves a 3-year old with a severe defect in TLR signaling, which rendered him defenseless to* S. pneumoniae infections. *Again, study of this "lesson from nature" points the way to knowledge of the norm! (See the review of this subject in* J Pediatr. *2004;144:421-429.)*
J. A. A.
Currie AJ, Davidson DJ, Reid GSD, et al: Primary immunodeficiency to pneumococcal infection due to a defect in toll-like receptor signaling.
J Pediatr. 2004;144:512-518. ♦♦

Immunologic and Clinical Findings in A-T: 100 Cases Reviewed

PATIENTS with ataxia-telangiectasia (A-T) have varying humoral and cellular immune abnormalities. The rarity of this genetic disorder makes it difficult to study the findings in a large group of well-characterized patients. The immunologic and clinical findings of 100 consecutive patients from an A-T referral center were analyzed.

The patients were referred between 1995 and 1999; median age at referral was 11.3 years. All but 1 of 80 patients tested had an elevated serum α-fetoprotein level. On analysis of immunoglobulin levels, 65% of patients had deficiency of IgG4, 63% of IgA, 48% of IgG2, 23% of IgE, and 18% of IgG. Seventy-one percent of patients had lymphopenia, while 75% had reduced B-lymphocyte numbers. CD4 T lymphocytes were reduced in 69% of patients and CD8 T lymphocytes in 51%.

The patients had many recurrent upper and lower respiratory infections, including otitis media, sinusitis, bronchitis, and pneumonia. Five patients developed sepsis, 2 during chemotherapy for cancer. Forty-four percent of patients had varicella infection with no complications, though the course was severe in 5%. There were no cases of *Pneumocystis jerovici* pneumonia, nor any complications related to live viral vaccines.

This large series of A-T patients documents many and varied immunologic abnormalities. However, rates of systemic bacterial and opportunistic infections are low and the immune defect does not appear to be progressive. More study will be needed to determine why some patients with A-T have high rates of infection.

COMMENT: *This is an impressive longitudinal study involving 100 cases of ataxia-telangiectasia (covering 1,127 patient years). Immunologlobulin deficiencies were common, especially IgG4, IgA, IgG2, and IgE. Also, lymphopenia occurred in three-fourths of patients. In spite of these deficiencies, many patients responded appropriately to childhood immunization, including live virus vaccines. Upper respiratory infections did not become more frequent over time, but the prevalence of lower respiratory infection increased with age. The risk of severe viral or opportunistic infections was low. An important observation was the lack of correlation between the degree of immune deficiency and the frequency of infections.*
J. A. A.
Nowak-Wegrzyn A, Crawford TO, Winkelstein JA, et al: Immunodeficiency and infections in ataxia-telangiectasia.
J Pediatr. 2004;144:505-511. ♦♦

The Beginning of Health Is Sleep

DAYTIME sleepiness is a common complaint in patients with seasonal allergic rhinitis. This symptom has been ascribed to trouble sleeping at night or to impaired sleep in general; there is debate over the contribution of obstructive sleep apnea. Subjective and objective sleep parameters were compared in patients with seasonal allergic rhinitis vs healthy controls.

The prospective study included 25 patients with seasonal allergic rhinitis and 25 healthy volunteers. Mean Epworth Sleepiness Scale score was 6.8 for the patients with allergic rhinitis vs 5.4 for healthy controls. The allergic patients also had significant decrements in most domains of quality of life on the SF-36. The changes in daytime sleepiness and quality of life were significantly related to each other.

However, polysomnography found no significant differences in oxygen saturation between allergic patients and controls. Although some sleep parameters were affected by seasonal allergic rhinitis, these were within normal limits and not considered clinically significant.

Patients with seasonal allergic rhinitis have increased daytime sleepiness and reduced quality of life com- ➤➤

pared with controls. However, there are no significant differences in objective sleep parameters. Daytime sleepiness appears to be related to seasonal allergic rhinitis itself, rather than to any problems with nighttime sleep.

COMMENT: *Daytime drowsiness is often mentioned as a problem by patients with seasonal allergic rhinitis. This study confirms significantly greater drowsiness compared to normal controls. Since sleep study events were unaltered in any clinically relevant way, the authors conclude that drowsiness is a direct effect of the allergic condition.*
R. J. M.
Stuck BA, Czajkowski J, Hagner A-E, et al: Changes in daytime sleepiness, quality of life, and objective sleep patterns in seasonal allergic rhinitis: a controlled clinical trial.
J Allergy Clin Immunol. 2004;113:663-668.

"Add-On" Antihistamine Therapy Is Beneficial in Atopic Asthma

FOR patients with asthma, second-line controller agents may be used in an attempt to minimize the necessary dose of inhaled corticosteroids (ICS). H_1 antihistamines, the mainstay of treatment for allergic rhinitis, are not usually recommended for asthma. This study compared the effects of the antihistamine fexofenadine with the leukotriene inhibitor montelukast for asthmatic patients receiving ICS.

The study included 18 patients with mild to moderate, persistent asthma. All were taking ICS therapy, mean dose 631 µg, which remained unchanged during the study. In randomized, crossover fashion, patients received 1 week of treatment with fexofenadine (180 mg), montelukast (10 mg), and placebo, with 1-week washout periods between treatments. The main outcome measure was the PC_{20} value in response to adenosine monophosphate (AMP) bronchial challenge.

Before each treatment, the AMP PC_{20} values were similar: around 70 mg/mL. Both active treatments brought significant improvements: 127 mg/mL with fexofenadine and 121 mg/mL with montelukast, compared to 78 mg/mL with placebo. Montelukast was associated with improved recovery after AMP challenge, with a 60-minute time-response curve of 352% min, compared to 758% min with fexofenadine and 683% min with placebo. Both fexofenadine and montelukast were associated with reduced exhaled nitric oxide levels, increased morning and evening peak expiratory flow, and reduced need for rescue salbutamol.

For asthma patients taking ICS, "add-on" therapy with fexofenadine offers significant improvement in bronchial responsiveness to AMP, as well as other inflammatory and diary outcomes. For many outcomes, the effect is comparable to that of "add-on" montelukast.

COMMENT: *Antihistamines are well known to have in vitro anti-inflammatory effects although the clinical relevance of these effects has not been generally accepted. In this crossover study, fexofenadine given as an "add-on" to inhaled corticosteroid therapy reduced both exhaled nitric oxide levels and bronchial responsiveness to adenosine. The effect was comparable to the "add-on" effect of montelukast. Additional studies using more traditional endpoints are necessary to validate the importance of these findings.*
S. A. T.
Lee DKC, Jackson CM, Haggart K, Lipworth BJ: Repeated dosing effects of mediator antagonists in inhaled corticosteroid-treated atopic asthmatic patients.
Chest 2004;125:1372-1377.

♦♦

Can Giving Medications at School Benefit Children With Asthma?

PARTICULARLY for young, urban children, poor compliance with asthma medications is a common problem. Various interventions have been tried to improve health outcomes for urban children with asthma. A program in which asthmatic children were administered inhaled corticosteroids in school was evaluated.

The study included 3- to 7-year-old children with mild to severe persistent asthma in an urban school district. Children randomized to the intervention group received daily inhaled corticosteroids at school, administered by the school nurse. Those in the control group received usual care, with no medications given at school. The main outcome measure was number of symptom-free days, as reported by parents.

A total of 184 children were enrolled from 54 schools; 180 had complete data for analysis. Parents of children in the intervention group reported greater improvement in quality of life: mean change score 0.63, compared with 0.24 in the usual care group. Children receiving-school-based care missed less school because of asthma, mean total difference about 2 days; and had more symptom-free days during the winter months, about 2 days per 2-week period. However, on post hoc analysis, all of the differences were attributed to children free from exposure to secondhand smoke at home. Nonexposed children in the intervention group also had improvement in overall symptom-free days, days in which rescue medication was needed, and acute visits for asthma.

Providing asthma medications at school improves symptom-free days and other outcomes for children with persistent asthma. However, the benefits are significant only for children not exposed to secondhand smoke.

COMMENT: *This paper attempted to study the effect of school-administered asthma medications in an asthma treatment program compared with routine outpatient care. Unfortunately, the study was able to analyze only 180 children and therefore was not powered to detect difference of 1 symptom-free day. Consequently, the results on the primary outcome measure of mean symptom-free days did not differ between the two groups. Although both groups had improvement in asthma symptoms in both groups, after post hoc analysis it was evident that the children who benefited from the school-based asthma program were those not exposed to secondhand smoke. The bottom line is* ➤➤

that school-based asthma treatment programs are feasible, although their benefit may be modest.
S. M. F.
Halterman JS, Szilagyi PG, Yoos L, et al: Benefits of a school-based asthma treatment program in the absence of secondhand smoke exposure.
Arch Pediatr Adolesc Med. 2004;158:460-467. ♦♦

REVIEWS OF NOTE

COMMENT: *Textbooks have been written on the subject of food allergies, but you can hardly do better than reading this 15-page review of the subject by one of the masters in the field. He covers the pathogenesis, clinical features, diagnosis, management, and prevention. The review is extensively referenced and full of interesting pearls.*
R. J. M.
Sampson HA: Update on food allergy.
J Allergy Clin Immunol. 2004;113:805-819. ♦♦

COMMENT: *This concise review summarizes articles in* JACI *2002-03 that dealt with the genetics, pathophysiology, and promoters of allergic respiratory disease. This is the "10,000-foot view" of important research in our specialty over the past 2 years.*
R. J. M.
Bochner BS, Busse WW: Advances in mechanisms of allergy.
J Allergy Clin Immunol. 2004;113:868-875. ♦♦

COMMENT: *The authors present a very useful review on an important clinical topic. The focus is a review on the published literature of nebulized budesonide, which has proven to be of great value in children who are too young to effectively use metered-dose inhalers.*
A. M.
Berger WE, Shapiro GG: The use of inhaled corticosteroids for persistent asthma in infants and young children.
Ann Allergy Asthma Immunol. 2004;92:387-399. ♦♦

COMMENT: *Our patients constantly ask us about what to do for their "severe" reactions to mosquito bites, and a subset actually do have systemic reactions. This is a thorough, well-referenced review of the subject, including an update on the development of recombinant allergens to aid in diagnosis and treatment.*
S. A. T.
Peng Z, Simons FER: Mosquito allergy: immune mechanisms and recombinant salivary allergens.
Int Arch Allergy Immunol. 2004;133:198-209. ♦♦

COMMENT: *This is an excellent summary of a recent NIH workshop on what needs to be done next in determining the relationship between obesity and asthma. Epidemiology as well as the mechanistic basis for airway responsiveness and risk for atopy are discussed. Mechanistic features--such as the role of leptin, the sympathetic nervous system, and genetic and gender influences--are all discussed. The article is extremely well referenced and provides the reader with a state-of-the-art review of what research directions are being pursued.*
G. D. M.
Weiss ST, Shore S: Obesity and asthma: directions for research.
Am J Respir Crit Care Med. 2004;169:963-968. ♦♦

COMMENT: *This executive summary provides a succinct review of the evidentiary strength supporting or refuting the relationship of potential side-effects to inhaled corticosteroid therapy. The references supporting the conclusions of the expert panel are not provided, but can be obtained in the complete publication (***Chest** 2003;124:2329-2340*).*
D. K. L
Leone FT, Fish JE, Szefler SJ, West SL: Systematic review of the evidence regarding potential complications of inhaled corticosteroid use in asthma: collaboration of American College of Chest Physicians, American Academy of Allergy, Asthma, and Immunology, and American College of Allergy, Asthma, and Immunology.
Chest. 2003;124:2329-2340. ♦♦

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