AllergyWatch®

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

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Salmeterol: More Good Than Harm!

THERE is continued controversy over whether overuse of β_2-agonists could contribute to the rising incidence of asthma-related mortality. Highly selective, third-generation β_2-agonists such as salmeterol and formoterol were developed to achieve long-lasting bronchodilator effects while reducing side effects. This randomized trial evaluated the effects of adding salmeterol to usual asthma care on asthma-related mortality and other safety outcomes.

The Salmeterol Multicenter Asthma Research Trial (SMART) included 26,355 patients aged 12 years or older with physician-diagnosed asthma. All patients were currently receiving asthma treatment, but those who had previously received long-acting β_2-agonists were excluded. Patients were assigned to receive salmeterol xinofoate--42 µg bid via metered-dose inhaler--or placebo, in addition to their usual drug treatment. The main study outcome was combined respiratory-related deaths or life-threatening experiences, ie, intubation and mechanical ventilation.

Because of safety concerns in African-American patients and problems with patient enrollment, the trial was halted after interim analysis of 26,355 patients. The overall risk of the main outcome was low and not significantly different between groups. However, patients assigned to salmeterol had small but significant increases in some outcomes, including asthma-related deaths, relative risk (RR) 4.37; and combined asthma-related deaths or life-threatening experiences, RR 1.71. Most of these increases occurred among African-American patients receiving salmeterol, with RRs of 4.10 for respiratory-related deaths or life-threatening experiences and 4.92 for asthma-related deaths or life-threatening experiences.

Overall safety outcomes are similar for asthma patients receiving salmeterol vs placebo added to their usual treatment. However, patients assigned to salmeterol show small but significant increases in some outcomes, including respiratory- and asthma-related deaths. The risk of such events appears higher in African-American patients--the reasons for this race-related difference in outcomes are unknown. ➤➤

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The following journals have been selected as the primary focus of review in the preparation of materials within "AllergyWatch®".

- Annals of Allergy, Asthma and Immunology
- Journal of Allergy and Clinical Immunology
- American Journal of Respiratory and Critical Care Medicine
- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
- Journal of Pediatrics
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal
- Pediatric Allergy and Immunology

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COMMENT: *Although it is tempting to explain away these data, the SMART study was a prospective trial powered to look at mortality. Salmeterol's association with mortality was observed in African-Americans after enrolling only half of the target number of study subjects. These facts compel us to take the data seriously. However, the drug's effect on mortality among asthma patients appears to be very small, and does not negate the fact that, when combined with inhaled corticosteroids, long-acting inhaled beta-agonists have arguably revolutionized the management of moderate to severe asthma in the past decade. How can we make sense out of these findings? Consider the choices we make when buying a car. Some of us choose a sports car over a sedan knowing that our risk of dying in a car accident is slightly higher with the smaller, lighter sports car. Others choose the sedan, forgoing any potential quality-of-life enhancements enjoyed by sports car drivers. It is unclear how the SMART study findings will impact our everyday practice. It may boil down to whether the patient wants (and can afford) a sports car or the full-sized sedan.*
S. A. T.

Nelson HS, Weiss ST, Bleecker ER, et al: The Salmeterol Multicenter Asthma Research Trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol.
Chest. 2006;129:15-26. ♦♦

ALTHOUGH short-acting inhaled β_2-adrenergic agonists can offer acute relief and short-term prevention of asthma symptoms, their regular use is ineffective in improving disease control. The newer long-acting β_2 agonists (LABAs) can be used regularly, without many of the problems related to short-acting drugs. Recent studies have raised the possibility of an increased risk of death in patients taking LABAs. The author reviews the literature and draws some conclusions regarding the benefits and potential problems of LABA treatment for asthma.

Several problems associated with the use of short-acting β-agonists have been identified, including unwanted receptor stimulation, the development of tolerance, declines in lung function, and an increased rate of cardiac events. The LABAs, in contrast, avoid these problems while providing a long-lasting bronchodilator effect with improved disease control. However, some recent prospective studies--notably including the "SMART" study--have suggested an increase in mortality among asthma patients receiving LABAs, especially African-Americans. These data have led the U.S. Food and Drug Administration to add a "black box" warning regarding an increased risk of asthma-related deaths to the labeling of salmeterol products.

In analyzing the SMART data, the author notes imbalances of asthma severity between the African-American and Caucasian patients enrolled. Most of the adverse outcomes in the study occurred in patients recruited in the first phase, a finding that is unexplained by racial differences in recruiting patterns. Although asthma-related deaths and other events were increased in the salmeterol group, these increases did not occur among patients who were receiving inhaled corticosteroids (ICS). Large case-control studies have found no link between LABA use and risk of hospitalization, ICU admission, or death.

The author questions the relationship between LABA use and increased risk of asthma-related deaths and other adverse outcomes. Rather than resulting from a direct toxic effect of β-agonists, these deaths may reflect limited access to medical care, if patients who derive symptom relief from β-agonist treatment delay seeking medical attention. The author suggests that LABAs should be used only in those asthma patients who are already taking ICS.

COMMENT: *The so-called SMART study of asthma has documented an association of fatal and near-fatal events with salmeterol use compared against placebo. This has resulted in a black-box warning in the package inserts for Serevent and Advair. In this analysis of the data, Dr. Harold Nelson, with his customary clarity and analytical precision, documents* ➤➤

the conclusions that can be drawn from the data. Like most therapies, a LABA can be a double-edged sword. LABAs with ICS provide better control than ICS alone, However, LABAs used without ICS might have a downside, perhaps especially in African Americans. The take-home: patients must use ICS with LABAs.
R. J. M.
Nelson HS: Is there a problem with inhaled long-acting beta-adrenergic agonists?
J Allergy Clin Immunol. 2006;117:3-16. ♦♦

The Die Is Cast Early in Asthma!

Studies suggest that most patients with persistent asthma develop symptoms in early childhood and that these symptoms track with age. Previous reports from the Tucson Children's Respiratory Study identified four phenotypes, based on the development of wheezing by age 3 years and active wheezing at age 6. Sixteen-year follow-up data of children in these four groups are presented.

Of 1,246 children enrolled in the population-based birth cohort study, 826 had complete follow-up data through age 16 years. Based on their findings at age 3 and 6, 425 children were classified as never-wheezers, 164 as transient early wheezers, 113 as persistent wheezers, and 124 as late-onset wheezers. Evaluations included a symptom questionnaire, conventional spirometry, and skin prick testing.

More than three-fourths of never-wheezers and transient early wheezers had no wheezing symptoms from age 8 to 16 years. In contrast, about half of persistent and late-onset wheezers reported wheezing at age 16. Atopy rates fell into a similar pattern. Compared with never-wheezers, forced expiratory flow between 25% and 75% of forced vital capacity at age 16 was decreased by a mean of about 260 mL/s for both the transient early wheezers and persistent wheezers. These groups also had significant reductions in FEV_1 and FEV_1/FVC ratio. For late-onset wheezers, pulmonary function at age 16 was similar to that of never-wheezers.

For children who develop asthma-like symptoms in the preschool years, the prevalence of wheezing and lung function values at age 6 years remain about the same through age 16. Children who wheeze by age 3 but not at age 6 are unlikely to wheeze later in childhood and adolescence, but they continue to have reduced lung function. The mechanisms determining lung function in early childhood may differ for transient early wheezers compared with persistent wheezers.

COMMENT: *This study again reinforces the significant value that the Tucson Children's Respiratory Study has provided us over the last 16 years. Supporting the Dunedin and Melbourne studies, levels of abnormal lung function were present by age 6 years and did not change by age16, in patients who had the phenotypic expression of asthma by age 6. This reinforces the need for early recognition in the hope that early intervention and treatment will change these trends.*
B. E. C.
Morgan WJ, Stern DA, Sherrill DL, et al: Outcome of asthma and wheezing in the first 6 years of life: follow-up through adolescence.
Am J Respir Crit Care Med. 2005;1253-1258. ♦♦

RECENT thinking suggests that asthma, traditionally regarded as a condition of reversible airway obstruction, may actually be associated with airway remodeling and permanent impairment. A group of children with moderate to severe allergic asthma were followed up to young adulthood.

Subjects were drawn from a group of 121 children, aged 5 to 12 years when enrolled in a randomized trial of immunotherapy as adjunct therapy for allergic asthma. Eighty-four subjects were available for re-examination at age 17 to 30 years. A week of high-dose oral prednisone followed by complete evaluation was offered to subjects whose postbronchodilator FEV_1, FVC, or FEV_1 was at or less than the 5th percentile, or who had two parameters at or less than the 10th percentile.

At follow-up, 48% of subjects had at least one spirometric result at or less than the 5th or 10th percentile. Of 28 subjects treated with prednisone and re-evaluated, 75% showed no improvement. Lung function results in childhood were significantly correlated with those in adulthood. Adults with abnormal spirometric results had a longer duration of asthma and increased methacholine responsiveness at the time of enrollment in the trial. They were also more likely to have been born prematurely, adjusted odds ratio 10.7. Adult lung function was no different for subjects receiving immunotherapy vs placebo as children.

Long-term follow-up demonstrates irreversible lung function deficits in adults who had moderate to severe allergic asthma as children. The spirometric findings in childhood are significantly correlated with the results in adulthood. Lung function parameters--along with other risk factors such as prematurity, longer duration of disease, and high methacholine sensitivity--might be useful in identifying asthmatic children whose airway obstruction is not easily reversible.

COMMENT: *These researchers report a longitudinal follow-up study of children diagnosed with asthma 20 years earlier. Data were collected on 84 of the original 121 patients. The most important finding was that lung function variables in adulthood directly correlated with those measured in childhood, indicating that chronic lung damage can begin early. Other risk factors included abnormal bronchial hyperreactivity as a child and prematurity. This study adds further support to the guidelines suggesting that vigorous anti-inflammatory therapy should begin early in childhood asthma.*
S. M. F.
Limb S, Brown K, Wood R, et al: Irreversible lung function deficits in young adults with a history of childhood asthma.
J Allergy Clin Immunol 2005;116:1213-1219. ♦♦

Can We Afford Not to Afford This Therapy?

RUSH immunotherapy (RIT) regimens offer important advantages over standard allergen-specific immunotherapy, but at a substantially increased risk of systemic reactions. The monoclonal anti-IgE antibody omalizumab was evaluated as an adjunct to increase the safety and efficacy of RIT.

The randomized, double-blind trial included 159 patients undergoing RIT for ragweed allergic rhinitis. Patients were assigned to 9 weeks of pretreatment with omalizumab, 0.016 mg/kg/IgE per month, or placebo pretreatment. They then underwent an active, 1-day RIT regimen, maximal dose 1.2 to 4.0 µg Amb a 1; or placebo immunotherapy. Treatment concluded with 12 weeks of omalizumab or placebo plus maintenance immunotherapy. Daily allergy severity scores and adverse events were compared among groups.

One hundred twenty-three patients received all study treatments, including 77% of the omalizumab plus immunotherapy group and 65% of the placebo plus immunotherapy group. Immunotherapy was associated with more than an 11-fold increase in ragweed-specific IgE levels, while omalizumab brought more than a 10-fold reduction in free IgE levels. Adverse events were less frequent and severe for patients receiving omalizumab plus immunotherapy, compared with immunotherapy alone. On post hoc analysis, adding omalizumab to active immunotherapy was associated with a 5-fold reduction in the risk of anaphylaxis. During the subsequent ragweed season, the omalizumab plus immunotherapy group had significantly lower allergy severity scores.

For patients undergoing RIT for ragweed allergic rhinitis, anti-IgE therapy with omalizumab can reduce the risk of serious allergic reactions. With further study, omalizumab pretreatment may provide a new approach to increasing the safety and effectiveness of allergen-specific immunotherapy.

COMMENT: *Allergen immunotherapy is a highly effective therapy for many IgE-mediated diseases, ranging from hay fever to asthma to venom allergy. Drawbacks include systemic reactions to the injections, and the long time to build up during conventional immunotherapy. Rush immunotherapy decreases the buildup time, but at the expense of more frequent systemic reactions. This study showed that 9 weeks of pretreatment with anti-IgE (omalizumab) significantly reduced the systemic reaction rate in an aggressive 1-day RIT with ragweed allergen. Pretreatment also improved the clinical severity scores during ragweed season, compared to patients not given omalizumab. In highly selected, special cases where the cost of omalizumab could be justified, this may be a strategy to consider.*

R. J. M.

Casale TB, Busse WW, Kline JN, et al: Omalizumab pretreatment decreases acute reactions after rush immunotherapy for ragweed-induced seasonal allergic rhinitis.

J Allergy Clin Immunol. 2006;117:134-140. ♦♦

Risk of Near-Fatal Reactions to Immunotherapy

FATAL reactions to allergen immunotherapy are rare, but do occur. Information on the incidence and characteristics of near-fatal reactions (NFRs) might help in developing preventive strategies. A survey of allergists was performed to investigate the occurrence of NFRs during allergen immunotherapy.

As part of a larger study of fatal and near-fatal reactions, a brief survey was mailed to 2,404 clinical practices affiliated with the American Academy of Allergy, Asthma, and Immunology (AAAAI). Of 646 respondents, 273 reported NFRs after immunotherapy injections--the study definition of NFR was respiratory compromise and/or hypotension requiring emergency treatment with epinephrine. A follow-up questionnaire elicited detailed information regarding the NFRs.

Analysis of 105 responses to the follow-up questionnaire suggested 68 confirmed NFRs, mean case incidence 4.7 per year. The incidence of confirmed NFRs was estimated at one event per 1 million immunotherapy injections--2.5 times more frequent than reported for fatal reactions. Most of the injections were prescribed by and occurred in the clinic of a board-certified allergist. Forty-six percent of patients with NFRs had asthma, compared to 88% of patients with fatal reactions. Eighty percent of NFRs were associated with hypotension and 10% with respiratory failure--all of these cases involved patients with asthma. Thirty percent of patients had no cutaneous signs. Epinephrine was delayed or not administered in 6% of NFRs, compared with 30% of fatal reactions.

The incidence of NFRs to allergen immunotherapy is estimated at one per 1 million injections. Prompt epinephrine administration is key to successful management of NFRs. The risk of severe respiratory compromise appears highest for patients with asthma and reduced lung function.

COMMENT: *Allergen immunotherapy is an effective therapy for properly screened patients, but is not without risk. The fatality rate has been estimated at one per 2 to 3 million injections. This retrospective survey study attempts to analyze "near-fatal reactions" (NFRs) and estimates them at one per 1 million injections. If we allergists are to obtain informed consent from immunotherapy patients, we need reliable data. This study suffers from being a retrospective survey (only 27% of AAAAI member practices responded) and from an imprecise definition of NFR ("severe respiratory compromise, hypotension, or both requiring…epinephrine"). One person's mere "systemic reaction" might be another's NFR. It is likely that only a prospective study can accurately gauge the true risks of immunotherapy. However, despite the shortcomings of this study's methods, it would be prudent to be aware of the association with dosing errors, high pollen seasons, and pre-existent severe asthma.*

R. J. M.

Amin HS, Liss GM, Bernstein DI: Evaluation of near-fatal reactions to allergen immunotherapy injections.

J Allergy Clin Immunol. 2006;117:169-175. ♦♦

United We Stand, Divided We Falter!

SKIN testing plays a central role in the diagnosis of allergic disease, but anecdotal evidence suggests wide variations in the way skin testing is performed. A survey of allergists was performed to investigate diversity in skin testing practices.

Three thousand U.S. members of the American Academy of Allergy, Asthma and Immunology were invited to complete the Internet survey. The response rate was 18%, with 539 responses. The allergists varied significantly in their skin test practices, including number of tests performed, extract concentrations and devices used, interpretation and recording of results, and quality assurance measures.

Eighty-five percent of respondents performed intradermal skin prick testing, but allergen extract concentrations varied widely. While about 60% of allergists used 1:1,000 dilutions, 20% used 1:100 dilutions and 10% used 1:500 dilutions. Fifty-four percent reported skin test results on a 0 to 4+ scale, while 28% measured orthogonal diameters. When reporting skin test results, only about half of allergists reported the extract concentration used. Less than one-third reported the extract manufacturer and skin test device.

Allergists vary widely in the way they perform, interpret, and report the results of skin testing. The survey identifies several areas of needed improvement in skin testing practice.

COMMENT: *Skin testing is the primary investigative tool used by allergists/immunologists, but there is a significant degree of variability in test methodology and reporting among experienced, board-certified clinicians. Significant progress toward standardization has been achieved, but we have a long way to go. The credibility of our specialty would be enhanced if we were able to agree on a consistent methodology and reporting. There is work to be done.*
D. K. L.

Oppenheimer J, Nelson HS: Skin testing: a survey of allergists.
Ann Allergy Asthma Immunol. 2006;96:19-23. ♦♦

Endotoxin: Protector vs Risk Factor for Asthma

EARLY childhood exposure to endotoxin may lower the risk of allergies, but its effects on risk of wheezing and asthma are unclear. The relationship between endotoxin exposure and asthma risk was evaluated as part of a national survey of U.S. housing.

The study used house dust specimens from a representative sample of U.S. homes, collected for the National Survey of Lead and Allergens in Housing. The analysis included a total of 2,456 subjects living in 831 housing units. Relationships between endotoxin exposure and asthma and allergy were assessed, along with housing characteristics associated with endotoxin.

Geometric mean levels of endotoxin in the study homes were 35.3 EU/mg in dust samples from bedroom floors, 18.7 EU/mg from bedding, 63.9 EU/mg from family room floors, 44.8 EU/mg from sofas, and 80.5 EU/mg from kitchen floors. On multivariate analysis, residents exposed to higher levels of endotoxin had higher rates of diagnosed asthma, asthma symptoms in the past year, current asthma medications, and wheezing. The risk of asthma associated with high endotoxin exposure was no different for residents with vs without allergies.

Higher exposure to household endotoxin is a significant risk factor for asthma. The main effect of endotoxin exposure appears to be airway inflammation, with little apparent effect on allergy risk. The effects of endotoxin on asthma and wheezing appear to be concentrated in adults.

COMMENT: *This study in 831 homes again shows us that early exposure to endotoxin is a risk factor for the development of persistent asthma, OR 2.83, (95% confidence interval 1.01 to 7.78). This adds strength to our recommendations for control of the indoor environment.*
B. E. C.

Thorne PS, Kulhánková K, Yin M, et al: Endotoxin exposure is a risk factor for asthma: The National Survey of Endotoxin in United States Housing.
Am J Respir Crit Care Med. 2006;172:1371-1377. ♦♦

Patient History Is Important in Venom Allergy

SKIN tests, along with specific IgE measurements and history of systemic reactions to insect stings, are the basis for decision making regarding venom immunotherapy (VIT). However, previous reports have raised questions about the reliability of skin testing for venom allergy. This study assessed the reproducibility of intradermal skin testing and specific IgE measurement in patients with venom allergy.

The analysis included 35 patients with a history of systemic reaction to an insect sting. On two occasions, 2 to 6 weeks apart, each patient underwent intradermal skin testing using honeybee, yellow jacket, and wasp venom. Measurement of serum Hymenoptera-specific IgE was performed twice in 27 patients. The initial test was performed a mean of 23 months after the systemic reaction.

In 66% of patients, the results of skin testing were reproducible between the two test occasions. The results of venom-specific IgE measurement were reproducible in 59% of patients. On evaluation of a total of 59 samples, the results of skin testing and venom-specific IgE measurement were concordant in 51% of cases.

In patients with a history of systemic reactions to insect stings, Hymenoptera venom skin testing and specific IgE measurement have relatively low reproducibility. Since decisions to perform venom immunotherapy are commonly based on a single test result, low reproducibility may lead to overtreatment or undertreatment. Further study is needed to assess the clinical significance of these results. ➤➤

COMMENT: *Previous studies have documented temporal variation in Hymenoptera allergy test results. In addition, individuals with convincing histories and positive tests have not reacted to stings; subjects with life-threatening reactions and negative tests, by one or more methods, have experienced life-threatening reactions to subsequent stings. The bottom line is that venom testing is not perfect, but immunotherapy is life-saving in highly allergic subjects. I am more comfortable with potential overtreatment rather than undertreatment as a result of test variability. In my opinion, a positive test--regardless if on the first, second or third attempt--justifies immunotherapy in a patient with the right history.*
D. K. L.
Graif Y, Ronit C-C, Goldberg A: Reproducibility of skin testing and serum venom specific IgE in Hymenoptera venom allergy.
Ann Allergy Asthma Immunol. 2006;96:24-29. ♦♦

Psychopathology and Asthma Exacerbations

PREVENTION of recurrent exacerbations, and their accompanying morbidity and costs, is a major goal of asthma treatment. Few comprehensive studies have evaluated the risk factors for recurrent exacerbations. Potential clinical and environmental risk factors for frequent exacerbations were evaluated in patients with difficult-to-treat asthma.

The study included 136 patients with difficult-to-treat asthma, mean age 45 years. All were symptomatic and had at least one severe exacerbation over the past year, or were dependent on maintenance therapy with oral prednisone. Thirteen potential contributors to frequent exacerbations were evaluated: current allergen exposure, food allergies, use of certain drugs, occupational sensitizers, severe chronic sinus disease, gastroesophageal reflux, recurrent respiratory infections, relative immune deficiency, hyperthyroidism, obstructive sleep apnea syndrome, hormonal factors, psychologic dysfunction, and poor inhaler technique. The findings of 39 patients with more than three severe exacerbations in the previous year were compared to those of 24 patients with just one exacerbation.

On logistic regression analysis, the variable most strongly associated with frequent exacerbations was psychologic dysfunction, defined as a score of 6 or higher on the General Health Questionnaire-12: adjusted odds ratio (OR) 10.8. Other significant factors were severe chronic sinus disease, (OR) 3.7; gastroesophageal reflux disease, OR 4.9; recurrent respiratory infections, OR 6.9; and obstructive sleep apnea, OR 3.4. When these five variables were incorporated into a single model, the independent risk factors were psychologic dysfunction, OR 11.7; and severe chronic sinus disease, OR 5.5. All patients with frequent exacerbations had at least one of the five risk factors, while more than half had at least three factors.

Several comorbid conditions are associated with frequent exacerbations in patients with difficult-to-treat asthma. Treatment for these conditions, such as psychologic dysfunction and obstructive sleep apnea, would likely reduce asthma exacerbations and improve quality of life for such patients.

COMMMENT: *This study allows for an in-depth analysis of factors that make a particular patient refractory to therapy. It is quite interesting that psychologic dysfunction is in fact the highest odds ratio for poor outcomes. It forces us to consider other factors than the usual comorbidities in determining why a particular patient is more difficult to treat.*
B. E. C.
ten Brinke A, Sterk PJ, Masclee AAM, et al: Risk factors of frequent exacerbations in difficult-to-treat asthma.
Eur Respir J. 2005;812-818. ♦♦

PSYCHOLOGIC factors seem to contribute to adverse outcomes associated with severe asthma. Several programs have been developed to promote treatment adherence and self-care skills, but few have addressed the psychosocial issues related to asthma. A psychoeducational intervention for adult asthma patients at risk of adverse outcomes was evaluated.

The randomized controlled trial included 92 patients with severe asthma who had a history of missed appointments or were considered to have poor treatment adherence. One group received the study intervention, while the other group received usual care. The psychoeducational intervention was delivered by a respiratory nurse specialist in a series of visits to the patients' homes over a 2-month period. Outcomes were evaluated at 6 months, including symptom control, disease-specific quality of life, and general health status.

Most study outcomes showed no significant effect of the psychoeducational intervention, with minimal differences in symptom control, physical functioning, and mental health. The intervention group showed a small but significant benefit in terms of asthma-specific quality of life, which was still present at 12 months. At the end of the study intervention, patients showed improvements in self-care, which were associated with short-term improvements in general health. These benefits were evident only after full adjustment for baseline outcome scores.

A nurse-delivered psychoeducational benefit shows little long-term benefit for asthma patients with poor treatment adherence. An alternative approach for this difficult group of patients might be to focus on "opportunistic" interventions in the primary care office or emergency department.

COMMENT: *This study focuses on a minority of patients with asthma who suffer from severe, poorly controlled disease. The authors developed a psychoeducational intervention program in an attempt to improve social and psychological problems leading to higher morbidity and mortality in such patients. The study uncovered significant difficulties faced by these patients, but yielded no clear evidence that the intervention had clinically important impacts on health outcomes over the long term.*
E. J. B.
Smith JR, Mildenhall S, Noble MJ, et al: The ➤➤

Coping with Asthma Study: a randomised controlled trial of a home based, nurse led psychoeducational intervention for adults at risk of adverse asthma outcomes.
Thorax. 2005;60:1003-1011. ♦♦

Is CIU Really Autoimmune?

SOME patients with chronic idiopathic urticaria (CIU) have circulating IgG antibodies against the α-subunit of the high-affinity IgE receptor or the IgE molecule itself, suggesting an autoimmune origin. However, nearly half of patients do not have autoantibodies against these targets, raising the possibility that other autoantigens are involved.

The random peptide library approach was used to screen for other relevant autoantigen peptides, using pooled IgG from 133 CIU patients. One particular peptide, recognized by the serum of most CIU patients, proved similar to the low-affinity IgE receptor (FcεRII/CD23) on lymphomonocytes and eosinophils. Purified IgG antibodies against this peptide bound cell-surface CD23 and induced histamine release from basophils, apparently mediated by the release of major basic protein from eosinophils.

Serum autoantibodies directed against CD23 are identified in most patients with CIU. By inducing the release of major basic protein after binding of the ligand on the eosinphil surface, these antibodies may play a key role in the maintenance of disease activity.

COMMENT: *These authors used a random peptide library technique to identify autoantibodies recognizing the low-affinity IgE receptor (CD23) in the sera of patients with CIU. They also suggest that in these patients hives result from histamine release induced by major basic protein after autoantibodies bind to CD23 on eosinophils. The prevalence of these autoantibodies is not known but it is possible that autoimmunity explains an even larger portion of "idiopathic" urticaria than previously thought.*
S. A. T.
Puccetti A, Bason C, Simeoni S, et al: In chronic idiopathic urticaria autoantibodies against FcεRII/CD23 induce histamine release via eosinophil activation.
Clin Exp Allergy. 2005;35:1599-1607. ♦♦

Tumor Necrosis Factor in Severe Asthma

TUMOR necrosis factor (TNF) α is an important therapeutic target in various chronic inflammatory diseases involving neutrophils and a Th1-type immune response. Whereas asthma is generally regarded as a Th2 type disorder associated with eosinophils, characteristics more typical of a Th1 response may develop in chronic and severe disease. In vitro and clinical studies were performed to explore the possible role of TNFα as a therapeutic target for severe persistent asthma.

Bronchoalveolar lavage specimens were obtained from 20 patients with severe, steroid-dependent persistent asthma, as well as from healthy controls and patients with mild asthma. Median TNFα level was 160 fg/mL in the specimens from severe asthmatics, compared with 117 fg/mL in controls and 111 fg/mL in patients with mild asthma. Levels of TNFα in endobronchial biopsy specimens were also higher in patients with severe persistent asthma. Expression of TNFα cells was localized mainly to mast cells.

In an open, uncontrolled clinical trial, 17 patients with severe persistent asthma received 12 weeks of treatment with the TNF-inhibitor etanercept. Fifteen study completers had a significant reduction in mean asthma control questionnaire score, from 26 to 11. Pulmonary function variables improved as well--including FEV_1, FVC, and morning and evening PEF--while methacholine PC_{20} increased by 2.5 doubling dilutions. The benefits were lost by 8 weeks after etanercept withdrawal.

Tumor necrosis factor α is a promising therapeutic target in severe persistent asthma. Treatment to block TNFα may yield significant improvements in disease control and lung function. Large, placebo-controlled trials are needed to evaluate approaches to TNFα blockade in patients with severe, steroid-dependent asthma.

COMMENT: *Patients with severe, steroid-refractory asthma are known to have an altered inflammatory profile involving neutrophils. TNFα is overexpressed in the airways of such patients, and treatment with etanercept is a reasonable strategy. Entanercept binds specifically to TNFα and TNFβ, preventing cytokine binding to cell-surface TNF receptors. These authors treated 15 subjects for 12 weeks, with a very significant improvement in FEV_1, FVC, and BHR. The encouraging results should prompt confirmation in future placebo-controlled studies.*
E. J. B.
Howarth PH, Babu KS, Arshad HS, et al: Tumor necrosis factor (TNFα) as a novel therapeutic target in symptomatic corticosteroid-dependent asthma.
Thorax. 2005;60:1012-18. ♦♦

Fluticasone vs Montelukast in Childhood Asthma

IN both children and adults with persistent asthma, the use of anti-inflammatory controller medications falls far short of recommended guidelines. There is a need for more outcomes data to guide the prescription of controller medications for asthmatic children. This randomized, controlled trial compared the outcomes of treatment with an inhaled corticosteroid (ICS) and a leukotriene receptor antagonist (LTRA) for school-aged children with asthma.

The Childhood Asthma Research and Education (CARE) Network trial included 144 children, aged 6 to 17 years, with mild to moderate persistent asthma. At baseline, all patients were using as-needed bronchodilators only. In crossover, placebo-controlled fashion, the children received 8 weeks of treatment with fluti- ➤➤

casone propionate, 100 µg twice daily; and 8 weeks of montelukast, 5 to 10 mg, depending on age. Clinical outcomes, pulmonary function variables, and anti-inflammatory markers were compared between groups.

By most measures, clinical asthma control improved with both treatments. However, fluticasone provided better clinical improvement than montelukast. Asthma-control days increased by a mean of 2.8 d/week with fluticasone and 2.1 d/week with montelukast. The percentage of children improving by at least 2 d/week was 59% with fluticasone vs 47% with montelukast; by at least 1 d/week, 29% vs 12%, respectively. Fluticasone also yielded greater improvement in pulmonary function and airway inflammation. Exhaled nitric oxide was a significant indicator of response, particularly to fluticasone.

For school-age children with mild to moderate persistent asthma, the ICS fluticasone provides a better response than the LTRA montelukast. The results provide research-based evidence that an ICS is the preferred frontline therapy for persistent asthma in children. Exhaled nitric oxide is a useful predictor of response, and may also aid in identifying children likely to have better disease control with ICS vs an LTRA.

COMMENT: *This report from the CARE Network demonstrates that children with persistent asthma treated with ICS had more favorable clinical, pulmonary and inflammatory responses than those treated with an LTRA. Although the crossover design is a strength with respect to assessing individual therapeutic response, it can also be a weakness since there may be carryover effects that could lead to statistical bias. Children with both mild-persistent and moderate-persistent asthma were included in the sample. The individual responses for each classification were not differentiated, although overall improvement with ICS was more favorable. The authors suggest that exhaled nitric oxide might be used as a predictor of clinical and pulmonary responses in children with persistent asthma.*
S. M. F.

Zeiger RS, Szefler SJ, Phillips BR, et al: Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma.
J Allergy Clin Immunol. 2006;17:45-52. ♦♦

Atopy, eNO, and EIB

ALTHOUGH the clinical features of atopic and nonatopic asthma differ, both types are associated with airway inflammation and bronchial hyperresponsiveness (BHR). Exhaled nitric oxide (eNO) is a useful indicator of airway inflammation, but its relationship to BHR remains unclear. The association between eNO and BHR was compared between subjects with atopic vs nonatopic asthma.

The study included 181 consecutive male conscripts referred for evaluation of suspected asthma. All were nonsmokers who had not previously been treated with steroids. Based on the results of evaluation including skin prick testing, 128 patients were atopic, 68 with asthma; and 53 were nonatopic, 19 with asthma. Other assessments included lung function studies, eNO measurement, and histamine and exercise challenge tests.

Median eNO was 21.2 ppb in the atopic patients vs 10.2 ppb in nonatopic patients. Nevertheless, eNO was elevated in 36% of nonatopic subjects. Bronchial responsiveness to histamine was similar between groups, but atopic subjects had a much stronger response to exercise challenge. On multivariate analysis, eNO was significantly related not only to atopy but also to the severity of exercise- and histamine-induced bronchoconstriction. Separate models suggested that the relationships with bronchial hyperresponsiveness were significant only for atopic subjects.

The results show a significant relationship between eNO and bronchial responses to exercise and histamine only in atopic patients with asthmatic symptoms, not in those without atopy. In patients with atopy, the severity of airway hyperresponsiveness and airway inflammation may be correlated with each other. In nonatopic asthmatics, other mechanisms of airway hyperresponsiveness may predominate.

COMMENT: *Previous studies have shown that airway inflammation can be assessed noninvasively with eNO. (See* AllergyWatch, *Nov/Dec 2005, pp 3 and 4.) The concentrations of eNO are elevated 10-fold in allergic asthma, and to a lesser extent in nonallergic asthma. These investigators showed a definite association between eNO and the severity of EIB in patients with suspected allergic asthma who had not been exposed to steroids. However, this association was not seen in nonallergic patients with similar symptoms. These observations support the view that mechanisms of bronchial hyperreactivity may differ between allergic and nonallergic asthma, suggesting that the optimal approach to anti-inflammatory treatment in these two groups may also differ.*
E. J. B.

Rouhos A, Ekroos H, Karjalainen J, et al: Exhaled nitric oxide (eNO) and exercise-induced bronchoconstriction (EIB) in young male conscripts: association only in atopics.
Allergy. 2005;60:1493-1498. ♦♦

Allergists Do It Best!

SOME reports have suggested that management by an allergist improves outcomes for patients with asthma, although these studies have had limitations. The effects of allergist care on asthma patients' outcomes were evaluated in a large patient population.

The study included a random sample of 3,568 patients with persistent asthma enrolled in a large staff-model HMO. In response to a survey, nearly half of patients reported that a primary care physician PCP was their regular source of asthma care, while one-fourth reported management by an allergist. Most of the rest had no regular contact for asthma care. Quality of life, disease control and severity, satisfaction, and other outcomes were compared among groups.

Younger and nonwhite patients were more likely to report no regular source of asthma care. Compared to patients managed by their PCP, those managed by ➤➤

an allergist had higher scores for generic and disease-specific quality of life. Allergist care was also associated with fewer problems with disease control, less-severe asthma, greater patient satisfaction, and better self-care knowledge. Hospitalizations and unscheduled visits for asthma were less frequent for patients managed by allergists, odds ratio (OR) 0.45 and 0.71, respectively. Patients reporting allergist care were less likely to overuse β-agonists, OR 0.47; and more likely to use inhaled steroids, OR 1.81.

For patients with persistent asthma, seeing an allergist for regular asthma care is associated with better outcomes, compared to patients managed by their PCP or with no regular source of asthma care. The improvement in outcomes may be related to processes of care, including increased use of inhaled steroids and better patient self-management. Patients managed by pulmonologists tend to have more severe asthma.

COMMENT: *Data from a questionnaire survey of physician-diagnosed asthma in a closed-panel HMO found that 47.1% of patients were primarily managed by their PCP, 24.8% by an allergist, and 5.5% by a pulmonologist, while 19.4% identified no regular source of asthma care. Analysis of data from validated outcomes questionnaires found that patients followed by allergists had much better control of their asthma than those with no regular care or, even those followed by PCPs. Although the limitations of the study are the lack of treatment assignment and absence of cost information, the large number of patients provides robust data. Last year the theme of the ACAAI was "Nobody does it better than the allergist." This study provides support for that statement.*
S. M. F.

Schatz M, Zeiger R, Mosen D, et al: Improved asthma outcomes from allergy specialist care: a population-based cross-sectional analysis.
J Allergy Clin Immunol. 2005;116:1307-1313. ♦♦

Listen to the Children; They're Better Historians!

THE "hygiene hypothesis" suggests that infants exposed to multiple infections may be protected against later development of allergic disease and sensitization. Among the many questions surrounding this hypothesis is which characteristics of infectious diseases might be responsible for the protective effect. The relationship between neonatal sepsis and later development of allergic disease was investigated.

The study included 339 infants hospitalized for sepsis or suspected sepsis between 1990 and 1995. In 2002, a questionnaire was sent to 196 families of these infants, of whom 140 responded. A parental questionnaire asked whether the children had received a physician's diagnosis of asthma, allergic rhinitis, or atopic dermatitis.

Seventy children met diagnostic criteria for neonatal early-onset sepsis (eg, positive blood culture); the remaining 70 children were hospitalized for suspected sepsis but did not meet the criteria. Lifetime prevalence of atopic dermatitis was 15.7% for children with sepsis and 21.4% for hospitalized children who did not meet the diagnostic criteria, compared with 5.2% in a control group of children with no hospitalizations during infancy. Hospitalized children without sepsis were more likely to receive a diagnosis of bronchial asthma, 7.1%; compared to children with sepsis, 4.3%; or controls. 1.9%. After adjustment for parental history of atopic disease and other factors, risk of allergic disease for normal-birth weight children was similar across groups. There was a marginal association between bronchial asthma and exposure to environmental tobacco smoke.

A history of hospitalization for sepsis during infancy does not affect the risk of developing allergic disease later in childhood. For normal-birthweight children, hospitalization for suspected sepsis does not seem to influence allergic disease risk, after adjustment for parental atopy.

COMMENT: *In this article, neonatal sepsis did not prove to be a protective factor in the development of atopic disease. Although these findings do not disprove the hygiene hypothesis, they raise important questions. One issue that remains unsettled is the value of parental questionnaires. The discordance between parental questionnaires and the children's own history needs to be noted when interpreting these and previous observations in this area.*
A. M.

Kopp MV, Semmler S, Ihorst G, et al: Hospital admission with neonatal sepsis and development of atopic disease: is there a link?
Pediatr Allergy Immunol. 2005;26:630-636. ♦♦

Impact of Penicillin Skin Testing

PENICILLIN allergy is a common problem in hospitalized patients, and some of these patients show cross-reactivity to cephalosporins. The findings of and treatment changes resulting from penicillin skin testing in hospitalized patients were analyzed.

The retrospective study included 101 hospitalized patients undergoing penicillin skin testing over a 6.6-year period. Testing was performed using penicillinoyl polylysine, penicillin G sodium, and sodium benzyl penicilloate--the latter two test solutions were made at the study hospital.

The test results were negative in 92 patients, positive in 5, and indeterminate in 4. Among the patients with negative penicillin skin tests, there were 96% reductions in the use of both vancomycin and fluoroquinolones. All patients with positive results were initially given vancomycin, while 3 of 5 received vancomycin after penicillin skin testing. Of 14 patients with a history of allergy to cephalosporins, all but 1 had a negative result on PST. No patient with a negative PST result experienced a serious adverse reaction to penicillin or a cephalosporin.

Penicillin skin testing is a useful tool in the management of hospitalized patients with a history of allergy to β-lactam drugs. Performing PST decreases the use of vancomycin and fluoroquinolone drugs while increasing the use of penicillin and cephalosporin antibiotics. ➤➤

In cases of suspected penicillin allergy, consultation with an allergist can lead to meaningful improvements in clinical care.

COMMENT: *This important paper reinforces the utility of penicillin skin testing even without the availability of a commercially available reagent. The findings further highlight the ability of skin test results to avoid unnecessary, expensive, and potentially dangerous antibiotics. In these days of increasing emergence of drug resistance, it is essential to treat with targeted therapy and avoid "shotgun" treatment.*
A. M.
Nadarajah K, Green GR, Naglak M: Clinical outcomes of penicillin skin testing.
Ann Allergy Asthma Immunol. 2005;95:541-545. ♦♦

CLINICAL TIDBITS

Allergic Alveolitis and Feather Duvets

BIRD fancier's lung (BFL), a type of hypersensitivity pneumonitis caused by inhaling bird-related antigens, is usually found in bird breeders. The findings of seven patients with BFL related to the use of feather duvets are reviewed. Lung disease was acute in 4 patients and chronic in 3. Chest x-rays showed diffuse ground-glass opacities in patients with acute disease; chronic cases showed reticular infiltrates and ground-glass opacities in the upper and lower lung fields, along with reduced lung volume. Antibodies to bird antigens were found only in acute cases, while all patients showed antigen-induced lymphocyte proliferation in peripheral blood or bronchoalveolar lavage cells. With the growing popularity of feather duvets, physicians should be aware of this source of avian antigens leading to BFL.

COMMENT: *The report of chronic hypersensitivity pneumonitis resulting from a few pet birds, as opposed to raising birds, suggests that low-level exposure to avian proteins may result in respiratory disease. These investigators present evidence suggestive of hypersensitivity pneumonitis caused by feather duvets. Although feather pillows do not appear to play a role in IgE-mediated respiratory disease, any history of exposure to avian proteins--even apparently minimal exposure--should be considered in subjects with restrictive lung disease and respiratory symptoms. Once again, the history is critical.*
D. K. L.
Inase N, Ohtani Y, Sumi Y et al. A clinical study of hypersensitivity pneumonitis presumably caused by feather duvets.
Ann Allergy Asthma Immunol. 2005;96:98-104. ♦♦

Polysorbate 80: Maybe Not So Benign

THE solubilizing agent polysorbate 80 (Tween 80) is widely used in products such as ointments, lotions, and medical preparations. The authors performed extensive investigations to identify the cause of anaphylactoid shock caused by IV infusion of a multivitamin product in a pregnant woman. Skin prick tests were strongly positive for the multivitamin preparation as well as for the polysorbate 80 it contained. There were no reactions to latex or preservatives. No polysorbate-specific IgE antibodies were found, confirming the nonimmunologic nature of the reaction. Previously regarded as inert, polysorbate 80 can cause severe, nonimmunologic anaphylactoid reactions. Other adverse effects have been reported as well.

COMMENT: *This is an extremely well-studied case that highlights the importance of the previously unknown. We all are asked to evaluate the possibility of drug-related anaphylaxis to preparations that are not classically associated with IgE-specific responses. Clinicians should be aware of this extremely ubiquitous solubilizing agent that can cause severe systemic anaphylaxis.*
A. M.
Coors EA, Seybold H, Merk HF, Mahler V: Polysorbate 80 in medical products and nonimmunologic anaphylactoid reactions.
Ann Allergy Asthma Immunol. 2005;95:593-599. ♦♦

Simple, Effective Test for Pulmonary Embolism

EVALUATION of patients with suspected pulmonary embolism poses a clinical challenge. A dichotomized version of the Wells clinical decision rule was used to divide 3,306 patients with clinically suspected acute pulmonary embolism into "unlikely" and "likely" groups. Two-thirds of patients fell into the "unlikely" group. After a normal D-dimer test, 1,028 patients were managed without anticoagulants--the resulting rate of nonfatal venous thromboembolism was 0.5%. In 1,505 patients, PE was ruled out by computed tomography--venous thromboembolism occurred in 1.3%. Seven patients had PE as a possible cause of death after a negative CT scan, a rate of 0.5%. The clinical decision rule evaluated in this study, along with D-dimer testing and CT scanning, is useful in the evaluation of clinically suspected pulmonary embolism.

COMMENT: *Allergists/immunologists do not evaluate and treat subjects with suspected pulmonary emboli, but we do see patients with shortness of breath and cough. This paper demonstrates the value of a negative D-dimer test in excluding the diagnosis of pulmonary emboli in low-probability subjects. Using this test would provide additional reassurance in the next patient you see with shortness of breath, cough, and minimal* ➤➤

reversibility on spirometry. The serious results of overlooking the diagnosis make this issue important for allergists/immunologists.
D. K. L.
Writing Group for the Christopher Study Investigators: Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography.
JAMA. 2006;295:172-179. ♦♦

Autism and Immunity

SEVERAL studies have reported immune system abnormalities in patients with autism, although results have been inconsistent. The findings of 24 children with autism or pervasive developmental disorders referred for immunologic evaluation are reported. Parents reported a history of frequent infections in 7 patients. Of 2 patients with abnormal immunoglobulin levels, one was later diagnosed with common variable immune deficiency. Five children had elevated IgE levels, consistent with clinical evidence of atopy. Some patients had low levels of diphtheria or tetanus antibodies, mainly related to vaccination status. Immunologic evaluation of autistic children should be performed only if clinical indications are present--ie, recurrent infections.

COMMENT: *Parents' concerns regarding potential allergic and/or immunologic mechanisms in autism frequently result in requests for immunologic consultation. These data further highlight that routine evaluation of immune function in autism is indeed low-yield!*
A. M.
Stern L, Fancoeur M-J, Primeau M-N, et al: Immune function in autistic children.
Ann Allergy Asthma Immunol. 2005;95:558-565. ♦♦

Hood Is as Good as a Mask...Less Traumatic Too!

IN infants with respiratory syncytial virus (RSV) bronchiolitis, aerosolized drugs are generally administered via a tight-fitting face mask. A hood device was tested for administration of inhaled bronchodilators in 49 infants with viral bronchiolitis. One group was randomly assigned to receive the "BabyAir" hood device, while the other received a face mask. Active drug and placebo were administered in crossover fashion. The two groups had similar and significant improvement in clinical severity scores from day 1 to 3. Eighty percent of parents preferred the hood over the mask. The BabyAir device is an effective and well-tolerated option for delivery of nebulized medications for infants.

COMMENT: *I still remember the 1960s, when in wintertime the pediatrics wards were filled with infants being treated for respiratory illnesses with O_2 and saline in mist tents enclosing the crib! This interesting study of bronchiolitis from Israel promotes a new delivery device for aerosols in infants, similar to a small mist tent. If the gold standard for aerosol drug delivery in an infant is through a tight-fitting mask, the use of a "hood" appears just as good, and less traumatic--to both the infant and the parents! Further studies using these devices seem warranted.*
J. A. A.
Amirav I, Oron A, Tal G, et al: Aerosol delivery in respiratory syncytial virus bronchiolitis: hood or face mask?
J Pediatr. 2005;147:627-631. ♦♦

Heliox in the ER

COMPARED with 100% oxygen, heliox--a 70% helium/30% oxygen combination--can increase delivery of aerosols and gases to the lung. Thirty children receiving emergency department care for moderate to severe asthma received an initial oxygen-driven dose of albuterol, along with oral steroid. They were then randomized to receive continuous albuterol delivered using heliox or oxygen via face mask. Over the first 4 hours, pulmonary index score increased by a mean of 6.67 with heliox vs 3.33 with oxygen. Patients assigned to heliox were also more likely to be discharged from the hospital within 12 hours, 73% vs 33%. Heliox-driven delivery of nebulized albuterol may promote clinical improvement for children seen in the emergency department for acute asthma.

COMMENT: *Attempts to improve the emergency care of severe life-threatening asthma in young children are laudable! The unique aspect of this small pilot study is the short-term use of helium/O_2 (heliox) instead of O_2 alone, to facilitate the aerosol delivery of a standard dose of albuterol. There is no doubt that the subjective asthma score was reduced over 4 hours in the treatment group. However, as the authors point out, such initial impressions need to be confirmed by larger blinded studies for this technique to be accepted as a safe, effective aerosol delivery method.*
J. A. A.
Kim IK, Phrampus E, Venkataraman S, et al: Helium/oxygen-driven albuterol nebulization in the treatment of children with moderate to severe asthma exacerbations: a randomized, controlled trial.
Pediatrics. 2005;116:1127-1133. ♦♦

Should Children With Asthma Have Influenza Vaccination?

YEARLY influenza vaccination is generally recommended for children with asthma, with the objective of preventing exacerbations and complications. This recommendation is not supported by randomized trials demonstrating any preventive benefit. Two studies using culture confirmation have confirmed that influenza-related exacerbations do occur in asthmatic chil- ➤➤

dren, but detected no serious complications. Trials in adults show that, while vaccine is effective in preventing serologically confirmed influenza, its effectiveness in preventing clinical influenza is much lower. These and other considerations suggest that the recommendation to vaccinate all asthmatic children should be reconsidered.

COMMENT: *Temporary shortages in the influenza vaccine supply the past 2 years have forced physicians to rethink the generally accepted notion that asthma is a risk factor for increased morbidity or mortality during influenza infection. Citing the relatively low incidence of influenza infection, the availability of antiviral agents to reduce the severity of influenza infection, and the absence of convincing proof of the vaccine's ability to prevent worsening asthma, this review/editorial takes to task the general recommendation that every child with mild-moderate asthma should receive an annual influenza vaccination.*
S. A. T.
Bueving HJ: Is influenza vaccination in asthmatic children helpful?
Clin Exp Allergy. 2006;36:21-25. ♦♦

Sexual Dysfunction and Rhinitis

RECENT reports have drawn attention to the problem of sexual dysfunction associated with chronic disease. Using specific questionnaires for women and men, sexual function scores were assessed in 43 sexually active patients with allergic rhinoconjunctivitis (ARC). For both sexes, sexual function scores were significantly lower for patients with continued ARC symptoms than for patients receiving treatment for ARC or for healthy controls. Improvement in nasal and conjunctival symptoms was significantly correlated with improvement in sexual function scores. Sexual dysfunction is an important quality-of-life issue for patients with ARC, and one that can be improved with treatment to reduce allergic symptoms.

COMMENT: *These findings give us another answer to insurers and patients who may question the need for allergic disease management. It appears that all aspects of patients' quality of life are affected by allergic disease!*
A. M.
Kirmaz C, Aydemir O, Bayrak P, et al: Sexual dysfunction in patients with allergic rhinoconjunctivitis.
Ann Allergy Asthma Immunol. 2005;95:525-529. ♦♦

REVIEWS OF NOTE

COMMENT: *The authors are to be congratulated for preparing a thorough review in a content area where definitive statements are few and far between. Nevertheless, this is a topic that patients frequently ask about and that it's important for our specialty to know about. If you see patients, you should read this article.*
D. K. L.
Wilson BG, Bahna SL: Adverse reactions to food additives.
Ann Allergy Asthma Immunol. 2005;95:499-507. ♦♦

COMMENT: *This review is very well done, giving the current state of understanding regarding the interaction between infection and the development and persistence of asthma. Although the answer is not clear, there is promising work in this area that may lead to better diagnosis and treatment over time.*
B. E. C.
Johnston SL, Martin RJ: Chlamydia pneumoniae *and Mycoplasma pneumoniase: a role in asthma pathogenesis?*
AM J Respir Crit Care Med. 2005;172:1078-1089. ♦♦

COMMENT: *This review is an update from the EAACI Interest Group on Insect Venom Hypersensitivity. It presents the European view relative to prevention and treatment of hymenoptera venom allergy.*
E. J. B.
Bonifazi F, Jutel M, Bilo BM, et al: Prevention and treatment of hymenoptera venom allergy: guidelines for clinical practice.
Allergy. 2005;60:1459-1470. ♦♦

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