AllergyWatch®

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

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

Volume 9, Number 2 March-April 2007

Chink in the Armor

REGULAR treatment with inhaled corticosteroids (ICS) to control airway inflammation has had a major impact on disease outcomes and quality of life for patients with asthma. It is often assumed that long-term changes in airway structure and function also result from inflammation, and thus that these changes can be prevented by ICS. This paper reviews the most recent evidence on the ability of ICS therapy to prevent loss of lung function in children and adults with asthma.

Dr. Martinez considers two recent trials designed to assess the effects of early ICS therapy on the natural course of asthma in children: the Childhood Asthma Management Program study and the Prevention of Early Asthma in Kids trial. Along with other studies from Europe, the results suggest that even very early ICS treatment does not alter the final level of pulmonary function. A study in adults with recently diagnosed asthma, by O'Byrne et al., has reached similar conclusions. Thus despite their effectiveness in controlling asthma symptoms, ICS do not seem to prevent or alter the changes in airway structure and function resulting from the disease.

The findings raise the possibility that the changes in airway function do not result from the airway inflammation that causes symptoms and responds to ICS treatment. Other lines of evidence support the absence of such an association: for example, there is no consistent relationship between pathologic indicators of airway remodeling and asthma duration and severity. Long-term follow-up studies suggest that the early presence of bronchial hyperresponsiveness determines the future growth of airway function, regardless of the presence of asthma symptoms.

Strong data now suggest that ICS therapy does not alter the clinical course of asthma, despite its efficacy in controlling symptoms. New lines of research are needed to find treatments capable of preventing the pathologic process leading to the "parallel pathways" of asthma symptoms and long-term airway changes. Studies are also needed to identify genetic and phenotypic markers of progressive asthma, and to compare the benefits of symptom-triggered versus daily anti-inflammatory treatment for children with mild persistent asthma. ➤➤

CONTENTS

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

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

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

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COMMENT: *There is no doubt at all that ICS control asthma symptoms better than any other pharmacologic agent. Therefore, their anti-inflammatory effects have been presumed to provide better long-term pulmonary outcomes. Not so. In this review, several studies are noted that agree that after several years of treatment with or without ICS, lung functions are similar. Thus we cannot assume any longer that ICS prevent airway remodeling. Asthma treatment does not equate to asthma prevention.*
R. J. M
Martinez FD: Asthma treatment and asthma prevention: a tale of 2 parallel pathways.
J Allergy Clin Immunol. 2007;119:30-33. ♦♦

PPI Treatment Linked to Hip Fracture Risk

THE introduction of proton pump inhibitors (PPIs) was a major advance in the treatment of gastroesophageal reflux disease; millions of patients now use these medications on a daily basis. Particularly in the elderly, long-term use of these medications could lead to hypochlorhydria, and thus possibly to abnormalities in calcium absorption. Alternatively, PPIs may inhibit osteoclastic vacuolar proton pumps, leading to decreased bone resorption. The relationship between long-term PPI treatment and hip fracture risk was evaluated in a population-based sample.

Based on the U.K. General Practice Research Database, the analysis included 13,556 patients aged 50 years or older with incident hip fracture and 135,386 matched controls without hip fracture. The effects of PPI exposure on hip fracture risk, compared to no use of acid-suppressing drugs, were assessed by conditional logistic regression. A similar analysis was performed for patients using histamine 2 receptor antagonists.

Patients taking PPIs had a higher rate of hip fracture: adjusted odds ratio (AOR) 1.44 for those with more than 1 year of PPI therapy. Risk was even higher for patients receiving long-term, high-dose PPI therapy: AOR 2.65. The strength of the association increased along with duration of PPI exposure: AOR 1.22 for 1 year, 1.41 for 2 years, 1.54 for 3 years, and 1.59 for 4 years. Histamine receptor 2 antagonist use did not affect hip fracture risk.

Older adults taking long-term PPI therapy, particularly at higher doses, appear to be at increased risk of hip fracture. Further studies are needed to confirm this association and determine its underlying mechanism. Pending the results of those studies, physicians should prescribe the lowest effective dose of PPI therapy and emphasize the need for increased calcium intake, preferably from dairy sources.

COMMENT: *Allergists/immunologists care for patients with persistent respiratory complaints that often are caused by or aggravated by gastroesophageal reflux. The combination of prolonged inhaled and nasal corticosteroid therapy, intermittent systemic corticosteroid therapy, and now, probably, PPI therapy creates the "perfect storm" for bone loss. It is incumbent upon us as specialists to be knowledgeable and proactive in addressing and treating such a serious problem as osteoporosis, which may be aggravated by the therapies we recommend.*
D. K. L.
Yang Y-X, Lewis JD, Epstein S, Metz DC: Long-term proton pump inhibitor therapy and risk of hip fracture. **JAMA**. 2006;296:2947-2953. ♦♦

Sharp Drop in Positive Penicillin Skin Tests in Children

ADVERSE reactions to penicillin and related antibiotics are common in children. However, only a small percentage of reported reactions ➤➤

are true IgE-mediated penicillin allergy, confirmed by skin testing. A 10-year prospective database was analyzed to report on trends in penicillin skin test reactivity, including the role of specific minor determinant reagents in diagnosing penicillin allergy.

The database included 359 patients referred to a children's hospital allergy clinic for penicillin skin testing from 1993 to 2003. During this time, three test reagents were used: the major determinant benzylpenicilloyl polylysine and the minor determinants penicillin G and sodium penicilloate. The results were compared with those of 562 children tested from 1979 through 1992.

Of 23 positive skin test reactions occurring from 1993 to 2003, all but one occurred in the first year of the experience. The 6% rate of positive results contrasted sharply with the 27% rate between 1979 and 1992. Thirty-five percent of positive reactions were to penicillin G and/or sodium penicillioate, while 8.5% were to sodium penicilloate alone. The clinical history--ie, the presence or absence of characteristics of IgE-mediated reactions--did not affect the likelihood of a positive skin test result.

This extensive experience suggests a significant drop in the rate of positive penicillin skin tests among children over the past two decades. Testing with the minor determinant reagents penicillin G and sodium penicilloate appears essential for detecting the presence of penicillin allergy. The clinical history is of little use in predicting the results of skin tests.

COMMENT: *This is an important study for many reasons. First, the scope is impressive, with more than 900 pediatric patients studied over a 10-year period. Second, it reminds us of the limitation of physician- or patient-diagnosed allergy and the importance of skin testing with major and minor determinants. Now if someone would only step up to the plate and manufacture reagents for us to use!*
A. M.
Jost BC, Wedner HJ, Bloomberg GR: Elective penicillin skin testing in a pediatric outpatient setting.
Ann Allergy Asthma Immunol. 2006; 97:807-812, 2006. ♦♦

Biphasic Anaphylaxis: Rates and Risk Factors

IT is increasingly recognized that anaphylaxis can follow a biphasic course. Reported incidences of biphasic anaphylaxis vary widely, and little is known about the predictive clinical features. These issues were addressed in a 3-year prospective study.

The experience included 134 patients with anaphylaxis seen at a Canadian tertiary care center from 1999 through 2001. Patients were contacted within 48 to 72 hours to assess diagnostic criteria for anaphylaxis, including the occurrence of biphasic reactions. Medical records were reviewed and the characteristics of uniphasic and biphasic anaphylaxis were compared.

Of 103 patients with complete follow-up data, 20 met criteria for biphasic reactions--a rate of 19.4%. Patients with biphasic reactions were younger, median age 25 versus 35 years. There was no difference in the inciting antigens between biphasic and uniphasic reactions. The second phase of the reaction took place at an average of 10 hours, with 40% occurring after 10 hours.

Biphasic reactions were associated with a longer time to initial symptom resolution, 133 versus 112 minutes. Most other characteristics were similar between groups. However, patients with biphasic reactions received less epinephrine, with a trend toward lower corticosteroid use. Fifty-five percent of the second-phase reactions were clinically similar to the initial phase. Forty percent included life-threatening symptoms, and 20% required more aggressive treatment than the first phase. No biphasic reactions occurred in patients who had complete responses to treatment within 30 minutes.

Nearly 20% of patients with anaphylaxis have biphasic reactions, this prospective study suggests. The second-phase reactions occur an average of 10 hours after the first phase, but may occur much later. Undertreatment of the initial reaction may be a contributing factor; epinephrine treatment leading to complete resolution within one half hour may protect against the occurrence of biphasic reactions.

COMMENT: *This paper provides additional support for aggressive management of all anaphylaxis, as individuals with resolution within 30 minutes did not experience biphasic reactions. Onset occurs after 10 hours in 40% of affected subjects, and 40% of biphasic reactions are life-threatening. These findings emphasize the need to provide epinephrine to anyone who requires more than 30 minutes to recover from the initial reaction.*
D. K. L.
Ellis AK, Day JH: Incidence and characteristics of biphasic anaphylaxis: a prospective evaluation of 103 patients.
Ann Allergy Asthma Immunol. 2007;98:64-69. ♦♦

Peanut Allergens Differ in Potency

THE role of specific peanut allergens, or of binding to multiple allergens, in causing severe clinical reactions is unclear. Sensitization to various peanut allergens was evaluated as a predictor of clinical reactivity.

The study included 30 adult patients with peanut allergy, confirmed by skin prick testing. Further skin prick tests were performed to assess sensitization to the peanut allergens Ara h 1, Ara h 2, Ara h 3, and Ara h 6. The findings were compared with the patients' clinical reactivity, assessed by double-blind placebo-controlled food challenge. In most patients, the eliciting dose of peanut was determined.

Rates of sensitization to specific peanut allergens were 87% to Ara h 6, 83% to Ara h 2, 53% to Ara h 1, and 50% to Ara h 3. All patients sensitized to one or both of the latter antigens were also sensitized to Ara h 6 and/or Ara h 2. More severe clinical reactions➤➤

were associated with a higher skin test response to Ara h 2 and Ara h 6 at low concentrations, ie, 0.1 µg/mL; and to Ara h 1 and Ara h 3 at high concentrations, ie, 100 µg/mL. Patients with more severe reactions were sensitized to a higher number of allergens and had a greater cumulative skin prick test response. Eliciting dose did not affect clinical severity of reactions.

Sensitization to specific peanut allergens affects the clinical severity of reactions. Ara h 2 and Ara h 6 appear to be more potent--sensitized patients have more severe reactions than those sensitized to Ara h 1 and Ara h 3. Oral challenge studies are needed to confirm these differences in potency.

COMMENT: *Skin testing and ImmunoCAP testing are good tools for helping predict the likelihood of having a clinical reaction to peanut, but we currently have little to help predict the severity of future clinical reactions. Studying the diversity of specific peanut IgE may be useful in this regard. This study helps confirm a previous finding that patients with more severe clinical reactions tend to have specific IgE to each of the four major peanut proteins. It also observes that patients with a prior history of severe peanut reactions had stronger skin test reactions to Ara h2 and Ara h6 at low concentrations than patients with less severe reaction histories. Perhaps in the future we will be performing a titrated skin test panel to a family of peanut allergens in clinic.*
S. A. T.
Peeters KABM, Koppelman SJ, van Hoffen E, et al: Does skin prick test reactivity to purified allergens correlate with clinical severity of peanut allergy?
Clin Exp Allergy. 2006;37:108-115. ♦♦

Montelukast Improves Distal Lung Function

DISTAL lung inflammation and remodeling likely play a role in the pathophysiology and symptoms of asthma. Montelukast is a systemically administered drug that has a greater impact on asthma symptoms and quality of life than on FEV_1. The current study evaluated the effects of montelukast on measures of distal lung function.

The randomized, crossover trial included 19 patients with mild asthma, treated with short-acting inhaled β_2-agonists only. After baseline examination including tests of pulmonary function and mechanics, the patients received 4 weeks of treatment with montelukast, 10 mg taken in the evening, and 4 weeks of treatment with placebo. Treatments were given in random order with a 2-week washout period. At the end of each treatment period, measures of proximal and distal lung function were assessed, along with symptoms.

Montelukast was associated with a 0.16 L increase in FEV_1, compared to a 0.05 L decrease with placebo. During montelukast treatment, the patients also had significant improvements in specific conductance, an increase of 7.2% predicted, compared to a decrease of 17% predicted with placebo; and percentage of predicted residual volume, with increases of 18.4% predicted on montelukast versus 3.0% predicted on placebo. Improvements in residual volume during montelukast treatment were correlated with reductions in wheezing, chest tightness, and other symptoms.

For patients with mild asthma, oral montelukast treatment is associated with improvements in both distal and proximal lung function. The improvements in distal lung function, particularly residual volume, are associated with reductions in asthma symptoms. Future trials of asthma treatments should incorporate measures of distal lung function.

COMMENT: *Montelukast has a moderate effect on FEV_1, a marker of both large and small airways. However, clinical outcomes seem to improve to a greater degree. Using residual volume as a marker for distal airways effect, these researchers demonstrated significant improvement, which correlated with clinical improvement. This may explain the discrepancy between clinical outcomes and traditional spirometry in response to montelukast.*
S. F. W.
Kraft M, Cairns CB, Ellison MC, et al: Improvements in distal lung function correlate with asthma symptoms after treatment with oral montelukast.
Chest. 2006;130:1726-1732. ♦♦

ICS Alone Is Best for Kids with Persistent Asthma

THE goal of treatment for mild to moderate persistent childhood asthma is to control symptoms using the lowest possible dose of inhaled corticosteroid (ICS). Alternative approaches include a leukotriene receptor antagonist (LTRA), such as montelukast; or adding a long-acting β agonist (LABA) to ICS. The Pediatric Asthma Controller Trial (PACT) compared these two alternatives to ICS monotherapy.

The randomized, double-blind trial included 285 children with mild to moderate persistent asthma. All had an FEV_1 of at least 80% predicted with a methacholine FEV_1 PC_{20} 12.5 mg/mL or less. Patients were assigned to receive monotherapy with fluticasone, 100 µg twice daily; fluticasone 100 µg plus salmeterol 50 µg twice daily; or montelukast 5 mg once daily. The main outcome of interest was asthma control days. Secondary outcomes included asthma exacerbations and pulmonary function variables.

The percentage of asthma control days was 64.2% with fluticasone monotherapy, 59.6% with fluticasone plus salmeterol, and 52.5% with montelukast. Both fluticasone alone and fluticasone plus salmeterol yielded more episode-free days than montelukast. However, several other outcomes were better with fluticasone alone, including the FEV_1/forced vital capacity ratio, maximum bronchodilator response, exhaled nitric oxide, and methacholine responsiveness. Growth was not significantly different between groups.

Fluticasone, alone or in combination with salmeterol, offers better disease control than montelukast in children with mild to moderate persistent asthma. However, other outcome measures appear superior ➤➤

with fluticasone monotherapy, compared to the combination regimen evaluated in this study. For children meeting the PACT enrollment criteria, fluticasone monotherapy appears to be the treatment of choice. Other approaches are needed for children whose asthma is not well-controlled on low-dose ICS monotherapy.

COMMENT: *The PACT was designed to determine whether persistent asthma in children could be controlled with a reduced steroid dose if a LABA was added (PACT combination) and also to study the efficacy and safety of the LTRA montelukast. Interestingly, monotherapy with an ICS was comparable to the PACT combination in asthma control days only. In all other parameters--including exhaled nitric oxide and spirometric measures--ICS monotherapy was superior to both the PACT combination and montelukast. The concerning point of this study is that even under optimal conditions, the childrenís symptoms were controlled only 64% of the time. There is a need to improve our therapeutic options for pediatric asthma.*
S. M. F.
Sorkness CA, Lemanske RF Jr, Mauger DT, et al: Long-term comparison of 3 controller regimens for mild-moderate persistent childhood asthma: the Pediatric Asthma Controller Trial.
J Allergy Clin Immunol. 2007;119:64-72. ♦♦

Promising Results with Egg Oral Immunotherapy

IN contrast to other types of allergic diseases, there is currently no active treatment for food allergies. Previous studies have reported some success with oral immunotherapy (OIT). Initial results of an OIT regimen for children with egg allergy are reported.

The study included seven children with egg allergy but no history of egg-induced anaphylaxis. The mean age was 44.7 months; all children had comorbid atopic dermatitis, while many had asthma and/or other food allergies. The OIT protocol included a modified rush phase and a buildup phase, with the goal of reaching a daily maintenance dose of 300 mg of egg protein. Assessment included double-blind placebo-controlled food challenges at 2 years' follow-up.

All seven patients completed the study. There were few problems during the modified rush and buildup phases, and no symptoms related to home treatment during the maintenance phase. Egg-specific IgG levels increased from 8.24 mg/L at baseline to 38.00 mg/L at 2 years' follow-up. Egg -specific IgE decreased in most cases, although the mean change from baseline was not significant. In food challenges, all patients tolerated a higher dose of egg protein than at baseline, or the dose associated with a typical accidental ingestion. Two patients passed all oral egg challenges.

Oral immunotherapy may offer a new approach to the treatment of egg allergy in children. The protocol used in this study protects against reactions to accidental egg exposure, and may even induce long-term tolerance in some cases. The authors plan larger studies of egg OIT, including patients with a history of more severe clinical reactions.

COMMENT: *This is an open-label, uncontrolled, proof-of-concept study of OIT in children with egg allergy without anaphylaxis. All had atopic dermatitis and manifested urticaria after egg ingestion; three of the seven patients had other symptoms as well. After a carefully conducted modified rush protocol and 2 years of daily low-dose egg protein ingestion, egg-specific IgG increased while egg-specific IgE decreased. All 7 children tolerated challenges with egg. The authors state that they are starting a larger, blinded, controlled study. Since OIT for foods could be a remarkable benefit for our food-allergic patients, we anxiously await their future results.*
S. M. F.
Buchanan AD, Green TD, Jones SM, et al: Egg oral immunotherapy in nonanaphylactic children with egg allergy.
J Allergy Clin Immunol. 2007;119:199-205. ♦♦

Immunologic Response to Dog Extract Is Dose-Dependent

HIGH-dose allergen immunotherapy is an effective treatment for patients with various types of allergies. Compared with other allergens such as cat dander, relatively little is known about the effectiveness of immunotherapy with dog extract. Immunologic responses to standardized dog extract at varying concentrations of Can f 1 were analyzed.

Twenty-eight patients receiving cluster immunotherapy for dog allergy were randomly assigned to receive extract containing one of three doses of Can f 1--0.6, 3.0, or 15.0 μg/0.5 mL--or placebo. Assessment included titrated skin-prick tests, late cutaneous response, allergen-specific IgE levels, lymphocyte proliferation in response to stimulation with dog allergen, and cytokine assays.

At 5 weeks, titrated skin-prick tests showed significant, dose-dependent suppression of the wheal response. Compared to baseline, the change was significant in the medium- and high-dose allergen groups, but not in the low-dose and placebo groups. There was a similar dose-response in suppression of the late cutaneous response. Dog-specific IgG_4 decreased significantly in the high- and low-dose allergen groups. Cytokine assays showed dose-dependent suppression of secreted tumor necrosis factor-α, with an increase in secreted transforming growth factor-β. Secreted interleukin-4 was significantly decreased from baseline in the high-dose allergen group. Because of a scoring problem, symptom scores were unchanged. There was no change in lymphocyte proliferation, other secreted cytokine levels, or intracellular cytokine production.

In patients undergoing immunotherapy with dog extract, a higher allergen dose provides a greater immunologic response. A Can f 1 dose of 15 μg provides the strongest and most consistent response. This is consistent with previous studies of cat extract showing the best response at the same dose of Fel d 1. ➤➤

COMMENT: *Using a relatively rapid build-up, cluster immunotherapy dosing schedule, these dog-allergic patients reached maintenance dose in 5 weeks. There was a dose-dependent response to immunologic parameters including titrated and late cutaneous skin tests, IgG_4, and TGF-β which represents T suppressor cell activity. Improvement in nasal allergen challenge could not be demonstrated because of a data collection scoring problem. The bottom line is that the higher the dose of allergen given for IT, the better the result.*
S. M. F.
Lent AM, Harbeck R, Strand M, et al: Immunologic response to administration of standardized dog allergen extract at differing doses.
J Allergy Clin Immunol. 2006;118:1249-1256. ♦♦

We Have More Work to Do...

DESPITE current guidelines, most children with asthma exacerbations seen in the emergency department (ED) are not currently receiving anti-inflammatory therapy. The pediatric ED is an appropriate place to initiate anti-inflammatory therapy, but involvement of the primary care physician (PCP) is essential to the success of such efforts. An ED intervention for children with asthma is reported, emphasizing promotion of appropriate follow-up care by the PCP.

The parents or guardians of 142 children seen in an urban pediatric ED with asthma exacerbations were asked to compete a survey regarding the child's asthma history and treatment. At the time of ED discharge, an ED attending physician provided persistent asthma patients with a 2-week sample of anti-inflammatory medication, based on the child's asthma severity classification. Each child's PCP was contacted to discuss the diagnosis of persistent asthma and the addition of anti-inflammatory medication. Parents were instructed to follow up with the PCP about further treatment, including a prescription for anti-inflammatory treatment. Follow-up evaluation included telephone calls, pharmacy data, and PCP office records.

Forty-seven children met criteria for persistent asthma and were enrolled. Seven were lost to follow-up; of the remaining 40 patients, 28 received follow-up care from their PCP. In 75% of these cases, the PCP continued the child's anti-inflammatory medication, including 88.9% of children with severe persistent asthma and 68.4% of those with mild to moderate persistent asthma. Overall, 13 of the 28 patients who followed up with their PCP had received, filled, and used a prescription for anti-inflammatory therapy at follow-up.

A pediatric ED intervention, in cooperation with PCPs, can promote the use of maintenance anti-inflammatory therapy among inner-city children with asthma. Patient nonadherence is a significant barrier--even when prescriptions are received from a PCP, many are not filled. Before leaving the ED, parents should be encouraged to follow up with the PCP, who should be identified as the primary source of asthma management and medication refills.

Lehman HK, Lillis KA, Shaha SH, et al: Initiation of maintenance antiinflammatory medication in asthmatic children in a pediatric emergency department.
Pediatrics. 2006;118:2394-2401. ♦♦

MANY children with persistent asthma do not receive recommended therapy with inhaled corticosteroids (ICS). Few studies of this issue have used pharmacy data as an objective indicator of whether ICS are available to these children. Pharmacy records were used to assess medication use among urban children with persistent asthma.

Patients were drawn from a sample of 221 children with persistent asthma participating in a clinical trial of an asthma educational intervention. Most of the children were African-America boys receiving Medicaid; the mean age was 4.5 years. Use of asthma medications during a 12-month follow-up period was assessed by parental questionnaires and pharmacy records. Asthma-related morbidity, health care utilization, and asthma care were assessed as well.

Of 180 children with complete data, 72% had at least one exposure to ICS. However, 20% received no asthma medications at all during the follow-up year, or received short-acting β agonists only. Just 20% of children received six or more ICS refills over the 12-month period studied; 40% received three or more refills. Children who had more short-acting β agonist refills and those receiving specialist care were more likely to have three or more ICS refills, after adjustment for age, asthma severity, and measures of asthma care.

This study documents very low rates of ICS use among an underserved population of children with persistent asthma, coupled with overuse of short-acting β agonists. Over 12 month's follow-up, pharmacy records suggest that adequate controller medications are available to only 1 in 5 children in this group. Efforts to improve daily asthma management might include review of pharmacy records, assessment of parents' ability to recognize symptoms, and appropriate referral to asthma specialists.

Butz AM, Tsoukleris M, Donithan M, et al: Patterns of inhaled antiinflammatory medication use in young underserved children with asthma.
Pediatrics. 2006;118:2504-2513.

COMMENT: *Despite a decade of widely promoting anti-inflammatory therapy as the cornerstone of persistent asthma control, there remain too many who do not receive maintenance medication, for a variety of reasons. Whatever the medical community can do to improve this situation will improve outcomes for these patients. The study by Lehman et al. outlines another potential approach in a pediatric population: partnering between emergency medicine and primary care to improve access to asthma maintenance therapy at the time of an ED visit, and continuity of care thereafter. Now, if we can only convince patients (and their parents) to make (and keep) follow-up appointments, and take the prescribed medications.* ➤➤

Which brings us to the study by Butz et al. Inhaled corticosteroid use was indirectly measured by examining pharmacy records of urban children with persistent asthma. Compliance with ICS was so poor that only 20% filled more than six monthly refills in a 12 month period. For study analysis, this required a change in comparators to those filling three or more ICS prescriptions versus those with fewer ICS refills (in 1 year)! Tragically, three children (1.4% of study population) died from asthma during the study period; two of these children had not received ICS.
K. R. M.

♦♦

Aspirin May Lower Risk of Adult-Onset Asthma

SOME studies have suggested that reductions in the use of aspirin--the result of concern about Reye's syndrome--may have contributed to the increase in pediatric asthma. In one large observational study, women reporting frequent aspirin use had a lower rate of newly diagnosed asthma than non-aspirin users. Randomized trial data were used to assess the effects of aspirin use on adult-onset asthma in men.

As part of the Physicians' Health Study, 22,071 male physicians were randomly assigned to take aspirin, 325 mg, or placebo every other day. At baseline, the men were 40 to 84 years old, apparently healthy, and tolerant of aspirin. The study was halted early after 5 years, when it became apparent that aspirin users had dramatically lower rates of myocardial infarction. Available follow-up data, totaling 109,035 person-years, were analyzed to compare the rate of adult-onset asthma between the aspirin and placebo groups.

A new diagnosis of asthma was reported by 113 men taking aspirin versus 145 in the placebo group. The associated hazard ratio of 0.78 and was unchanged by adjustment for smoking, body mass index, age, or other baseline characteristics. The preventive benefit of aspirin was somewhat greater in younger men and those who never smoked.

Taking aspirin may reduce the risk of adult asthma in healthy, aspirin-tolerant men. Confirmatory studies are needed to specifically test this apparent preventive benefit of aspirin. There is no evidence that aspirin improves symptom status in patients with existing asthma.

COMMENT: *This study is important in that it allows further benefit from regular aspirin therapy. It should be noted that 325 mg was taken on alternate days, It is not clear if 81 or 162 mg daily will have the same effect.*
B. E. C.
Barr RG, Kurth T, Stampfer MJ, et al: Aspirin and decreased adult-onset asthma: randomized comparisons from the Physicians' Health Study.
Am J Respir Crit Care Med. 2007;175:120-125. ♦♦

Arginine-16 Polymorphism Affects Response to Salmeterol

THE arginine-16 polymorphism of the β_2 adrenoreceptor gene *ADRB2* may affect responses to inhaled β_2 agonists. Studies suggest that the presence of the homozygous arginine-16 variant (Arg/Arg) reverses the benefits of regular short-acting β_2 agonist therapy in adult asthma patients, compared with the homozygous glycine-16 genotype (Gly/Gly). The contribution of this polymorphism to the risk of asthma exacerbations in children and young adults was investigated, including the relationship to use of long-acting β_2 agonists.

The cross-sectional study included 546 children and young adults seen in Scottish asthma clinics during 2004-05. All patients provided DNA mouthwash samples for genotyping at position 16 and 27 of the *ADRB2* gene. Genotype was Arg/Arg16 for 15% of patients, Arg/Gly16 for 45%, and Gly/Gly16 for 38%. The findings were compared with the rates of asthma exacerbations over the previous 6 months, including comparison of patients who were and were not taking regular inhaled salmeterol therapy.

Across the four steps of the British Thoracic Society asthma treatment guidelines, the rate of asthma exacerbations was increased for patients who were homozygous for the Arg16 variant, either Arg/Arg or Gly/Gly: odds ratio 2.05. The risk was even higher among Arg16 homozygotes treated with salmeterol, odds ratio 3.40. Genotype at position 27 of *ADRB2*, ie, the Glu27Gln polymorphism, was unrelated to the exacerbation rate.

Among young patients with asthma, those who are homozygous for the arginine-16 genotype of the *ADRB2* gene are at increased risk of asthma exacerbations. This risk appears particularly pronounced in patients taking regular inhaled salmeterol, possibly reflecting genotype differences in salmeterol-induced downregulation and impaired receptor coupling. Other second-line controllers, such as montelukast or theophylline, might be more effective in patients with a homozygous arginine-16 genotype.

COMMENT: *While there are significant differences of opinion in this area of research, this research group presents very provocative data. In a large cohort of children, homozygotes for the Arg/Arg β_2 receptor genotype receiving salmeterol appeared to do less well than other genotypes. While this signal in the literature continues to be investigated, it appears that LABA therapy remains safe for most asthmatics. Clinicians must be aware of this potential mechanism in patients whose asthma is not well controlled on ICS/LABA combinations or regular use of short-acting β_2 agonist.*
A. M.
Palmer CNA, Lipworth BJ, Lee S, et al: Arginine-16 β_2 adrenoceptor genotype predisposes to exacerbations in young asthmatics taking regular salmeterol.
Thorax. 2006;940-944, 2006. ♦♦

FOCUS ON PREVENTION

Early Antibiotic Exposure Linked to Wheezing Risk

IT has been suggested that early-life exposure to antibiotics might influence the development of atopic disease. This potential association was evaluated in a large Dutch birth cohort study.

The "KOALA" cohort included 2,764 infants of women recruited during pregnancy in 2000. Follow-up included questionnaires regarding antibiotic use during the first 6 months--including exposure to maternal antibiotics via breast-feeding and oral antibiotics prescribed for the infant--and the occurrence of eczema and wheezing through age 2 years. Blood samples were obtained from a subset of infants for measurement of total and allergen-specific IgE levels.

By age 2 years, 32% of the infants had had eczema, 11% had recurrent wheezing, 5% had prolonged wheezing, and 27% were sensitized to at least one common allergen. Rates of antibiotic exposure by age 6 months were 11% via breast milk and 20% through oral antibiotic treatment. Antibiotic exposure through breast-feeding was associated with increased risk of recurrent wheezing, adjusted odds ratio (OR) 1.55, though not of prolonged wheezing. Oral antibiotics were associated with increased risks of both recurrent and prolonged wheezing, OR 2.65 and 2.32, respectively. The associations with oral antibiotics remained significant after exclusion of infants who wheezed during the same period in which they received antibiotics. Neither route of antibiotic exposure was related to eczema or sensitization.

Antibiotic treatment during the first 6 months of life is associated with an increased risk of wheezing by age 2. No such association is noted for eczema or allergic sensitization. Exposure to maternal antibiotics via breast milk may increase the risk of recurrent wheezing.

COMMENT: *This epidemiologic study from the Netherlands attempts to assess a potential relationship between early exposure to antibiotics and atopic manifestations. Recurrent wheeze was associated with early antibiotic exposure via oral prescription for the infant and to a lesser degree maternal use, with exposure via breast-feeding. Neither atopy nor atopic dermatitis was associated with such early antibiotic exposures. Certainly, recurrent wheeze may not be predictive of future asthma or atopy, and a 2-year study time is insufficient to assess these risks. Let's hope for additional longitudinal reports from this cohort.*
K. R. M.

Kummeling I, Stelma FF, Dagnelie PC, et al: Early life exposure to antibiotics and the subsequent development of eczema, wheeze, and allergic sensitization in the first 2 years of life: The KOALA Birth Cohort Study. **Pediatrics**. 2007;119:225-231. ♦♦

Which Comes First, the Chicken or the Egg?

THE recognized link between obesity and asthma could be related to reduced physical activity. Little is known about factors affecting physical activity in asthmatic children, including the role of mental health and other confounders. The relationship between physical activity and body mass index (BMI) was studied in school-aged children with asthma.

The study included 56 children, aged 7 to 14 years, receiving outpatient care for asthma. Sixty-one children receiving care at ENT or dermatologic clinics were studied for comparison. Assessments included BMI, a child-rated physical activity questionnaire, and a parental rating of child mental health.

Mean BMI was 20.78 for children with asthma versus 18.82 in the comparison group. Median number of physical activities per day was 4 versus 6, respectively. Asthma was the factor most strongly associated with physical activity level. Children with asthma had more emotional problems; within the asthma group, more active children had better mental health. Asthma was cited as a barrier to exercise by more than 60% of the children with asthma and their parents.

Children with asthma have higher BMI and lower physical activity levels than children with other health problems. Interventions to increase physical activity could have both physical and mental health benefits for asthmatic children.

COMMENT: *In this study from the United Kingdom, having asthma is significantly associated with overweight status or obesity in children. Asthma is perceived as a barrier to physical activity by both parents and children, and not surprisingly, is associated with a negative impact on mental health. These results parallel similar studies done in adults.*
K. R. M.

Glazebrook C, McPherson AC, Macdonald IA, et al: Asthma as a barrier to children's physical activity: implications for body mass index and mental health. **Pediatrics**. 2006;118:2443-2449. ♦♦

Skinny Farmers Do Better!

OBESITY and reduced exposure to microbial agents have both been suggested as risk factors for allergic sensitization, but few studies have looked at their possible combined effects. The effects of the farm environment on allergy risk were compared for obese versus nonobese adults.

As part of a German population-based study, 1,861 adults living in a rural area were studied. Rates of allergic sensitization and allergic rhinitis were compared for subjects with and without recent obesity, defined as a body mass index of 30 kg/m^2 or higher; and with and without childhood farm contact during the first 3 years of life.

Among subjects with childhood farm exposure, the rate of allergic sensitization was significantly lower ➤➤

for obese versus nonobese subjects, odds ratio 0.6. Among obese subjects, there was no significant protective effect of farm exposure. A similar pattern was found on analysis of allergic rhinitis.

Although childhood farm exposure protects against allergic sensitization, this effect may be reduced or lost for subjects who are obese as adults. Obesity might help to explain the high rate of respiratory allergies in inner-city populations.

COMMENT: *Using data from a questionnaire survey of rural adults, these German researchers found that contact with farm animals as a young child had a protective effect on adult allergy sensitization in nonobese adults. There was no significant benefit of exposure to farm animals in subjects who were obese; therefore obesity seems to diminish or cancel out the protective effect of childhood farm animal exposure. The authors suggest that dietary factors or nonspecific inflammation could be responsible for the higher incidence of atopy in obese adults.*
S. M. F.
Radon K, Schulze A: Adult obesity, farm childhood, and their effect on allergic sensitization.
J Allergy Clin Immunol. 2006;118:1279-1283. ♦♦

Dirty Dogs

PREVIOUS studies have suggested a lower rate of asthma among children from homes with dogs. However, these studies have not looked at the concomitant effect of dust endotoxin levels, which are higher in homes with dogs.

This issue was addressed in a study of 532 infants having at least one parent with confirmed atopy. The prevalence of wheezing at age 1 was not significantly related to the presence of a dog or cat in the home, nor to the level of endotoxin in house dust samples. The rate of positive skin prick tests was 28.6%.

On univariate analysis, wheezing outcomes were related to daycare attendance, number of siblings, respiratory infections, maternal smoking, and parental asthma. Logistic regression analysis found a significantly lower risk of recurrent wheezing in children from homes with high dust endotoxin levels and two or more dogs. Similar associations were noted for other wheezing outcomes.

In infants with a family history of atopy, exposure to pets or endotoxin does not independently risk of allergic sensitization of wheezing. However, exposure to higher endotoxin levels and multiple pets may be linked to lower rates of wheezing in these at-risk infants.

COMMENT: *This report tests the Hygiene Hypothesis using early data from the Cincinnati Childhood Asthma and Air Pollution study. The data do not support the effect of pet ownership in reducing wheezing and allergen sensitization. However, pet ownership--particularly two or more dogs--in conjunction with high endotoxin levels in the home was conducive to reduced wheezing in the infants. The Cincinnati study is a major effort including over 500 children from allergic families, and we will look for future reports as this group continues to collect data.*
S. M. F.
Campo P, Kalra HK, Levin L: Influence of dog ownership and high endotoxin on wheezing and atopy during infancy.
J Allergy Clin Immunol. 2006;118:1271-1278. ♦♦

Probiotics: Pro and Con

THE well-known Hygiene Hypothesis leads to speculation that supplementation with probiotics--nonpathogenic intestinal bacteria--may reduce the development of atopy. This randomized trial evaluated a combination of probiotics for the prevention of allergic disease in infants at high genetic risk.

The trial included 1,223 pregnant women with physician-diagnosed allergic disease. For 2 to 4 weeks before delivery, one group received a supplement containing a mix of four probiotics while controls received placebo After birth, 905 newborns were randomly assigned to 6 months of treatment with the same probiotic mix plus galacto-oligosaccharides, or with placebo.

When the infants were 2 years old, the cumulative rate of allergic disease was similar between groups, although infants fed probiotics tended to have a fewer IgE-associated diseases--odds ratio 0.71. Infants in the probiotic group had significantly lower rates of eczema and atopic eczema--odds ratio 0.74 and 0.66, respectively. Fecal samples showed higher rates of colonization with *Lactobacillus* and *Bifidobacterium* species in the probiotic group.

The combination probiotic regimen evaluated in this study lowers the risk of eczema for infants at high genetic risk of allergic disease. Despite a trend toward a lower rate of IgE-mediated diseases with probiotics, the overall effect on allergic disease risk was nonsignificant in this trial.

COMMENT: *In this Finnish study, atopic mothers were given probiotic supplements or placebo for 2 to 4 weeks before delivery, and the babies for the first 6 months of life. At 2 years, there was no difference in the cumulative incidence of all allergic diseases (asthma, rhinitis, eczema, or food allergy) or allergen sensitization. However, the specific incidence of eczema was reduced.*
R. J. M.
Kukkonen K, Savilahti E, Haahtela T, et al: Probiotics and prebiotic galacto-oligosaccharides in the prevention of allergic diseases: a randomized, double-blind, placebo-controlled trial.
J Allergy Clin Immunol. 2007;119:192-198. ♦♦

THE potential for probiotics to prevent allergic disease remains unclear. A *Lactobacillus acidophilus* supplement was evaluated for prevention of allergic diseases in infants of atopic mothers.

Two hundred thirty-one high-risk infants were randomly assigned to receive the *Lactobacillus* supple-➤➤

ment or placebo daily for the first 6 months of life. One hundred seventy-eight infants completed their assigned supplementation. Infants in the probiotic group had a higher rate of intestinal colonization with *Lactobacillus*.

However, there was no significant difference in the rate of atopic dermatitis at 6 months: 25.8% in the probiotic group and 22.7% in the placebo group. At 12 months, the overall rate of positive skin prick tests plus atopic dermatitis was higher for children receiving *Lactobacillus*. The probiotic group also had a higher rate of sensitization. The presence of culturable *Lactobacillus* in feces at age 6 months was associated with a higher risk of later sensitization to cow's milk.

Lactobacillus supplementation during the first 6 months of life does not reduce the risk of atopic dermatitis for infants at high genetic risk. Further study is needed to clarify the higher rate of allergic sensitization observed in the probiotic-treated infants in this trial.

COMMENT: *In this study, infants of allergic mothers were given probiotics or placebo for the first 6 months of life. Unfortunately, the supplemented group actually had a higher rate of allergen sensitization, wheezing, and cowís milk sensitivity by 1 year of age. Probiotics did not reduce the development of atopic dermatitis.*
R. J. M.
Taylor AL, Dustan JA, and Prescott SL: Probiotic supplementation for the first 6 months of life fails to reduce the risk of atopic dermatitis and increases the risk of allergen sensitization in high-risk children: a randomized controlled trial.
J Allergy Clin Immunol. 2007;119:184-191. ♦♦

Whole Grains and Fish Lower Asthma Risk

CHANGES in the Western diet--particularly decreased consumption of fruits, vegetables, and fish--may have contributed to increased asthma rates. Data from the International Study on Allergy and Asthma in Childhood 2 were used to analyze associations between diet and asthma risk, including clinical as well as questionnaire assessments of asthma.

The analysis included 598 Dutch children aged 8 to 13 years. Information on diet was provided by parent-completed food frequency questionnaires. Endpoints included not only questionnaire data on current wheezing and asthma, but also clinical assessments of bronchial hyperresponsiveness (BHR) and atopic sensitization.

Children who ate more whole grains and more fish had lower rates of asthma. On logistic regression analysis, the adjusted odds ratio for current asthma was 0.46 for children in the highest category of whole-grain consumption and 0.34 for those in the highest category of fish consumption. Odds ratios for atopic asthma with BHR were 0.28 and 0.12, respectively. Whole grains and fish also had protective effects on current wheezing and atopic wheezing with BHR. Asthma and other outcomes were unrelated to consumption of fruits, vegetables, or dairy products.

A diet high in whole grains and fish is associated with a lower risk of asthma in school-aged children. No conclusions can be drawn about whether these are causal associations; prospective studies of dietary factors are needed.

COMMENT: *The recent literature suggests that the Hygiene Hypothesis is unlikely to be the only explanation for the increased prevalence of asthma in Western societies. Along with increasing weight and sedentary lifestyles, Western diets are clearly changing. It appears that intake of a diet rich in fish and whole grain confers greater than 50% protection against developing asthma!*
A. M.
Tabak C, Wijga AH, de Meer G, et al: Diet and asthma in Dutch school children (ISAAC-2).
Thorax. 2006;61:1048-1053. ♦♦

CLINICAL TIDBITS

Exhaled NO Predicts Respiratory Symptoms in Infants of Atopic Mothers

EXHALED nitric oxide is a clinically useful marker of asthma, but its pathogenetic role before the appearance of symptoms is unclear. Exhaled NO was prospectively measured in a birth cohort of 164 healthy newborns and evaluated as a predictor of respiratory symptoms appearing later in life.

For 61 infants whose mothers had a history of atopic disease, elevated NO levels during the newborn period predicted an increased likelihood of respiratory symptoms: risk ratio 7.5 per 1 nL/s increase in NO output. Exhaled NO also predicted respiratory symptoms in infants of mothers who smoked, RR 6.6. For infants with both risk factors, the RR increased to 21.8.

For infants of atopic mothers and/or mothers who smoke, elevated NO levels during the newborn period predict an increased risk of respiratory symptoms during the first year of life. Further studies may help to clarify nitric oxide's role in the development of respiratory disease.

COMMENT: *This study allows us to reaffirm the potential adverse outcomes in children born to smoking mothers with a family history of asthma. As this monitoring device becomes more widely accepted, such studies may provide the basis for modification of our practice patterns.*
B. E. C.
Latzin P, Kuehni CE, Baldwin DN, et al: Elevated exhaled nitric oxide in newborns of atopic mothers precedes respiratory symptoms.
Am J Respir Crit Care Med. 2006;174:1292-1298. ♦♦

Is Home Monitoring Useful in Asthma?

RECENT studies have questioned the value of home peak expiratory flow (PEF) monitoring in asthma management. Use of an electronic home spirometer for daily measurement of FEV_1 was evaluated in 36 children with mild to moderate persistent asthma. Each day, the children recorded an asthma severity score in a diary and performed an FEV_1 maneuver using the home spirometer, which automatically recorded the results. Patients also measured PEF twice daily. Bronchial responsiveness was assessed at baseline, and bronchodilator response and disease-specific quality of life were assessed at the end of the 3-month study.

The PEF measurements were significantly but weakly correlated with bronchial responsiveness and bronchodilator responses. However, PEF was unrelated to symptom severity or quality of life. Within individual patients, associations between severity scores and home spirometry measures and between PEF and FEV_1 varied widely. Like PEF monitoring, home FEV_1 measurements appear to be of limited value in self-management of childhood asthma.

Brouwer AFJ, Roorda RJ, Brand PLP: Home spirometry and asthma severity in children.
Eur Respir J. 2006;28:1131-1137. ♦♦

ALTHOUGH peak flow monitoring is recommended in asthma management guidelines, few studies have compared with symptom monitoring alone in asthmatic older adults. This issue was addressed in a randomized trial including 296 adults with moderate to severe asthma, age range 50 to 92 years. All received a personalized action plan, emphasizing the use of symptoms or peak flow rate for disease monitoring.

At 2 years' follow-up, none of the study outcomes evaluated--including health care utilization, asthma-specific quality of life, or pulmonary function measures--differed significantly different between groups. This was so whether peak flow monitoring was performed on a twice-daily or as-needed basis. The study educational interventions were associated with significant improvements in both groups, including in the proper use of asthma inhalers. As part of a comprehensive asthma management program, peak flow monitoring offers no advantage over symptom monitoring in older adults with asthma.

Buist AS, Vollmer WE, Wilson SR, et al: A randomized clinical trial of peak flow versus symptom monitoring in older adults with asthma.
Am J Respir Crit Care Med. 2007;174:1077-1087. ♦♦

COMMENT: *These two studies point out that measures of airflow limitation taken at one point in time do not appropriately categorize patients regarding asthma severity and are not useful in developing a home asthma management strategy. The results are very important as they help to minimize the attendant cost of home monitoring for asthma.*
B. E. C.

Anti-IL-5 Therapy Improves Eosinophilic Esophagitis

PATIENTS with eosinophilic esophagitis (EE) have epithelial hyperplasia associated with high numbers of eosinophils in the esophagus. Interleukin (IL)-5 plays a key role in the pathogenesis of this condition. The authors report an open-label, phase I/II trial of anti-IL-5 therapy in 4 patients with EE associated with dysphagia and esophageal strictures. All patients received three infusions of mepolizumab, a humanized monoclonal IgG_1 antibody against human IL-5, 750 mg IV monthly. Anti-IL-5 therapy was associated with significant reductions in peripheral blood eosinophil count and percentage of CCR3+ cells. A 9-fold decrease in esophageal eosinophilia was accompanied by improvements in diet and other clinical outcomes and in quality of life. Initial clinical experience supports the safety and efficacy of anti-IL-5 therapy with mepolizumab for patients with EE.

COMMENT: *Eosinophilic esophagitis is one of a spectrum of infiltrative eosinophilic diseases affecting various parts of the gastrointestinal tract. Treatment of EE currently includes dietary manipulations and topical or systemic corticosteroids, both of which have tolerability or toxicity problems. In this study of four patients, anti-IL-5 had pronounced effects on most measures of improvement and was relatively well-tolerated. Long-term data are still lacking, but this is promising.*
R. J. M.
Stein ML, Collins MH, Villanueva JM, et al: Anti-IL-5 (mepolizumab) therapy for eosinophilic esophagitis.
J Allergy Clin Immunol. 2006;118:1312-1319. ♦♦

Anti-Inflammatory Therapy Reduces Staph Colonization in AD

PATIENTS with atopic dermatitis (AD) are highly susceptible to staphylococcal skin colonization and infection. This randomized trial compared AD severity and *Staphylococcus aureus* colonization between patients treated with topical 0.05% fluticasone propionate or 0.03% tacrolimus, including the effects of complementary topical fusidic acid therapy. Sixty patients with moderate to severe AD were enrolled. With both anti-inflammatory drugs, the colonization rate and density of *S. aureus* on the skin decreased in correlation with AD severity score. Tacrolimus yielded similar clinical improvement fluticasone, although the reduction in *S. aureus* numbers was slower to occur. Adding fusidic acid therapy produced no further benefit; 2 of 5 patients with persistent staphylococcal colonization developed fusidic acid-resistant *S. aureus*. Topical anti-inflammatory therapy for AD reduces *S. aureus* colonization as it improves the allergic inflammation of the skin. Topical antibiotics appear unnecessary unless clinical skin infection is present.

COMMENT: *Various studies confirm the importance of skin bacteria, particularly* Staphylococcus ➤➤

species, in aggravating AD. The role of long-term antibiotic therapy to attempt a change in skin flora is not supported. This study confirms that, in clinically uninfected skin, there is no role for topical antimicrobials. Furthermore, the development of bacterial resistance to the topical agent in 40% of patients is an additional negative concern. The bottom line is to use clinical judgment, not culture data alone, when deciding about antibiotic treatment of AD.
D. K. L.
Hung S-H, Lin Y-T, Chu C-Y, et al: Staphylococcus *colonization in atopic dermatitis treated with fluticasone or tacrolimus with or without antibiotics.*
Ann Allergy Asthma Immunol. 2007;98:51-56. ♦♦

REVIEWS OF NOTE

COMMENT: *This paper provides a single source for most of the relevant literature concerning leukotriene receptor antagonists. We struggle with the decision as to where this class of drugs fits into our armamentarium. There is still controversy; this paper does not answer all of the questions but provides a source of information to help the clinician decide.*
D. K. L.
Currie GP, McLaughlin K: The expanding role of leukotriene receptor antagonists in chronic asthma.
Ann Allergy Asthma Immunol. 2006;97:731-742.

COMMENT: *This is well-written, succinct review of an important topic. Changes I am considering in my practice after reading include more frequent measurement of diffusion capacity to predict early pulmonary fibrosis, screening for partial α1-antitrypsin deficiency, and culturing for* Pseudomonas *species to anticipate the higher likelihood of progressive lung disease.*
D. K. L.
Busse PJ, Farzan S, Cunningham-Rundles C: Pulmonary complications of common variable immunodeficiency.
Ann Allergy Asthma Immunol. 2007;98:1-9. ♦♦

COMMENT: *This is a concise review of beta lactam skin testing and includes both a review of the literature and a discussion of the importance of making penicilloyl-polylysine (PPL) available again.*
S. A. T.
Blanca M, Romano A, Torres MJ, et al: Continued need of appropriate betalactam-derived skin test reagents for the management of allergy to betalactams.
Clin Exp Allergy. 2007;37:166-173. ♦♦

COMMENT: *Since the Womenís Health Initiative reported in 2002 that hormones increase the risk of serious diseases, allergists have often been confronted with the use of alternative integrative medicine options by their patients. The search for safer, effective treatment for menopausal symptoms has led to increased use of phytoestrogens, botanicals, and other treatments for vasomotor symptoms. This paper presents a 1-year randomized, double-blind, placebo-controlled herbal alternative for menopausal symptoms. Three hundred fifty women, 45 to 55 years of age, were randomly assigned to treatment with black cohosh (*Actaea or Cimicifuga racemosa*), a multibotanical preparation with or without dietary soy, hormone therapy, or placebo. Vasomotor symptoms did not differ between the herbal interventions and placebo. The study reinforces the need to evaluate new biologically plausible agents and behavioral treatments in multiethnic populations of women. There were limitations in that the trial did not consider the "whole-person" approach used by naturopathic physicians and could not exclude differences of less than 1.5 vasomotor symptoms between treatment groups.*
M. F.
Newton RM, Reed SD, LaCroix AZ, et al: Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo: a randomized trial.
Ann Intern Med. 2006;145:869-879. ♦♦

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