AllergyWatch®

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

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Some Patients with Insect Sting Allergy Are Skin-Test Negative but RAST-Positive, Study Finds

As many as 30% of patients with a clear history of anaphylactic reaction to insect stings will have a negative skin test result. However, some of these patients will go on to have a serious reaction to a subsequent sting. Participants in a large sting challenge trial were studied to assess the frequency and clinical importance of negative skin test results.

The investigators screened 307 subjects with a history of systemic reaction to an insect sting. Thirty-two percent of these patients had a negative response on intradermal venom skin testing at a dose up to 1 µg/mL.

The patients also underwent a sensitive radioallergosorbent test (RAST) for venom-specific IgE. Of the 99 patients with a negative skin test, 43% had a positive RAST result. The RAST result was low-positive (1 to 3 ng/mL) in 36 of these patients, but high-positive (4 to 243 ng/mL) in 7.

The history of systemic reaction was comparable for patients with positive vs negative skin tests: the reaction was rated mild in about 25%, moderate in 55%, and severe in 20%. Eleven patients with a negative skin test reacted to a challenge sting: the previous systemic reaction was rated mild in 6 of these, moderate in 4, and severe in 1.

Patients with a history of systemic reaction to an insect sting may have negative results on venom skin testing, yet go on to have another systemic reaction. These skin-test-negative patients may be positive for venom-specific IgE antibodies on RAST. Patients with a negative skin test should undergo repeat skin-testing, followed by an IgE antivenom serologic test. The authors call for improved skin test reagents.

COMMENT: *In the published literature, about one-third of subjects with a history of systemic reactions to insect stings have negative venom skin tests and are excluded from immunotherapy. Yet some may still suffer anaphylaxis from a subsequent sting. In this* ➤➤

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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
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- Mayo Clinic Proceedings

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study (using a unique RAST), 43% of patients with a positive history and negative skin test had a "positive" RAST. Even among those with concordant negative skin test and RAST, 14% had positive sting challenges. The respected authors conclude that diagnostic sensitivities of both skin test and RAST are inadequate to rule out anaphylactic sensitivity completely, and that we need improved test reagents. In the meantime, even with negative tests, never say never.
R. J. M.
Golden DBK, Kagey-Sobotka A, Norman PS, et al: Insect sting allergy with negative venom skin test responses.
J Allergy Clin Immunol 107:897-901, 2001. ♦♦

Rubber Medication Stoppers Linked to Positive Skin Tests in Latex-Allergic Subjects

NATURAL rubber stoppers are commonly used on medication vials. This raises the possibility that latex allergen may be released from a rubber stopper into the medication, thus producing a reaction in a patient with latex allergy (LA). Skin tests were performed in 12 volunteers with and 11 without LA to evaluate this possibility.

The subjects were skin-tested with phenol-saline-natural human albumin that had been stored in vials with natural rubber or synthetic stoppers. Some of the vials were repeatedly punctured 12 to 24 hours before skin testing.

All subjects without LA had negative skin test results. Positive skin test results occurred in 5 of 12 LA subjects on testing with solution from rubber-stoppered vials that had been punctured. Furthermore, 2 of 12 subjects had reactions even to solutions from rubber-stoppered vials that had not been punctured. Two LA subjects had inexplicable, nonreproducible reactions to solutions from vials with synthetic stoppers. In vitro inhibition analysis confirmed the presence of latex allergen in extracts of rubber stoppers.

The use of natural rubber stoppers on pharmaceutical vials may allow latex proteins to be released into the medication. In some cases, the latex-contaminated solution may induce a reaction in patients with LA. The findings support the elimination of natural rubber from medication vial stoppers.

COMMENT: *The Johns Hopkins group demonstrates the importance of using latex-free stoppers in pharmaceutical vials. Although only half of the patients with latex sensitivity reacted to intradermal skin testing with saline from vials with natural rubber stoppers, it was surprising to see the large reactions from vials that had not been punctured. Although the FDA resisted a call for eliminating natural rubber stoppers in pharmaceuticals in 1997, I would be surprised if they don't revisit this policy in future.*
S. M. F.
Primeau M-N, Adkinson NF Jr, Hamilton RG: Natural rubber pharmaceutical vial closures release latex allergens that produce skin reactions.
J Allergy Clin Immunol 107:958-962, 2001. ♦♦

Could Tacrolimus Be a Useful Antiasthma Drug?

WHEREAS tumor necrosis factor (TNF)-α activates inflammatory cells and induces adhesion molecule expression, interleukin (IL)-5 induces eosinophil maturation and differentiation. The mechanism of action of the immunosuppressive drug tacrolimus involves an inhibitory effect on inflammatory cell production of cytokines. However, the effects of tacrolimus ➤➤

on the cytokines and chemical mediators involved in asthma are unknown. A series of experiments were performed to assess the effects of tacrolimus on IL-5 and TNF-α production, in comaprison with the steroid dexamethasone.

Excised human lung tissue was passively sensitized using serum from patients with mite allergy, then preincubated with varying concentrations of tacrolimus or dexamethasone. When stimulated with mite antigen, the lung fragments released a high level of histamine, an effect that was largely blocked by preincubation with tacrolimus. Similarly, mite antigen induced a sharp rise in leukotriene E4, which was blocked by tacrolimus. Furthermore, tacrolimus blocked degranulation of sensitized mast cells, preventing a drop in tryptase-positive cells after stimulation. Dexamethasone preincubation had none of these effects.

Antigen stimulation also resulted in increased expression of TNF-α and IL-5 mRNA and associated protein production. These effects were inhibited by both tacrolimus and dexamethasone.

This in vitro model suggests that tacrolimus is a strong inhibitor of cytokine production and release of chemical mediators associated with asthma. The anti-inflammatory effects of tacrolimus may be even stronger than those of steroids. Tacrolimus warrants further study as a possible antiasthma medication.

COMMENT: *Despite the growth in asthma treatment options, we continue to face the clinical reality that some of our patients do not respond completely to current therapies. Pharmacologic agents affecting the inflammatory cascade at a variety of points are attractive alternatives for asthma management. Tacrolimus, a therapy useful in the management of graft rejection, is now an approved topical agent for atopic dermatitis. Cyclosporine, a more toxic drug that is similar to tacrolimus, has steroid-sparing effects in select subjects with asthma. These investigators demonstrate that tacrolimus in vitro not only affects lymphocytes, but directly reduces mediator release from passively sensitized human mast cells. Tacrolimus is a therapeutic agent with potential in asthma, but we will need double-blind studies confirming this effect.*
D. K. L.

Matsuo N, Shimoda T, Mitsuta K, et al: Tacrolimus inhibits cytokine production and chemical mediator release following antigen stimulation of passively sensitized human lung tissues.
Ann Allergy Asthma Immunol 86:671-678, 2001. ♦♦

Study Links IEI to Panic-Related Cholecystokinin Allele

PATIENTS with "idiopathic environmental intolerance" (IEI) exhibit many of the symptoms associated with panic attacks, including anticipatory anxiety and phobic avoidance of perceived triggers. Nevertheless, some reports advance a toxicogenic explanation, claiming that the symptoms result from exposure to chemicals in the environment. This study compared the neurogenetic backgrounds of patients with IEI to normal controls.

The study included 11 patients meting DSM-IV criteria for panic disorder and the same number of matched controls. Genomic DNA was obtained to assess the presence of cholecystokinin B (CCK-B) receptor alleles, which have been previously been linked to panic disorder. A standard polymerase chain reaction assay found the CCK-B reeptor allele in 41% of alleles from IEI patients, compared with 9% of alleles from matched controls.

There was no difference in the presence of personality trait-associated dopamine D4 receptor polymorphisms.

The results show that patients with IEI have an increased prevalence of a CCK-B receptor allele that has been associated with panic disorder. In answer to advocates of the toxicogenic theory--who attribute panic symptoms to the stress of dealing with an environmental illness--the new findings suggest that patients with IEI are genetically predisposed to panic disorder. Under appropriate psychiatric care, some of the treatments used for panic disorder might be helpful in patients with IEI.

COMMENT: *Idiopathic environmental intolerance (IEI) is the new name for what used to be called "multiple chemical sensitivity." It is thought* not *to be a toxic or immunologic disorder, but rather a psychophysiologic disorder with prominent features of anxiety, panic, and somatization. Cholecystokinin (CCK) is a recognized panicogenic neuropeptide, the receptor for which is polymorphic, with receptor allele 7 proven to be associated with panic disorder. This study shows that the same CCK receptor allele 7 is associated with IEI patients compared to normal controls. This lends support to other data suggesting that IEI may be a variant of panic disorder, with neuropsychiatric correlates.*
R. J. M.

Kinkley K, King N, Poonai N, et al: Idiopathic environmental intolerance: increased prevalence of panic disorder-associated cholecystokinin B receptor allele 7.
J Allergy Clin Immunol 107:887-890, 2001. ♦♦

Prospective Study Assesses Risk of On-the-Job Sensitization to OAAs

ORGANIC acid anhydrides (OAAs) are a common cause of occupational sensitization and provide a good model in which to study the association between exposure and allergic airway sensitization. This prospective study examined the exposure-response relationships for specific IgE and IgG among workers exposed to OAAs, including the effects of atopy and smoking.

One hundred sixty-three previously unexposed workers at three plants were enrolled in the study. The workers had new occupational exposure to epoxy resins using hexahydrophthalic, methylhexahydrophthalic, and methyltetrahydrophthalic anhydride curing agents. Follow-up included periodic measurement of serum specific IgE and IgG, as well as airborne OAA monitoring.

With a mean follow-up of 32 months, the ➤➤

workers had a mean combined OAA exposure level of 15.4 µg/m³. Thirteen percent became positive for specific IgE. Their median induction time was 8.8 months; sensitization incidence was 4.1 cases/1,000 months at risk.

Twenty-three percent of the workers were atopic. For this group, the risk of sensitization was elevated 5.4-fold. The greater the level of exposure, the higher the risk of sensitization. Workers who were RAST-positive were more likely to be smokers, although this relationship was nonsignificant. The rate of a positive skin-prick test to common allergens was 53% among IgE-positive subjects vs 14% among IgE-negative subjects.

This prospective study demonstrates a significant exposure-response relationship among workers exposed to OAAs. Atopy and intensity of exposure are both important predictors of sensitization risk: risk is similarly high for atopic subjects and those at the highest level of exposure. Smoking has no important effect.

COMMENT: *There are very few truly prospective studies looking at the induction of occupational asthma by work-related antigens. This represents such a study of 163 previously unexposed persons to a variety of epoxy resins containing OAAs. An incidence of IgE sensitization of 4.1 cases/1,000 months at risk was found. There was a correlation between risk of sensitization and increasing intensity of exposure. Atopy was found as an important risk factor for sensitization.*
E. J. B.

Welinder H, Nielsen J, Rylander L, Stählbom B: A prospective study of the relationship between exposure and specific antibodies in workers exposed to organic acid anhydrides. **Allergy** 56:506-511, 2001.

Montelukast vs Inhaled Beclomethasone: Long-Term Follow-Up in Three Clinical Trials

THERE are few long-term studies of the efficacy of antileukotriene drugs in asthma, and few direct comparisons of antileukotriene drugs with inhaled corticosteroids. Data from the extension phases of three placebo-controlled clinical trials of montelukast were combined to analyze the long-term safety and efficacy of this antileukotriene drug.

There were two adult studies, in which 436 and 374 patients, respectively, entered the extension phase; and one pediatric study, in which 245 patients went into the extension phase. The adult studies used an oral montelukast dosage of 10 mg once daily; children received a 5 mg chewable tablet once daily. Alternatively, the patients took inhaled corticosteroids: adults took beclomethasone 200 µg twice daily while children took beclomethasone 100 µg, or its equivalent, three times daily. Follow-up was 37 and 156 weeks in the adult studies and 112 weeks in the pediatric study.

Both treatments brought significant improvement in asthma control at up to 2 years' follow-up. In adults, montelukast and beclomethasone were both associated with reductions in airway obstruction and daytime asthma scores, reduced need for rescue β-agonists, and reduced nocturnal awakenings. Beclomethasone brought greater initial improvement in FEV_1, but the difference narrowed over time. Some of the apparent loss of effectiveness of beclomethasone may have reflected reduced compliance with ongoing inhaled medication use.

These data support the long-term effectiveness of montelukast and inhaled corticosteroids in controlling mild to moderate chronic asthma. Both are well tolerated, with similar relative effectiveness under open-label conditions. Future studies should specifically address the impact on adherence with these controller medications.

COMMENT: *This report summarizes extension data for three separate trials comparing the effects of montelukast and inhaled corticosteroids in mild asthma. As a group, subjects treated with montelukast retained their improvements in FEV_1 and symptoms throughout the extension periods. The inhaled corticosteroids generally had superior efficacy in the first three months, but the differences were much less pronounced during longer treatment periods. While there is still controversy regarding whether the leukotriene modifiers are adequate controller therapy for all patients with mild, persistent asthma, this report provides evidence that the vast majority of these patients do quite well on montelukast.*
S. A. T.

Williams B, Noonan G, Reiss TF, et al: Long-term asthma control with oral montelukast and inhaled beclomethasone for adults and children 6 years and older. **Clin Exp Allergy** 31:845-854, 2001.

♦♦

Nasal Fluticasone Is Beneficial in Pediatric OSA

CORTICOSTEROID therapy is generally regarded as ineffective in the treatment of obstructive sleep apnea (OSA) in children. One recent study found that nasal steroids reduced adenoidal size and symptoms of nasal airway obstruction, although that study did not specifically address OSA. A randomized, placebo-controlled trial was performed to assess the efficacy of topical nasal corticosteroids in the treatment of pediatric OSA.

The study included 25 children, aged 1 to 10 years, with a diagnosis of OSA. Each patient had adenoidal hypertrophy plus symptoms such as loud snoring, difficulty breathing, and witnessed episodes of apnea. On polysomnography, each patient had a mixed/obstructive apnea/hypopnea index of greater than 1. The patients were randomized to receive 6 weeks of treatment with fluticasone propionate or placebo. The fluticasone dosage was one 50 µg spray per nostril twice daily for the first week, then once daily for the next 5 weeks. The main outcome measure was the change in the frequency of mixed and obstructive apneas and hypopneas.

With fluticasone, the mean mixed/obstructive apnea/hypopnea index decreased from 10.7 to 5.8 ➤➤

over the 6-week treatment period. In contrast, in the placebo group the index increased from 10.9 to 13.1. Overall, 92% of children in the fluticasone group had a reduction in mixed/obstructive apnea/hypopnea index, compared with 50% of those in the placebo group. Fluticasone was also associated with greater reductions in the frequency of hemoglobin desaturation and respiratory movement/arousals, but there were no significant differences in tonsillar size, adenoidal size, or symptom score.

For children with OSA, 6 weeks of nasal fluticasone treatment significantly reduces several indicators of severity, including episodes of airway obstruction and desaturation. Adenotonsillar hypertrophy and symptom score are not significantly reduced, however. Topical nasal steroids are a promising treatment alternative for pediatric OSA because of their documented safety in children.

COMMENT: *Obstructive sleep apnea (OSA) affects about 2% of preschool children and can cause significant sequelae including cognitive impairment, failure to thrive and cor pulmonale. Adenotonsillectomy is usually curative, but is associated with a variety of complications in 16% to 27% of patients. This prospective study demonstrates a decreased frequency of mixed and obstructive apneas with fluticasone. In mild cases it may be the treatment of choice, or provide relief until surgery is carried out at a later time.*
J. B.-M.
Brouillette RT, Manoukian JJ, Ducharme FM, et al: Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea.
Pediatrics 138:838-844, 2001. ♦♦

Is Chronic Idiopathic Urticaria an Autoimmune Disease?

RECENT evidence suggests that up to one-half of cases of chronic idiopathic urticaria (CIU) are autoimmune in nature. Heparin inhibits the response to skin testing with autologous serum in these patients. The results of autologous serum skin testing and other investigations in 306 patients with CIU are reported.

All patients underwent intradermal testing with autologous serum; 57 were also tested with autologous heparinized plasma. Sixty-seven percent of patients had a wheal-and-flare reaction in response to autologous serum, while 14% reacted to heparinized plasma. All patients with a positive response to serum skin testing had a positive response to plasma.

In an in vitro study, sera from 121 CIU patients were used to induce histamine release from normal donor basophils. Seventeen percent of CIU sera induced significant histamine release, including 22% of samples taken from patients with a positive serum skin test. Heparin inhibited the release of histamine induced by CIU sera and plasma in a dose-dependent fashion.

Most patients with CIU have a positive response to autologous serum skin testing. Sera from about one-fifth of these patients induce significant histamine release from normal basophils, probably reflecting the presence of functional autoantibodies. The differences between the in vivo and in vitro findings may indicate the presence of a mast-cell-specific factor that does not induce histamine release from donor basophils. Complement may play an important role in the histamine-releasing activity of CIU sera.

COMMENT: *Over two-thirds of 306 consecutive patients with idiopathic urticaria had positive wheal-and-flare reactions to intradermal injections of their own serum. Control testing with saline was negative except in four patients with severe dermatographia. These results suggest that most cases of chronic idiopathic urticaria have an autoimmune etiology.*
J. R. B.
Asero R, Tedeschi A, Lorini M, et al: Chronic urticaria: novel clinical and serological aspects.
Clin Exp Allergy 31:1105-1110, 2001. ♦♦

Noneosinophilic Asthma: Induced Sputum Findings

ALTHOUGH eosinophilic airway inflammation is recognized as a key feature of asthma, noneosinophilic forms are increasingly reported. Some of these studies have found neutrophilic inflammation, which may be induced in response to interleukin-8 (IL-8). Sputum induction was used to assess the presence of eosinophilic vs noneosinophilic inflammation in asthma.

Along with sputum induction, spirometry and hypertonic saline solution challenge were performed in 56 nonsmoking adult patients with persistent asthma--rated mild in 11 patients, moderate in 26, and severe in 19--and 8 healthy controls. Forty-one percent of asthma patients had the typical eosinophilic pattern of inflammation. The remaining 59% had noneosinophilic asthma.

The value for percentage neutrophils was 64% in patients with noneosinophilic asthma, compared with 14% in those with eosinophilic asthma and 34% in controls. Absolute neutrophil counts were 283, 41, and 49 x 10^6/mL, respectively. Both asthma groups had elevated myeloperoxidase. Levels of sputum IL-8 were 45 ng/mL in the patients with noneosinophilic asthma, compared with 9.6 ng/mL in those with eosinophilic asthma and 3.5 ng/mL in controls. Sputum IL-8 and neutrophil levels were significantly correlated with each other. Levels of supernatant eosinophil cationic protein were 2,685 ng/mL in patients with eosinophilic asthma and 1,081 ng/mL in those with noneosinophilic asthma, compared with 110 ng/mL in controls.

Sputum induction studies in a sample of adult patients with asthma suggest that a noneosinophilic pattern of inflammation is more common than an eosinophilic one. Noneosinophilic asthma is associated with elevated numbers of neutrophils, which may be mediated by IL-8.

COMMENT: *Prior biopsy studies have shown a predominance of neutrophilic inflammation rather than eosinophilic inflammation in a subset of patients* ➤➤

with severe asthma. Gibson et al. provide evidence that a relatively noninvasive technique such as sputum induction may differentiate these phenotypes in asthma of all severities. Further studies are necessary to determine the utility of these induced sputum markers in making treatment decisions.
S. A. T.
Gibson PG, Simpson JL, Saltos N: Heterogeneity of airway inflammation in persistent asthma: evidence of neutrophilic inflammation and increased sputum interleukin-8. **Chest** 119:1329-1336, 2001. ♦♦

Nebulized IL-4 Receptor: a New Th2 Inhibitor for Asthma Treatment?

INTERLEUKIN-4 (IL-4) plays a critical role in the development of asthma--it induces the isotope switch to IgE production and expression of vascular cell adhesion molecule-1, among other effects. Measures to neutralize excess IL-4 have the potential to block diverse inflammatory pathways at the point of Th2 differentiation, thus preventing an allergic response. Recombinant human soluble IL-4 receptor (IL-4R) was studied as an inhaled IL-4 antagonist for use in asthma treatment.

The randomized, double-blind, dose-finding trial included 62 patients with steroid-dependent asthma, with an FEV_1 of greater than 65% predicted. They were randomized to 12 weeks of once-weekly treatment with nebulized IL-4R--0.75, 1.5, or 3.0 mg--or placebo. At the start of treatment, patients discontinued inhaled steroid use; after a single exacerbation, they were required to withdraw from the study.

By 4 weeks, the withdrawal rate was 50% with placebo, 47% with IL-4R 0.75 mg, and 50% with IL-4R 1.5 mg, compared with 33% with IL-4R 3.0 mg. By 12 weeks, withdrawal rates were not significantly different: 56%, 67%, 69%, and 47%, respectively. After discontinuing steroid treatment, the placebo group had a significant decrease in FEV_1: -0.4 L or -13% predicted. This decline was effectively prevented in the IL-4R 3.0 mg group, in which FEV_1 decreased by only -0.1 L or -2% predicted. High-dose IL-4R was also beneficial in terms of patient-measured morning FEV1 and symptom scores. Serum IL-4R concentration increased with dose in linear fashion.

Used as a Th2 inhibitor, nebulized IL-4R has promising clinical effects in the treatment of steroid-dependent asthma. It prevents declines in FEV_1 after steroid discontinuation, without side effects. Further studies are needed to assess the effects of IL-4R on airway inflammation and remodeling.

COMMENT: *The concept of targeting specific mediators of inflammation for the treatment of allergic disease has been a goal even before the development of antihistamines. Borish et al. used recombinant IL-4 receptors to bind excess IL-4 in steroid-dependent asthmatics. There was an impressive effect of the IL-4R, which was nebulized weekly, in maintaining asthma symptom scores and patient-monitored pulmonary function after steroid withdrawal. Although this study focused on pulmonary function and asthma symptom scores, it will be of interest to see what effects IL-4R--which may be considered a Th2 inhibitor--may have on other immunologic processes. As our knowledge of the inflammatory process expands, the potential for new and more specific therapeutic approaches is exciting.*
S. M. F.
Borish LC, Nelson HS, Corren J, et al: Efficacy of soluble IL-4 receptor for the treatment of adults with asthma. **J Allergy Clin Immunol** 107:963-970, 2001.

Tobacco Smoke Exposure May Reduce the Risk of Atopy

EXPOSURE to tobacco smoke is an important risk factor for many respiratory health problems in children. Some European studies have suggested that exposure to environmental tobacco smoke also increases the risk of atopic sensitization. However, other studies have yielded conflicting results, even suggesting that tobacco smoke exposure reduces the risk of atopy.

A Swedish population data base was used to further evaluate the relationship between tobacco smoke exposure and atopic sensitization. The analysis included data on 6,909 adults, aged 16 to 49 years when studied in 1996-97; and 4,472 of their children, aged 3 to 15 years. The rate of daily smoking was 25% among women and 18% among men. Smoking rates were highest for subjects in their forties.

In study interviews, 4% of adult subjects reported allergic asthma while 22% reported allergic rhinoconjunctivitis. In the youngest age group, 16 to 29 years, rates of these disorders were 6% and 25%, respectively. Nine percent of the children studied had eczema, 8% had food allergies, and 4% had allergic asthma.

Among the adults, current smokers had lower rates of allergic asthma and allergic rhinoconjunctivitis than former smokers and nonsmokers. Light smokers (less than 10 cigarettes/d) had a somewhat higher rate of allergic asthma than nonsmokers and former smokers. Children whose parents smoked 15 or more cigarettes/d had lower rates of all allergic diseases, compared to the children of nonsmokers, former smokers, or lighter smokers.

Current exposure to tobacco smoke is associated with a reduced risk of atopic disorders, both for the smokers themselves and for their children. Adults show evidence of a dose-response effect, whereas children show no association below a threshold of 15 cigarettes/d. The findings may indicate a protective effect of tobacco smoke against atopy. On the other hand, they may reflect reporting bias or a tendency of allergic individuals to refrain from smoking.

COMMENT: *While there is good evidence that active and passive exposure to tobacco smoke increases the risk of developing asthma, the relationship between smoke exposure and clinically relevant IgE sensitization to aeroallergens is less clear. This large, cross-sectional study from Sweden adds to the literature arguing that tobacco smoke exposure reduces the risk of developing allergic asthma and rhinoconjunctivitis. The main* ➤➤

weakness of the study is the lack of objective confirmation of atopy.
S. A. T.
Hjern A, Hedberg A, Haglund B, Rosén M: Does tobacco smoke prevent atopic disorders? A study of two generations of Swedish residents.
Clin Exp Allergy 31:908-914, 2001. ♦♦

Increasing Body Mass Index Linked to Prevalence of Asthma

MANY patients with asthma have other medical problems as well, such as obesity, hypertension, arthritis, and diabetes. These associations suggest a possible link between obesity and asthma. Data from a large military managed care data base were used to assess the relationship between body mass index (BMI) and asthma.

From the data base, the investigators identified 2,788 cases with asthma and 39,637 controls. For an additional substudy, a random sample of 1,000 subjects from each group were linked to a computerized record system to check whether they had been prescribed antiasthma medications. The latter analysis included 386 verified cases and 744 controls. Logistic regression to examine associations between asthma and BMI, among other risk factors.

In both the larger study and the verified subsample, increasing BMI was a significant predictor of asthma. This relationship was linear and independent of potential confounders. Other independent predictors included younger age, female sex, non-active duty status, and arthritis. Gastric ulcer, depression, hypertension, and Caucasian race were also significant predictors in the larger study. Smoking was not associated with asthma risk.

Increasing BMI is a significant, independent risk factor for asthma. Further studies are needed to determine whether this association is etiologic in nature; if so, then obesity may be a potentially modifiable risk factor. In addition, studies are needed to see if weight-loss interventions can reduce symptoms in overweight patients with asthma.

COMMENT: *There is mounting evidence that the prevalence and morbidity of asthma have risen in the last several decades. A variety of causal factors have been linked to this observation; dietary factors have been identified as a possible contributor. Recent studies have also identified obesity as a key predictor of the prevalence of asthma. The importance of this observation is that if obesity is determined to be etiologically related to asthma, it is clearly a potentially modifiable risk factor. Further studies are needed.*
E. J. B.
Young SYN, Gunzenhauser JD, Malone KE, McTiernan A: Body mass index and asthma in the military population of the northwestern United States.
Arch Intern Med 161:1605-1611, 2001. ♦♦

Postmarketing data link itraconazole to congestive heart failure

THE antifungal medication itraconazole is approved for use in the treatment of onychomycosis and systemic fungal infections. There is evidence to suggest that intravenous itraconazole has negative inotropic effects. This report describes 58 cases of congestive heart failure (CHF) potentially related to itraconazole therapy reported to the U.S. Food and Drug Administration (FDA).

The cases were reported to the FDA's Adverse Event Reporting System between 1992, when itraconazole was approved, and 2001. Twenty-eight patients developed CHF severe enough to require hospitalization; 13 died. However, 43 of the patients had other CHF risk factors or comorbid conditions potentially confounding the association with itraconazole.

Under revised labeling, itraconazole is now contraindicated for use in treating onychomycosis in patients with signs of ventricular dysfunction. Those receiving itraconazole for systemic fungal infections should be re-evaluated if they develop clinical evidence of heart failure. The authors call for formal studies to assess the risk of congestive heart failure associated with itraconazole.

COMMENT: *Allergists have always seen patients with suspected fungal disease of the sinuses and lungs, eg, aspergillosis. This short report warns that animal and clinical pharmacology studies have observed negative inotropic effects with itraconazole. The FDA received 58 reports of potential cases of congestive heart failure associated with itraconazole between 1992 and April, 2001. These preliminary observations should dictate vigilance.*
E. J. B.
Ahmad SR, Singer SJ, Leissa BG: Congestive heart failure associated with itraconazole.
Lancet 357:1766-1767, 2001. ♦♦

Cooking Method Affects Allergenicity of Peanuts

THE rate of sensitization and reactivity to peanuts is far lower in China than in the United States, even though the two countries have similarly high rates of peanut consumption. The difference is probably not explained by genetic factors, as Chinese-Americans have a similar rate of peanut allergy to the U.S. population. Peanuts are generally dry-roasted for consumption in the United States, whereas in China they are more often fried or boiled. This study compared the effects of these three cooking techniques on the allergenicity of peanuts.

Peanuts were roasted, boiled, or fried in the laboratory. On SDS-PAGE, the relative amount of the peanut allergen Ara h 1 was significantly higher in roasted peanuts than in fried or boiled peanuts. Roasting also resulted in greater IgE-binding intensities to the Ara h 1 monomer and trimer. Fried and boiled peanuts ➤➤

showed significantly reduced IgE binding to the Ara h 2 and Ara h 3 allergens, even though the total protein concentration was unaffected by cooking technique.

Frying or boiling peanuts, as done in China, is associated with lower allergenicity than roasting peanuts, as done in the United States. The Chinese methods of cooking eliminate the Ara h 1 trimer almost completely; in contrast, large amounts of this allergen are found in roasted peanuts and in peanut butter. The effects of cooking techniques may help to explain the differing prevalence of peanut allergy in the United States and China.

COMMENT: *Heat usually denatures proteins. These authors demonstrate that in the case of peanut allergen, heat enhances allergenicity. More extractable Ara h 1 was found in roasted peanuts (cooked at 170° C) than in peanuts that were fried (at 120° C) or boiled (at 100° C). The authors compare peanut consumption in the United States with that in China. They suggest that the difference in preparation techniques--roasting peanuts in the United States, compared with boiling or frying in China--may reflect the higher incidence of peanut allergy in the United States, even though the average consumption rate is similar. Although this suggestion is speculative, it is food for thought.*
S. M. F.

Beyer K, Morrow E, Li X-M, et al: Effects of cooking methods on peanut allergenicity.
J Allergy Clin Immunol 107:1077-1081, 2001. ♦♦

"Last-to-First" PEF Ratio Predicts Length of Stay in Acute Asthma

PATIENTS with acute exacerbations of asthma were studied to determine whether the change in peak expiratory flow (PEF) over three consecutive blows can help in predicting the severity of the exacerbation. The study included 43 consecutive patients hospitalized for acute exacerbations of asthma. Each underwent measurement of PEF using a mini-Wright flowmeter. The investigators divided the PEF measured on the third blow by that measured on the first to calculate a last-to-first PEF ratio. This was related to length of hospital stay using multiple logistic regression.

The last-to-first PEF ratio was less than 1 in 15 patients; the remaining 28 patients had a ratio of 1 or greater. Patients with a ratio of less than 1 had a median hospital stay of 3 days, compared to 1 day for those with a ratio of 1 or greater.

In patients hospitalized for acute asthma exacerbations, the last-to-first PEF ratio over three successive blows is independently related to the patients' length of hospital stay. This simple ratio may provide a simple means of identifying patients with a significant difference in outcome who are similar in conventional prognostic indicators.

COMMENT: *Patients with exacerbations of asthma have difficulty performing spirometry. These British physicians demonstrated that some patients with severe asthma, which required hospitalization for therapy, had even greater worsening of their peak flow rates after a forced expiratory maneuver. Patients with more severe asthma--who also required longer hospitalizations--had lower PEF on the third blow compared with the first. Although we require consistency for relevant spirometric results, it may be useful to document this peak flow sequence to predict more severe uncontrolled asthma.*
S. M. F.

Birring SS, Heartin E, Williams TJ, et al: Peak expiratory flow sequence in acute exacerbations of asthma.
BMJ 322:1281, 2001. ♦♦

Boiled Lentil Extracts Increase the Sensitivity of Skin-Prick Testing

THE prevalence of food allergy is affected by the dietary habits of the community. In Spain, lentils and other legumes are generally boiled or roasted before eating. In previous enzyme-linked immunosorbent assay inhibition studies, the authors reported greater inhibition capacity in boiled than in crude lentil extracts. These two extracts were compared for use in skin-prick testing for the clinical diagnosis of lentil allergy.

The study included 36 patients, median age 8 years, with a history of allergic reactions after lentil ingestion. Each patient underwent skin-prick testing with a battery of allergens, including crude and boiled lentil extracts. Thirty-three patients underwent oral challenge with lentils on the same day.

Overall, 78% of patients had positive skin-test responses to pollen extracts. Twenty patients had a positive response to lentil challenge; another 3 had a clear history of recent lentil anaphylaxis. Eighty-three percent of these patients had a positive skin-prick response to the crude lentil extract, as did 92% of patients with negative oral challenge. In contrast, when the boiled lentil extract was used, the rate of positive skin-prick test results was 100% for clinically sensitive patients vs 84% for clinically tolerant patients. With the boiled extract, mean wheal sizes were significantly larger in patients with a positive oral challenge than in those with a negative challenge.

In skin-prick testing for lentil allergy, the use of boiled lentil extract appears to be more clinically sensitive. Based on their results, the authors recommend a concentration of 0.5 or 5.0 mg/mL. Using boiled lentil extracts in clinical practice may help to reduce the need for oral food challenges.

COMMENT: *Most allergens are proteins or glycoproteins and are denatured by heating. Thermostable allergens have been described, particularly in food. The idea of heat increasing the allergenicity of substances is less recognized but is relevant to both food and selected airborne allergens. For example, heating of soybean hulls increases the allergenicity of the airborne husk responsible for asthma outbreaks during loading and unloading of soybeans. The possibility of allergen modification needs to be kept in mind when testing is negative--using aller-* ➤➤

gen vaccines prepared with standard techniques--but the clinical history is highly suggestive of sensitivity.
D. K. L.
San Ireneo MM, Sandín MDI, Fernández-Caldas E, et al: The diagnostic value of crude or boiled extracts to identify tolerant versus nontolerant lentil-sensitive children.
Ann Allergy Asthma Immunol 86:686-690, 2001. ♦♦

Adding Salmeterol to Inhaled Steroid Reduces Airway Wall Vascularity in Asthma

FEW studies have addressed the effects of antiasthma treatments on long-term airway remodeling, ie, disease-related structural changes occurring in the airway wall. One useful measure of the airway remodeling process may be increased vascularity. This study compared the effects of low-dose inhaled corticosteroids with and without a long-acting β_2-agonist on airway wall vascularity.

The randomized trial included 45 asthma patients who remained symptomatic despite low-dose inhaled corticosteroids, 200 to 500 µg twice daily. At baseline, bronchoscopy and airway endobronchial biopsy were performed for immunohistochemical staining of vascular structures. Patients were then randomized to receive one of three treatments in addition to their usual dose of inhaled corticosteroid: placebo, salmeterol 50 µg twice daily, or fluticasone propionate 100 µg twice daily. Posttreatment biopsies were then obtained. The final analysis included 34 patients, along with 28 nonasthmatic controls.

At baseline, asthma patients had 524 vessels/mm^2 of lamina propria, compared with 425 vessels/mm^2 in controls. In patients assigned to salmeterol, vessel density decreased from 535 to 400 vessels/mm^2. The placebo and fluticasone groups showed no significant change, and were not significantly different from each other. None of the groups had an increase in vessel density.

Three months of treatment with the β_2-agonist salmeterol produces a significant reduction in airway wall vascularity in asthma patients. Salmeterol's effect on airway vascularity appears complementary to that of inhaled corticosteroids, possibly mediated by effects on angiogenic growth factors.

COMMENT: *The authors' contention is that increased subepithelial vascularity is a significant part of the structural changes (aka remodeling) seen in chronic asthma, In this study they demonstrate that the addition of salmeterol to treatment with an inhaled corticosteroid results in a reduction of blood vessel density that was not achieved by increasing the corticosteroid dose. The therapeutic significance of this is uncertain, for although salmeterol-treated patients had fewer blood vessels per millimeter there was no change in the percentage area of the lamina propria occupied by vessels, perhaps because of β-agonist-induced vasodilation.*
J. R. B.
Orsida BE, Ward C, Li X, et al: Effect of a long-acting β_2-agonist over three months on airway wall vascular remodeling in asthma.
Am J Respir Crit Care Med 117-121, 2001. ♦♦

Studies Show Effectiveness of Once-Daily Budesonide in Different Groups of Asthma Patients

TWO studies assessed the effectiveness of once-daily budesonide via Turbuhaler in two distinct populations of patients with asthma: adults with persistent asthma who had not previously received inhaled corticosteroids and children who had been taking inhaled corticosteroids.

Banov et al. studied 177 adult patients who had not received inhaled corticosteroids within 12 weeks. They were randomized into groups receiving once-daily budesonide 400 µg or placebo. The two groups were similar at baseline, with FEV_1% predicted of 71.9% and 70.6%, respectively. Over 12 weeks, FEV_1 improved to a significantly greater extent in the budesonide group: 0.31 vs 0.17 L. Budesonide also yielded greater improvements in morning peak expiratory flow, symptom scores, and albuterol use.

In the study by Shapiro et al., 274 children who had been taking oral corticosteroids for at least 16 weeks were randomized to receive 12 weeks of treatment with placebo or budesonide, 200 or 400 µg once daily. Budesonide brought significant improvement in mean FEV_1: by 2.65% in the 200 µg group and 3.29% in the 400 µ group, compared with a decrease of 1.49% in the placebo group. The budesonide groups also had significant improvement in other pulmonary function measures, along with symptom scores and β_2-agonist use.

The two studies demonstrate the efficacy and safety of budesonide via Turbuhaler in two diverse groups of asthma patients. The ability to give budesonide once daily simplifies dosing, potentially improving treatment compliance and benefit.

COMMENT: *These two articles present similar data showing efficacy of once-daily budesonide in moderate asthma. The observations are not novel: prior once-daily data are available for beclomethasone dipropionate, budesonide, flunisolide, fluticasone, mometasone, and triamcinolone. The clinical effectiveness of inhaled corticosteroid therapy is enhanced by the simplicity of the regimen. Divided dosages of inhaled corticosteroids are more effective and appropriate for moderately severe and severe asthma. These articles reinforce the observation that once-daily inhaled cortiocosteroids are a useful asthma treatment strategy for adults or children and in subjects with or without prior inhaled corticosteroid therapy.*
D. K. L.
Banov CH, Howland WC III, Lumry WR: Once-daily budesonide via Turbuhaler improves symptoms in adults with persistent asthma.
Ann Allergy Asthma Immunol 86:627-632, 2001.
Shapiro GG, Mendelson LM, Pearlman DS: Once-daily budesonide inhalation powder (Pulmicort Turbuhaler) maintains pulmonary function and symptoms of ➤➤

asthmatic children previously receiving inhaled corticosteroids.
Ann Allergy Asthma Immunol 86:633-640, 2001. ♦♦

Anaphylactic Reaction to a COX-2 Inhibitor: Case Report

THERE have been few reports of anaphylaxis and related reactions among patients taking the newer selective cyclo-oxygenase-2 (COX-2) inhibitors. A patient with an anaphylactic reaction to celecoxib is reported.

The patient was a 55-year-old woman who had taken celecoxib for Achilles tendinitis. The medication was effective and she used it occasionally for intermittent symptoms. Then she took a 200 mg celecoxib capsule for the first time in 3 months. She developed symptoms of a reaction within 15 minutes, including pruritus, urticaria, respiratory distress, and hypotension. She had no history of allergic reactions to medications, and had taken aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) without problem. There was no evidence of an IgE-type reaction. The patient's condition improved with epinephrine, corticosteroids, and IV fluids. She was instructed to avoid all NSAIDs, including COX-2 inhibitors; oral challenge with celecoxib was not attempted.

This is the first reported case of anaphylaxis caused by the COX-2 inhibitor celecoxib. Reactions to NSAIDs appear to occur through non-IgE mechanisms; rather, they may involve a series of events related to inhibition of intracellular COX enzymes. Hypokalemia, which is listed as an adverse effect of celecoxib, results from unknown causes.

COMMENT: *Lipoxygenase inhibitors are increasingly used as anti-inflammatory and analgesic medications. While they are generally safe, this case report highlights the possibility of life-threatening anaphylaxis in patients who had previously tolerated other NSAIDs without difficulty. This observation balances those reported in* AllergyWatch *July/August 2001, p. 2.*
A. M.
Levy MB, Fink NJ: Anaphylaxis to celecoxib.
Ann Allergy Asthma Immunol 87:73-73, 2001. ♦♦

Floor Insulation and Other Housing Factors Affect Mite Allergen Levels

A PREVIOUS study from New Zealand, which has a high prevalence of wheezing among young people, found that carpeted floors were strongly related to floor Der p 1 levels. However, there was significant, unexplained variability in allergen levels in carpeting between homes. Homes from the previous study were revisited to assess the effects of housing construction and other characteristics on Der p 1 levels.

The study included 78 New Zealand homes from which dust samples had been taken from the carpet only in the previous study, 4 years earlier. In that study, 42 of the homes had high levels of Der p 1 measured while 36 had low levels. For the new study, living room dust from a 1 m^2 area was sampled for 1 minute, and from the whole floor at 5 m^2/min. Der p 1 levels were measured and correlated with questionnaire data on housing characteristics.

Geometric mean Der p 1 level was higher in the 1 m^2 sample than in the whole room sample, 40.0 vs 53.4 $\mu g/m^2$, respectively. However, the results of the two techniques were significantly correlated. The allergen levels measured in the two study years were weakly but significantly correlated with each other. In both samples, the Der p 1 concentration was reduced by about half in houses with insulation or a room or garage below the living room, after controlling for potential confounders. In the 1 m^2 sample, houses with more than 2 children had higher allergen levels. The Der p 1 concentration was also higher in rooms with a carpet underlay thinner than 8 mm: 3-fold higher in the 1 m^2 sample and 1.6-fold higher in the whole room sample.

Floor insulation appears to have a major impact on the Der p 1 level on carpeted floors. Mite allergen levels also appear lower in homes with a room or garage below the living room or a thick underlay below the carpet. These factors may reduce Der p 1 levels by providing a barrier between the carpet and ground moisture. Der p 1 measurements based on a 1 m^2 sample taken in the center of the room may not adequately reflect the level in the whole room.

COMMENT: *As allergists we pride ourselves in our ability to advise our patients effectively regarding which environmental control measures to employ. Determining the best ways to reduce symptoms resulting from dust mite exposure is one of our most challenging responsibilities. This New Zealand study found that the dust in living rooms with insulated floors contained only roughly half of the levels found in other homes. A correlation with symptoms was not evaluated, though this finding could lead to recommended changes in home construction and/or remediation of existing homes.*
S. A. T.
Wickens K, Mason K, Fitzharris P, et al: The importance of housing characteristics in determining Der p 1 levels in carpets in New Zealand homes.
Clin Exp Allergy 31:827-835, 2001. ♦♦

Cleaning With Bleach Solution Doesn't Reduce Cockroach Allergen in Inner-City Homes

FOR inner-city children with asthma, exposure to cockroach allergen is associated with high levels of sensitization and morbidity. This study evaluated a new approach to cockroach allergen abatement: professional extermination followed by cleaning with bleach solution.

Seventeen inner-city Baltimore homes with cockroach infestation participated in the study. ➤➤

Three homes, serving as controls, were left untreated. The 14 intervention homes underwent professional pest extermination using 0.05% abamectin applied two times at 2-week intervals. Before and after extermination, the homes were professionally cleaned, using 0.5% hypochlorite solution on all washable surfaces. The homes were inspected monthly, including dust sampling.

Levels of *Blatella germanica* allergen 1 in dust decreased significantly in the treated homes. Median allergen levels decreased by 91% in the kitchen, by 78% in the bedroom, and by 77% in the living room of intervention homes, whereas control homes saw a gradual increase in allergen levels. However, cleaning with sodium hypochlorite did not appear to further reduce allergen levels, compared with a previous study using professional extermination without the cleaning regimen.

The results confirm that professional extermination sharply reduces cockroach allergen levels in infested inner-city homes. However, a protocol of cleaning with sodium hypochlorite solution does not achieve further improvements. Even with professional extermination, many homes will continue to have allergen concentrations above the threshold level of 8 U/g of dust.

COMMENT: *There is little question that cockroach allergen is an important trigger of asthma in many environments. Unfortunately, specific environmental control measures for cockroach abatement are difficult and infrequently done. In this study, the authors show that commonly available household bleach solutions are ineffective.*
A. M.

Wood RA, Eggleston PA, Rand C, et al: Cockroach allergen abatement with extermination and sodium hypochlorite cleaning in inner-city homes.
Ann Allergy Asthma Immunol 87:60-64, 2001. ♦♦

Allergy to Asian Edible Bird's Nests: Immunochemical Study

BIRD'S nest, also known as yen wo, is a Chinese delicacy made from the nests of four species of *Callocalia* swiftlets, found in Southeast Asia. The nests are made using saliva from the birds' sublingual salivary glands and consist mainly of glycoproteins. At the authors' hospital in Singapore, bird's nest is the most common cause of anaphylaxis. The immunochemical findings of bird's nest allergy are reported.

The study used sera from 25 children with clinically allergy to bird's nest. Extracts were made from three sources of commercially available bird's nest from Malaysia, Thailand, and Indonesia. The serum studies showed significant differences in IgE binding to the three different sources of commercially available bird's nest. Those from Malaysia showed the highest levels of specific IgE, and were cross-reactive with the nests from Thailand.

Further studies in unprocessed bird's nests from Malaysia identified a distinct IgE-binding proteins and a major 66 kD allergen. IgE binding ability was lost in the presence of periodate, suggesting that the carbohydrate moiety is a key contributor to the allergenic epitopes.

The allergens contained in edible bird's nests from different sources in Southeast Asia are allergenically dissimilar. A putative 66 kD major allergen is identified, and may be homologous to a domain of an ovoinhibitor precursor in chicken.

COMMENT: *Truth can be stranger than fiction. At the National University Hospital in Singapore, the most common cause of anaphylaxis is reported to be edible birds' nests. Not just any nests, but those from four species of swiftlets found in Southeast Asia. The nests, sold commercially as delicacies, are eaten by many ethnic Chinese around the world, with North America being the second-largest market. The study documents the immunochemical heterogeneity of the allergens, probably from the birds' saliva. This is great stuff for allergy trivia contests, but also may be important in areas of the United States with ethnic Chinese populations. Moreover, this makes me wonder, if we looked hard enough, whether we could explain all cases of so-called "idiopathic" anaphylaxis.*
R. J. M.

Goh DLM, Chua KY, Chew FT, et al: Immunochemical characterization of edible bird's nest allergens.
J Allergy Clin Immunol 107:1082-1088, 2001. ♦♦

Short-Course, High-Dose Amoxicillin Reduces Carriage of Resistant Pneumococci

THE rise of drug-resistant *Streptococcus pneumoniae* is reducing the effectiveness of penicillin against various pneumococcal infections. To combat the spread of resistant pneumococci, some authors have suggested the use of short courses of high-dose antibiotics. However, the effects of such approaches on nasopharyngeal carriage of pneumococci are uncertain. This randomized trial assess the effects of short-course, high-dose amoxillicin on carriage of resistant pneumococci in children.

The study included 795 children receiving antibiotics for respiratory tract infections in a clinic in the Dominican Republic. They received amoxicillin in a dosage of either 90 mg/kg/d for 5 days or 40 mg/kg/d for 10 days. The microbiologic effects on carriage of penicillin-nonsusceptible pneumococci were determined at up to 28 days; the study did not address clinical outcomes.

By 28 days, 24% of children receiving short-course, high-dose amoxicillin were carrying penicillin-nonsusceptible pneumococci, compared with 32% of those receiving the standard regimen. The associated relative risk was 0.77. The protective effect was greater among patients from households with 3 or more children, relative risk 0.72.

In children with respiratory tract infections, a regimen of short-course, high-dose amoxicillin may help to reduce the spread of drug-resistant pneumococci. This regimen may also reduce carriage of strains nonsusceptible to other drugs, especially trimetho- ➤➤

prim-sulfamethoxazole. The effects of short-course, high-dose regimens will depend on many factors, including the antibiotic used, the rate of pneumococcal carriage, and the level of resistance in the community.

COMMENT: *Acute otitis media and sinusitis can be effectively managed without antibiotic therapy. Short-course, high-dose (double the usual dosage) regimens are effective in acute, uncomplicated otitis media, sinusitis, bronchitis, and tonsillitis. The reduction in carriage of penicllin-resistant organisms following short-course vs routine antibiotic therapy is encouraging. However, resistance increased compared to baseline with both treatments, again emphasizing the need to be judicious in any course of treatment. Reduction of resistant organisms in this paper was greatest in children with siblings, suggesting that the benefits of short-course regimens are secondary to effects on close contacts.*
D. K. L.

Schrag SJ, Peña C, Sánchez J, et al: Effect of short-course, high-dose amoxicillin therapy on resistant pneumococcal carriage: a randomized trial. **JAMA** 286:49-56, 2001. ♦♦

REVIEWS OF NOTE

Aalberse RC, Akkerdaas JH, van Ree R: Cross-reactivity of IgE antibodies to allergens. **Allergy** 56:478-490, 2001.

COMMENT: *As these authors point out, cross-reactivity between IgE antibodies has enormous clinical implications. However, the key questions relate to the relative avidity of any given IgE antibody toward two or more allergens and--more importantly--what is the threshold avidity for biologic relevance of the cross-reactivity? It is the latter answer that is needed to translate an immunologically defined cross-reactivity into clinically relevant information. The review will acquaint the reader with this and other important perspectives.*
E. J. B.

Cianferoni A, Novembre E, Mugnaini L, et al: Clinical features of acute anaphylaxis in patients admitted to a university hospital: an 11-year retrospective review (1985-1996). **Ann Allergy Asthma Immunol** 87:27-32, 2001.

COMMENT: *While there are many recent reviews of anaphylaxis, this review highlights many important features of this life-threatening condition. The apparent under-utilization of epinephrine remains of great concern.*
A. M.

Ispas L, Henriksen RA, Metzger WJ: The many faces of systemic mastocytosis. **Ann Allergy Asthma Immunol** 87:6-15, 2001.

COMMENT: *This outstanding update reviews an important topic in allergy. While mastocytosis is uncommonly seen, it is useful to review the important symptoms and disease associations. The potential use of newly available biologic response modifiers such as FK506 is discussed.*
A. M.

Warner HA: Status asthmaticus in children: a review. **Chest** 119:1913-1929, 2001.

COMMENT: *An interesting review of management of critically ill patients with asthma, which includes comments on heliox, intubation, inhaled anesthetics, ketamine, extracorporeal life support, bronchoscopy, and bronchial lavage.*
J. B.-M.

Salvi SS, Krishna MT, Sampson AP, Holgate ST: The anti-inflammatory effects of leukotriene-modifying drugs and their use in asthma. **Chest** 119:15233-1546, 2001.

COMMENT: *There has been considerable disagreement regarding whether the leukotriene-modifying agents act principally as anti-inflammatory agents or bronchodilators. In this review, the authors provide an up-to-date and thorough review of asthma pathophysiology and the therapeutic role of the leukotriene modifiers relative to corticosteroids.*
S. A. T.

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