AllergyWatch®

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

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Study Shows Benefit of Grass Pollen Immunotherapy for Seasonal Asthma

SEASONAL asthma is a common finding in patients with severe hay fever. Some studies have shown that immunotherapy can be beneficial for selected asthma patients, but safety remains a concern. This randomized trial assessed the benefits of grass pollen immunotherapy in patients with seasonal rhinitis and asthma. It included 44 patients with severe summer hay fever, including 36 with seasonal chest symptoms and 28 with seasonal bronchial hyperresponsiveness. After one untreated summer, the patients received either immunotherapy with depot grass pollen vaccine or matched placebo injections. Injections were given in a 4-week rapid-updosing cluster regimen, then monthly for 2 years. The effects of immunotherapy on symptoms, bronchial hyperresponsiveness, and quality of life were assessed.

Thirty-seven patients completed the study, with a total of 471 grass pollen injections in the active treatment group. Hay fever symptoms decreased by 49% with immunotherapy vs 15% with placebo. Immunotherapy was associated with an 80% reduction in medication requirements, compared with 18% in the placebo group. The reduction in chest symptoms was 90% vs 11%, respectively. Immunotherapy had a significant advantage in 5 of 7 quality-of-life domains. At the end of treatment, patients in the immunotherapy group showed no seasonal decrease in methacholine PC_{20}. There were no immediate systemic reactions or large local reactions to grass pollen vaccine.

The findings demonstrate numerous benefits of grass pollen immunotherapy in patients with severe hay fever and seasonal asthma. Quality-of-life assessments show significant improvements in various domains. The rapid updosing cluster injection protocol used in this study reduces the number of hospital visits necessary and is well accepted by patients.

COMMENT: *Does immunotherapy help asthma? This English study proved that 2 years of immunotherapy for seasonal grass allergy and asthma signif-* ➤➤

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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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icantly reduced chest symptoms, medication use, and the expected seasonal increase in bronchial hyperresponsiveness. This adds to the body of evidence that immunotherapy provides clear benefits for allergic asthma when used in properly selected patients.
R. J. M.
Walker SM, Pajno GB, Lima MT, et al: Grass pollen immunotherapy for seasonal rhinitis and asthma: a randomized, controlled trial.
J Allergy Clin Immunol 107:87-93, 2001. ♦♦

Short-term Anti-inflammatory Therapy Does Not Prevent Asthma in Wheezing Infants

THE long-term effects of early anti-inflammatory therapy for infants with wheezing are unknown. This issue was addressed in a randomized trial including 89 infants (less than 2 years old) hospitalized for infection-related bronchial obstruction and wheezing. Two groups received 16 weeks of early anti-inflammatory therapy: cromolyn sodium in 29 patients and budesonide in 31. The remaining 29 patients received no anti-inflammatory medication. The children were followed up 3 years for the development of asthma, defined as 3 or more episodes of physician-diagnosed wheezing plus either an episode of wheezing during the preceding year or continued anti-inflammatory therapy for asthma.

At follow-up, the proportion of children with current asthma was 48% in the cromolyn group, 48% in the budesonide group, and 55% in the control group. A wide range of factors were significant predictors of asthma, including age older than 12 months, risk ratio (RR) 4.1; history of wheezing, RR 6.8; atopic dermatitis at baseline, RR 3.4; and a positive skin-prick test at age 16 months, RR 9.5. Eighteen of 18 children sensitized to furred pets developed asthma. The rate of asthma was reduced in patients positive for respiratory syncytial virus (RSV), RR 0.3; and those who had early contact with a furred pet at home.

In infants hospitalized for wheezing, 16 weeks of anti-inflammatory therapy does not reduce the rate of asthma at 3 years' follow-up. Asthma risk is higher for children with early sensitization to pets and other indoor allergens and those with atopic dermatitis. Children whose initial wheezing episode is related to RSV infection appear less likely to develop asthma.

COMMENT: *Though recent studies have suggested that early intervention with anti-inflammatory treatment in asthma may reduce loss of lung function, such therapy cannot be begun until the diagnosis is made. That is why early predictors of asthma would be helpful. Though pediatricians are reluctant to label patients with asthma after a single episode of wheezing, 3 or more episodes generally are considered diagnostic. This study investigated the question of whether early treatment in those patients can prevent further episodes. The authors found that a short course (4 months) of inhaled cromolyn or budesonide did not reduce the incidence of wheezing 1 and 3 years later. For the RSV group that did not have recurrent wheezing, this is not surprising. For the non-RSV group that did have a higher risk of subsequent wheezing, the lack of benefit after 4 months of treatment isn't too surprising because asthma is a chronic condition that usually requires ongoing treatment. The real take-home message here is that short-term intervention won't prevent the development of asthma. Treatment needs to be long-term to be effective.*
J. M. P.
Reijonen TM, Kotaniemi-Syrjänen A, Korhonen K, Korppi M: Predictors of asthma three years after hospital admission for wheezing in infancy.
Pediatrics 106:1406-1412, 2000. ♦♦

Peanut Allergy Resolves in Some Children

PEANUT is one of the most common causes of serious allergic reactions to food, with an estimated prevalence of 0.6% in the U.S. population. ➤➤

Questions remain about the natural history of peanut allergy--although previous reports suggest that peanut allergy is lifelong, a recent study suggested that the allergy resolves over time in some children. The authors reviewed 293 children with a clinical history of allergic reaction to peanut allergy and/or a positive skin test. Of these, 46 underwent open peanut challenge a mean of 1.8 years after their last clinical reaction. The peanut butter challenge started at a dose of 0.15 mL, which was doubled every 15 to 20 minutes until the patient either reacted or tolerated a dose of 15 mL.

Thirty-three patients had a history of peanut allergy and a positive skin test. Tolerance developed in 9 of 17 patients with a previous history of urticaria on peanut ingestion, compared to none of 5 with a history of anaphylactic reactions to peanut. Tolerance also developed in 4 of 10 patients with a history of peanut-induced flaring of atopic dermatitis. Thirteen patients had a positive skin test but a clinical history of persistent refusal to eat peanuts: 5 of these patients had a positive challenge result.

Some children with early-onset peanut allergy may later develop tolerance of peanuts. Such resolution is less likely in patients whose clinical history includes anaphylaxis. Concerns about false-positive reactions to open challenges may be alleviated by the use of specific, nonsubjective endpoints.

COMMENT: *This article addresses the important clinical issue of the natural history of peanut allergy. While it has been generally accepted that one never "outgrows" peanut allergy, this paper suggests otherwise in* some *patients. The authors show quite convincingly with oral challenges that over half of the patients with urticaria following peanut ingestion developed tolerance, while* no *patient with anaphylaxis developed tolerance. "Once anaphylactic to peanut, always anaphylactic" still holds true.*
A. M.

Spergel JM, Beausoleil JL, Pawlowski NA: Resolution of childhood peanut allergy.
Ann Allergy Asthma Immunol 85:473-476, 2000. ♦♦

Montelukast Pretreatment Does Not Fully Protect Against Reactions to Aspirin

PATIENTS with aspirin (ASA)-sensitive respiratory disease (ASRD) have respiratory mucosal inflammation and bronchospasm in response to aspirin. Oral ASA challenge is the only accurate diagnostic test. Previous studies have suggested that leukotrienes play an important role in ASA-induced respiratory reactions, and some report that pretreatment with leukotriene modifiers has some protective effect against responses to ASA in patients with ASRD. This study assessed whether pretreatment with montelukast could inhibit ASA-induced respiratory reactions, even at ASA doses above the threshold dose.

The study included 10 patients with confirmed ASRD who completed baseline ASA challenges. These challenges produced a naso-ocular reaction, mean score 2.6, in all patients. The mean change in FEV_1 was 19.5%

Each patient was pretreated with montelukast 10 mg/d. Oral ASA challenges were then repeated, starting at the patient's threshold dose and then escalating up to a total of 650 mg. The repeat challenges induced naso-ocular reactions, mean score 2.4, in all patients but 1. In addition, 4 of 9 patients had asthmatic reactions.

Thus montelukast pretreatment achieved "silent" ASA desensitization in only 1 of 10 patients with ASRD. Although montelukast has a partial protective effect against lower airway reactions, it has little or no impact on upper airway reactions. Patients with ASRD who are taking montelukast for asthma control remain at risk of respiratory reactions to ASA.

COMMENT: *The potential protection from aspirin ingestion of aspirin-sensitive subjects with asthma is an attraction for the use of leukotriene-modifier therapy. Several studies show a reduced response to aspirin challenge with a variety of leukotriene modifiers. This paper confirms that the protection from aspirin challenge is only one of degree, placing subjects at risk with aspirin or nonsteroid anti-inflammatory drug ingestion unless they are desensitized. The observation that protection was greater for asthma exacerbation than for upper airway symptoms suggests that the mechanism by which symptoms develop may vary in differing tissues. The experience with leukotriene modifiers and aspirin challenge implies that mediators other than leukotrienes are important in aspirin intolerance.*
D. K. L.

Stevenson DD, Simon RA, Mathison DA, Christiansen SC: Montelukast is only partially effective in inhibiting aspirin responses in aspirin-sensitive asthmatics.
Ann Allergy Asthma Immunol 85:477-482, 2000. ♦♦

Specificity of Skin Wheal Diameters for Predicting Positive Food Challenges Assessed

SOME authors have questioned the specificity of allergen skin testing for diagnosis of clinically relevant food allergy. Under current recommendations, a wheal measuring 3 mm or greater is considered to represent a positive reaction. This study evaluated the ability of allergen wheal diameters of a specific diameter to predict which children will react to an open food challenge.

The prospective study included 555 food challenges and skin prick tests performed in 467 children referred for evaluation of suspected food allergy. The lancet technique was used to perform allergen skin prick testing to cow's milk, egg white, and peanut extract. Open food challenges were subsequently performed: 339 to cow's milk, 121 to egg, and 95 to peanut. If any objective signs developed, the challenge was considered positive; if the child tolerated normal quantities of the food, the challenge was considered negative.

The challenge results were positive in 55% of cases, negative in 37%, and inconclusive in 8%. Challenges were more likely to be positive in children with greater skin wheal sizes, expressed in terms of either wheal diameter or histamine equivalent score. This was so for patients older or younger than 2 years. Food challenges were always positive when the skin diameter was 8 mm for cow's milk, 7 mm for egg, and 8 mm for peanut. However, some children had posi- ➤➤

tive challenges even with a skin wheal diameter of 0 mm.

As previously reported, a positive allergen skin test per se is not a good predictor of clinically relevant food allergy. However, the study identifies skin wheal diameters for milk, egg, and peanut allergen that are 100% specific in predicting a positive reaction to oral challenge. Children with wheals at or above the defined limits need not undergo further evaluation; those with lesser wheal diameters may undergo challenge testing.

COMMENT: *This study complements recent U.S. serologic studies defining levels of specific IgE measured by the CAP system that are highly specific for positive food challenges. As a rule of thumb, a skin test wheal diameter greater than 7 mm or CAP system result greater than 6 kU/L (egg), 31 kU/L (milk), or 15 kU/L (peanut) is highly specific for true food allergy in a high-risk referral population.*
S. A. T.

Sporik R, Hill DJ, Hosking CS: Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children.
Clin Exp Allergy 30:1540-1546, 2000. ♦♦

Reactions to MSG Are Not Reproducible

THE terms "Chinese restaurant syndrome" or "MSG symptom complex" refer to symptomatic reactions to ingestion of the flavor enhancer monosodium glutamate (MSG). However, in the absence of adequately controlled challenge studies, much of the evidence regarding reactions to MSG remains anecdotal. This multicenter study performed various kinds of MSG challenges in 130 patients reporting a previous reaction after an Asian meal that might have contained MSG. In the first of 4 sequential protocols, all subjects were challenged with 5 g of MSG and placebo on separate test days; MSG was added to a citrus-flavored drink to disguise the taste.

Eighty-six patients had a positive response, defined as 2 or more symptoms from a list of 10 reported to occur after MSG ingestion. These patients completed another challenge to assess the consistency and dose dependency of reactions. Twelve patients who responded to MSG but not placebo participated in a third challenge study. Finally, 2 patients participated in a fourth protocol in which MSG was given in food.

In the initial challenge study, 38.5% of patients responded to MSG only, 13.1% to placebo only, and 14.6% to both MSG and placebo. In the second protocol, using increasing doses of MSG, the response rate increased. However, only about half of patients who responded to MSG but not placebo in the first protocol had a similar response in the second. Two patients responded to all MSG challenges but not placebo through the 3 nonfood protocols, although their symptoms were not reproducible. In the food protocol, both patients responded to only 1 of 3 MSG challenges.

In patients with self-reported reactions to MSG, the symptom response rate to a large dose of MSG given without food is higher than the response rate to placebo. However, repeated testing shows no reproducible pattern of responses to MSG. In addition, the reactions that do occur are not serious in nature.

COMMENT: *This cleverly designed double-blind, placebo-controlled, multiple challenge study did find that patients reporting sensitivity to MSG initially reported more symptoms after ingesting MSG in a citrus-flavored beverage. However, after multiple challenges with MSG--either in food or in a capsule--the patient responses were not consistent. We are told that the double-blind, placebo-controlled food challenge is the "gold standard" for determining clinically significant food sensitivity. This study shows that large doses of MSG may produce more symptoms than placebo; however, they are neither reproducible nor serious.*
S. M. F.

Geha RS, Beiser A, Ren C, et al: Multicenter, double-blind, placebo-controlled, multiple challenge evaluation of reported reactions to monosodium glutamate.
J Allergy Clin Immunol 106:973-980, 2000. ♦♦

Local Reactions to Immunotherapy Do Not Require Dose Adjustments

LOCAL reactions to allergen immunotherapy are a common occurrence, with a reported rate of 0.7% to 4.0% per 100 injections. A 1998 World Health Organization position paper states that local reactions do not predict later systemic reactions. However, many practitioners continue to make dose adjustments for immunotherapy patients who experience local reactions. This study compared the effects of 2 policies in dealing with local reactions to immunotherapy--dose adjustments vs no adjustments--on the rate of subsequent systemic reactions.

In 1997, the authors' allergy clinic altered its policy in managing local reactions to allergy vaccine injection. Before the policy change, patients with immediate swelling of 15 to 19 mm received the same dose; those with immediate swelling of 20 to 25 mm received the last dose that produced no reaction; and those with immediate swelling of greater than 25 mm or any swelling lasting longer than 12 hours received a 50% dose reduction. After the policy change, no dose adjustments were made for patients with immediate or late local reactions. The 9-month periods before and after the policy change were reviewed to examine the impact on systemic reaction rates.

Throughout the 18-month study period, clinic patients received a total of 12,926 immunotherapy injections. The systemic reaction rate was 0.80% before the policy change and 1.01% afterward; the difference was nonsignificant. On review of patients who experienced systemic reactions, the rate of local reactions occurring immediately before a systemic reaction was 18.8% before and 10.5% after the policy change. This difference was also nonsignificant. Local reactions were only 15% sensitive in predicting a systemic reaction at the next immunotherapy injection.

In patients receiving immunotherapy, a local reaction is not a strong predictor of a subsequent systemic reaction. This experience supports a policy of not adjusting the immunotherapy dose in response to local reactions. Dose adjustments do not reduce the risk of subsequent systemic reactions. In addition, they ➤➤

delay treatment, increase costs, and increase the risk of dosing errors.

COMMENT: *Although the WHO position paper has recommended that allergen immunotherapy dose need not be adjusted after local reactions, many allergists have continued to make dose adjustments after these types of reactions. A change in policy at their allergy clinic afforded an opportunity for this group to compare systemic reaction rates after local reactions from immunotherapy. They reaffirm previous data showing that local reactions are a very insensitive predictor of subsequent systemic reactions. In light of medical-legal pressures, more definitive prospective studies such as this one are needed before we see a widespread change in practice patterns.*
S. M. F.

Tankersley MS, Butler KK, Butler WK, Goetz DW: Local reactions during allergen immunotherapy do not require dose adjustment.
J Allergy Clin Immunol 106:840-843, 2000. ♦♦

Der p 1 Allergen Crosses the Placental Barrier

PREVIOUS studies have demonstrated allergen-specific reactivity in umbilical cord blood mononuclear cells. However, the route of in utero allergen exposure remains unknown. The investigators used an enzyme-linked immunosorbent assay to measure Der p 1 allergen in matched samples of maternal blood and amniotic fluid from women undergoing amniocentesis at 16 to 17 weeks' gestation.

Of 406 maternal blood samples tested, 21% had detectable levels of Der p 1. Der p 1 was also detected in amniotic fluid from 56% of 43 mothers with circulating levels of the allergen. All mothers in the latter group had plasma Der p 1 concentrations exceeding 5 µg/L. Testing also showed Der p 1 in 63% of 24 umbilical cord blood samples. Levels of Der p 1 in amniotic fluid were significantly lower than in matched plasma samples.

The findings suggest the Der p 1 can cross the placenta to reach the umbilical cord blood. Levels of allergen in the fetal circulation are higher than in the maternal circulation. The findings may help to explain the phenomenon of allergen transfer to the fetus in utero.

COMMENT: *These investigators found Der p 1 in matched maternal blood and amniotic fluid samples at 16 to 17 weeks' gestation, and in matched maternal and umbilical cord blood at term. Over half the amniotic fluid samples were positive if the plasma contained greater than 5 µg/L of Der p 1. These observations provide incentive for allergic mothers to pursue aggressive avoidance measures during pregnancy in the hope of inhibiting the initiation of allergic disease in utero.*
E. J. B.

Holloway JA, Warner JO, Vance GHS, et al: Detection of house-dust-mite allergen in amniotic fluid and umbilical-cord blood. **Lancet** 356:1900-1902, 2000. ♦♦

Risks of Exemption from Immunizations Assessed

MANY states permit personal or religious exemptions from mandatory vaccination for children. Many parents--few of whom have ever encountered a child with a serious, vaccine-preventable illness--seek exemption based on fear of an adverse reaction to vaccines. Colorado has a high rate of personal or religious exemptions: 1.4% in 1994, compared with a national average of 0.6%. This study assessed the personal and community risks associated with personal exemption from immunizations.

The investigators reviewed standardized data on all cases of measles and pertussis occurring in Colorado during 1997-98. Children classified as "exemptors" were at elevated risk of measles (relative risk [RR] 22.2, 95% confidence interval [CI] 15.9 to 31.1) and pertussis (RR 5.9, 95% CI 4.2 to 8.2). These risks rose to 62-fold and 16-fold, respectively, among day-care to primary school-age children. Exemptors also played an prominent role in disease outbreaks, accounting for 14.5% of patients involved in the index and first generation of measles outbreaks. Overall, about 11% of vaccinated children involved in measles outbreaks were infected by contact with an exemptor.

This study documents the risks associated with exemption from measles and pertussis immunization, not only for the individual but also at the population level. Children exempted from vaccination place vaccinated children at risk. Parents concerned about the risks of having their child vaccinated should also be informed of the risks of not doing so.

COMMENT: *The control of vaccine-preventable diseases reduces the likelihood of personal experience--for the patient, family, and physician--with these severe, life-threatening illnesses. Allergist/immunologists often are asked to evaluate subjects for vaccine intolerance or allergy. Frequently an atmosphere of anxiety and concern about side effects dominates the assessment. When parents are making the decision to administer or withhold vaccination, the physician may help to maintain the risk-benefit balance by sharing data concerning the risk of serious infectious disease, including a 62-fold increase in risk of pertussis and a 16-fold risk of measles in young, unvaccinated children. This study also shows that vaccinated subjects are placed at risk from nonvaccinated individuals. Vaccines are our friends and deserve our respect.*
D. K. L.

Feikin DR, Lezotte DC, Hamman RF, et al: Individual and community risks of measles and pertussis associated with personal exemptions to immunization.
JAMA 284:3145-3150, 2000. ♦♦

Inhaled Fluticasone Offers Better Therapeutic Ratio Than Budesonide

INHALED corticosteroids are a highly effective treatment for bronchial asthma, with a lower rate ➤➤

of systemic side effects compared with systemic steroids. Few previous studies of inhaled corticosteroids have sought to establish a therapeutic ratio--that is, assessed efficacy and side effects at the same time. This study compared the therapeutic ratios of fluticasone propionate and budesonide in the treatment of bronchial asthma.

The randomized trial included 66 adult patients with clinically stable asthma, FEV_1 60% predicted or better. All were well maintained on inhaled corticosteroids--fluticasone 200 to 500 µg/d or beclomethasone dipropionate/budesonide 400 to 1,000 µg/d--at study entry. In double-blind fashion, the patients received three consecutive 2-week periods of treatment with fluticasone (250, 500, and 1,000 µg twice daily) or budesonide (400, 800, and 1,600 µg twice daily). Fluticasone was administered by Diskhaler and budesonide by Turbuhaler. Primary outcome assessments were bronchial methacholine challenge and plasma and urine cortisol measurements; serum osteocalcin and blood eosinophils were measured as well.

Thirty-one patients in the fluticasone group and 30 in the budesonide group completed the study. Both drugs had a clear dose-response effect on bronchial responsiveness. However, primary outcome measures favored fluticasone, with a relative PD_{20} potency of 2.51 and a relative 24-hour urinary cortisol potency of 0.60. Based on these 2 outcome measures, the differential therapeutic ratio was 4.18 (95% confidence interval, 1.16 to 15.03).

The study is the first to establish the differing dose-response relationships of fluticasone and budesonide in patients with asthma. Assessed in terms of bronchial responsiveness and endogenous corticosteroid production, the therapeutic ratio clearly favors fluticasone. The study population was specifically selected to be steroid sensitive--ie, to have stable lung function and symptoms on baseline inhaled corticosteroid therapy, but room for improvement in bronchial responsiveness.

COMMENT: *These results indicate that inhaled fluticasone has a greater pulmonary effect and less systemic effect than inhaled budesonide. This is one of only a few studies comparing therapeutic ratios of different inhaled steroid preparations. Change in bronchial hyperreactivity, as determined by methacholine challenge, was the measure of therapeutic effect favoring fluticasone. Study patients had well-controlled asthma on inhaled corticosteroids before the study. During the study period the 2 groups did not differ with respect to symptoms, peak flow measurements, or use of rescue* β*-agonists.*
J. R. B.

Nielsen LP, Dahl R: Therapeutic ratio of inhaled corticosteroids in adult asthma.
Am J Respir Crit Care Med 162:2053-2057, 2000. ♦♦

Do Metal Allergies Increase the Risk of Restenosis After Coronary Stenting?

STENT placement reduces the rate of restenosis in patients undergoing coronary angioplasty. However, about 10% of patients will experience in-stent restenosis, characterized by a fibroproliferative and inflammatory response to insults to the arterial wall. The finding of immunocompetent cells suggests a local immune response with an inflammatory reaction to foreign material. Most stents are made of 316L stainless steel, which contains potentially sensitizing metals such as nickel, chromium, and molybdenum. The possible relationship between in-stent stenosis and allergic reactions to stent materials was assessed.

The study included 131 patients with a total of 171 coronary stents made of 316L stainless steel. A mean of 6 months after stent placement, all patients were undergoing follow-up angiography for suspected restenosis. At the same time, epicutaneous patch tests for nickel, chromate, molybdenum, manganese and small 316L stainless steel plates were performed using the Finn Chamber method.

Eighty-nine patients had in-stent restenosis of 50% or greater. On skin testing, 4 patients reacted to molybdenum and 7 to nickel. All 10 patients with positive patch tests had recurrent angina pectoris requiring revascularization of the target vessel.

For patients with coronary stents, the frequency of in-stent restenosis may be elevated for those with delayed-type hypersensitivity to metals, particularly nickel. A history of allergy to nickel and other metals should be elicited in patients being considered for stent placement. Certain groups may be at particularly high risk: women, young patients, those with eczematous skin diseases, and those with pierced ears.

COMMENT: *Stainless steel implants can cause inflammatory hypersensitivity reactions to metal. This study included 131 patients with 171 coronary stainless steel stents who underwent repeat coronary angiography 6 months after stenting for suspected restenosis. Epicutaneous patch tests for nickel, chromate, molybdenum, manganese, and small stainless steel plates were performed. Restenosis occurred in 89 patients, and all 10 patients with positive patch tests had restenosis. A higher frequency of in-stent restenosis was found in patients with hypersensitivity to nickel (6) and molybdenum (4).*
E. J. B.

Köster R, Kiehn M, Sommeraurer M, et al: Nickel and molybdenum contact allergies in patients with coronary in-stent restenosis.
Lancet 356:1895-1897, 2000. ♦♦

Study Finds High Rate of Enzyme-Induced Asthma in Detergent Workers

PREVIOUSLY, the use of enzymes in detergent manufacturing was associated with high rates of occupational asthma. The introduction of enzyme encapsulation is credited with dramatically reducing this problem. However, from 1994 to 1997, the authors diagnosed 6 cases of enzyme-induced asthma among workers at a detergent factory that used encapsulated enzymes. This prompted a survey of enzyme sensitization and respiratory symptoms in the factory.

The survey sought information on symp- ➤➤

toms of asthma and upper respiratory disease in 350 detergent-factory employees, representing 81% of the workforce. Skin-prick tests were performed in 342 workers. Twenty-six percent of workers had a positive skin-prick test to 1 or more detergent enzymes. Workers were more frequently sensitized to amylase than to protease or cellulase. Of 22 workers sensitized to a single enzyme, 14 were sensitized to amylase. Sixty-eight percent of workers had work-related upper respiratory symptoms plus enzyme sensitization, a rate of 19%. Of these, 54 had lower-respiratory symptoms as well, a rate of 16%.

The findings question whether enzyme encapsulation has truly eliminated enzyme-induced allergy and asthma in the detergent industry. Rather, the engineering improvements introduced alongside enzyme encapsulation may have played the key role in reducing protease-induced asthma. The new study suggests that amylase is the most frequent sensitizing enzyme.

COMMENT: *Enzyme encapsulation is believed to have eliminated occupational asthma in the detergent industry. This survey of 350 employees of a large detergent factory detected work-related allergic rhinitis with enzyme allergy in 68 patients (19%), including 54 (16%) with occupational asthma. Sensitization to amylase was most common. These observations suggest our initial complacency may have been misplaced.*
E. J. B.
Cullinan P, Harris JM, Newman Taylor AJ, et al: An outbreak of asthma in a modern detergent factory.
Lancet 356:1899-1902, 2000. ♦♦

Esophageal Acid Instillation Increases Airway Hyperresponsivness

PREVIOUS studies suggest a strong association between gastroesophageal reflux and asthma exacerbations. The effects of local acid perfusion of the esophagus on airway responsiveness were studied in 7 patients with bronchial asthma. In random order at 1-week intervals, the patients underwent esophageal perfusion with either 0.1 N hydrochloric acid solution or saline solution. The solutions were instilled via a naso-esophageal tube with the patient seated. A pH meter was used to measure esophageal pH, and airway responsiveness by methacholine challenge. Spirometric measures were obtained as well.

Esophageal acid perfusion was associated with a significant increase in airway hyperresponsiveness. Acid perfusion was associated with significant reductions in geometric mean airway sensitivity or in the methacholine concentration causing a 35% decrease in respiratory conductance. Spirometric values were unchanged.

In patients with asthma, acid stimulation of the esophagus is associated with a significant increase in airway hyperresponsiveness. This is the first study to examine the effects of esophageal acid instillation, with pH monitoring, on changes in airway responsiveness. Even in patients without reflux disease, esophageal reflux may be an important factor in aggravating asthma.

COMMENT: *This is the first study to evaluate changes in airway responsiveness during instillation of acid into the esophagus while monitoring esophageal pH. The investigations showed that airway responsiveness increased significantly after acid perfusion of the esophagus in patients with mild asthma. None of the patients had symptoms of esophageal reflux. There is little doubt that reflux plays a critical role in aggravating asthmatic symptoms (see* AllergyWatch *Sept-Oct 2000, p. 2).*
J. B.-M.
Wu D-N, Tanifuji Y, Kobayashi H, et al: Effects of esophageal acid perfusion on airway hyperresponsiveness in patients with bronchial asthma.
Chest 118:1553-1556, 2000. ♦♦

Follow-up Study Tracks Development of SAR in Children

ALTHOUGH cross-sectional studies have been performed, there are few longitudinal data on the development of seasonal allergic rhinitis (SAR) in children. This prospective study--part of the Multicenter Allergy Study--examined the development of sensitization and symptoms of SAR in a birth cohort of 587 children. Annual follow-up information on each child was collected up to age 7 years.

During follow-up, 15% of the children developed SAR. In the early childhood years, the incidence and prevalence of symptoms and sensitization were lower than 2%--but increased steadily thereafter. All children developing SAR by age 2 were born in spring or early summer, and thus had gone through at least 2 pollen seasons. On multivariate analysis, the risk of SAR was higher for boys, children with atopic parents, first-born children, and those with early sensitization to food or atopic dermatitis. Early childhood wheezing was not a risk factor for SAR.

This prospective birth cohort study suggests that the prevalence and incidence of SAR in children increase steadily from age 2 to 7 years. Early symptoms of rhinitis more likely reflect respiratory infections than allergy. The study identifies risk factors for childhood development of SAR--for children with certain constellations of risk factors, the probability of developing SAR may be as high as 75%.

COMMENT: *This prospective cohort analysis from Germany reconfirms that the prevalence of SAR in young children is 15%. Symptoms of nasal congestion, rhinorrhea, and sneezing in children less than 5 years usually indicated transient and not chronic disease. Allergic diathesis and at least 2 seasons of pollen exposure predispose chuildren to SAR. Interestingly, early wheezing is not associated with SAR. As most allergists, know, infants and toddlers with rhinitis usually do not have seasonal allergens triggering their symptoms.*
S. M. F.
Kulig M, Klettke U, Wahn V, et al: Development of seasonal allergic rhinitis during the first 7 years of life.
J Allergy Clin Immunol 106:832-839, 2000. ♦♦

High-Dose Mometasone Has Few Systemic Effects

INHALED glucocorticoids bind to cytosolic receptors, raising the potential for adverse effects if systemic glucocorticoid levels become high enough. The development of inhaled glucocorticoids whose therapeutic activity in the lung greatly exceeds their potential for systemic effects is a priority. Mometasone furoate, delivered by breath-actuated dry powder inhaler (DPI), is highly effective in the treatment of mild to moderate persistent asthma. This study examined the potential for systemic effects of mometasone--delivered by DPI or metered-dose inhaler (MDI)--at clinical and higher doses.

Three separate studies were performed. In the first study, 60 asthma patients received mometasone via DPI at doses of 200, 400, 800, or 1,200 µg/d, or placebo. Plasma mometasone levels were around the lower limit of detection at the 400 µg/d dose, and about 250 pg/mL at the 1,200 µg/d dose. At all doses, the area under the curve for 24-hour serum cortisol concentration (AUC_{24}) was unchanged.

In the second study, 64 patients received mometasone 400 or 800 µg bid, oral prednisone 10 mg/d, or placebo. Only at the higher mometasone dose was there any consistent evidence of low-level systemic exposure. Some patients in this group had moderate reductions in mean serum cortisol AUC_{24} and failure to achieve a normal response to cosyntropin. The effects of inhaled mometasone were far less than those of oral prednisone. In the third study, 64 patients took mometasone 400 or 800 µg bid or fluticasone 880 µg bid via MDI, or placebo. The effects were similar to those produced by mometasone via DPI. The higher dose had a slight systemic effect on the hypothalamic-pituitary-adrenal (HPA) axis.

Inhaled mometasone therapy produces very low plasma levels. Even in doses up to 1,200 µg/d, the systemic effects on HPA axis function are inconsistent and modest. These effects are significantly lower than those caused by oral prednisone or inhaled fluticasone. The study findings apply only to patients with mild to moderate persistent asthma.

COMMENT: *This study helps validate claims that inhaled mometasone furoate has superior safety characteristics. While serum cortisol and cosyntropin stimulation measurements are not the only indicators of systemic steroid effects, the results clearly favoring mometasone 800 µg bid over fluticasone 880 µg bid are quite interesting.*
S. A. T.
Affrime MN, Kosoglou T, Thonoor CM, et al: Mometasone furoate has minimal effects on the hypothalamic-pituitary-adrenal axis when delivered at high doses. **Chest** 118:1538-1546, 2000. ♦♦

Severe Zafirlukast-Related Liver Injury: Three Cases

THE leukotriene receptor antagonist zafirlukast has become widely used in asthma treatment. Few toxic side effects are reported. Although clinical trials showed asymptomatic increases in serum liver enzymes in 1.5% of patients, none developed severe hepatotoxicity. Three cases of severe hepatitis developing in patients taking zafirlukast are reported.

The patients were 3 women with chronic asthma, aged 42 to 49 years. All developed symptoms--including flulike symptoms and jaundice--only after several months of zafirlukast therapy. Other possible causes of acute hepatitis were excluded. In all 3 cases, liver injury persisted for a period of weeks after withdrawal of zafirlukast. One patient developed progressive hepatitis, eventually requiring liver transplantation 3 months after zafirlukast was withdrawn. This patient had evidence of systemic hypersensitivity, including rash, fever, and eosinophilia. One patient recovered, but developed severe relapse when inadvertently given zafirlukast again. The third patient improved rapidly after a course of high-dose IV methylprednisolone. Histologic examination of liver tissue in 2 cases showed evidence of drug-related injury.

These cases illustrate the potential for severe hepatoxicity in patients taking zafirlukast for asthma. This is an idiosyncratic reaction affecting a small number of patients; however, all patients taking zafirlukast should be monitored for signs and symptoms of hepatitis.

COMMENT: *This important article serves as a reminder that zafirlukast may rarely cause significant hepatocellular changes. In early clinical trials, 5% of patients receiving zafirlukast had mainly mild asymptomatic elevations of liver enzymes. In these three cases much more significant hepatocellular injury occurred, with one patient progressing to hepatic failure and liver transplantation.*
A. M.
Reinus JF, Persky S, Burkiewicz JS, et al: Severe liver injury after treatment with the leukotriene receptor antagonist zafirlukast.
Ann Intern Med 133:964-968, 2000. ♦♦

Several Tests May Be Needed to Demonstrate Latex Sensitization

SEVERAL important latex allergens have been identified, including the 58 kD rubber elongation factor; the 14 kD hevein and the 20 kD prohevein; and a 27 kD natural rubber latex protein. The past decade has seen a sharp rise in latex allergy, especially among health care workers. A group of selected hospital employees were studied to assess IgE sensitization to various latex components.

A questionnaire regarding symptoms of latex allergy was given to 200 hospital employees. Thirty-four patients had clinical evidence of latex sensitization: ie, symptoms plus a positive specific IgE test or a positive leukocyte histamine release test. No challenge studies were performed. In vitro studies for sensitization to 5 different latex extracts were performed.

Thirty-four health care workers (17%) were identified as latex sensitive. Twenty-six of this group (76%) showed leukocyte histamine release in response to at least 1 latex extract. Thirty-eight percent had a ➤➤

positive specific IgE result on Pharmacia CAP testing, 58% were positive on the Hytec RAST, and 78% had positive results on IgE immunoblotting. Eight nonatopic controls showed no IgE binding. On immunoblotting, the only protein to which most allergic subjects reacted was a 30 to 35 kD protein, and then only when tested using Stallergene extract. Subjects also reacted to proteins with molecular weights of 14, 21, and 42 kD. Three patients with a negative histamine release response still had IgE antibodies confirmed by specific IgE tests.

This study confirms the high rate of latex sensitization among health care workers. However, it also points out that testing with a combination of latex extracts is needed to identify all sensitized individuals. This may reflect a large variety of latex epitopes and/or differences in the analytical sensitivity of techniques used to demonstrate IgE sensitization.

COMMENT: *Allergic reactions to natural rubber latex (NRL) continue to provide a diagnostic challenge to the clinician. It has been apparent that not only are there multiple proteins in NRL to which a sensitized individual may react, but that some patient populations have unique patterns of reactivity. This paper highlights the importance of recognizing that a latex-sensitive individual may recognize multiple epitopes on NRL, and that in some patients multiple tests may be necessary. The paper also points out the importance of recognizing that a substantial number of patients with a convincing history may have* no *reactivity to any NRL epitopes, despite aggressive testing.*
A. M.

Nielsen PS, Nissen D, Skov PS, et al: Assessment of IgE allergen specificity among latex-allergic health care workers: review of IgE-binding components of various latex extracts.
Ann Allergy Asthma Immunol 85:489-494, 2000. ♦♦

High Rate of Generalized Reactions to Skin Prick Testing in Young Infants

SKIN prick testing is a quick, convincing, and inexpensive technique for diagnosing IgE-mediated hypersensitivity in children. Though safe, skin prick testing can induce rare systemic reactions in highly sensitive patients. In a large series of pediatric skin prick tests, the authors identified 6 cases of generalized allergic reactions, all occurring in infants less than 6 months old.

The patients were encountered over a 2-year period, from a series of 1,152 skin prick tests in patients aged 0 to 19 years. The 6 patients with generalized allergic reactions ranged in age from 2.5 to 5 months. The babies all had eczema of varying severity, and all had a family history of atopic disease. None had a history of wheezing, though 2 had a cold at the time of testing. The generalized allergic reaction occurred within 20 minutes after the test. All of the reactions occurred after skin prick testing to fresh food specimen. The rate of generalized reactions was 0.52% overall, but 6.5% for children less than 6 months old.

This experience suggests a significant rate of generalized allergic reactions after skin prick testing with fresh food specimens in infants under 6 months old. Such reactions may be associated with active eczema, a positive reaction to food items, and a family history of allergy. Special precautions are recommended in testing of very young infants, especially those with eczema, perhaps including testing with only 1 allergen per visit.

COMMENT: *The safety of prick or percutaneous allergy skin testing has been convincingly documented. The need for testing infants less than 6 months of age is usually because of suspected food sensitivity. Six percent of children less than 6 months of age experienced a systemic cutaneous reaction following fresh-food skin prick testing. This reaction rate is more than 10-fold greater than in older children or adults. This risk does not prohibit testing, but special attention is advisable.*
D. K. L.

Devenney I, Fälth-Magnusson K: Skin prick tests may give generalized allergic reactions in infants.
Ann Allergy Asthma Immunol 85:457-460, 2000. ♦♦

Bronchial Hyperresponsiveness Appears After Initial Asthma Attack in Infants

PREVIOUS studies have described an association between bronchial hyperresponsiveness (BHR) and infantile wheezing. Infants who are genetically predisposed to atopy are more likely to develop wheezing in the presence of respiratory viral infection or bronchiolitis, and viral infections may induce continued BHR after the initial asthma attack. The authors used a transcutaneous oxygen pressure ($tcPO_2$) monitoring technique to assess the age at development of BHR in asthmatic children.

Two hundred five asthma-free children, aged 6 months to 6 years, underwent $tcPO_2$ monitoring during methacholine inhalation challenge. Eighteen children developed asthma during follow-up; they, along with a group of 15 age-matched children without asthma, were tested twice using methacholine inhalation challenge. Two inhalation challenges were also administered to 39 age-matched children with atopic-type asthma. The challenge studies were performed while the children were asleep, with sequential doses of inhaled methacholine administered by oxygen until a 10% decrease in $tcPO_2$ from baseline was reached. The groups were compared in terms of the cumulative dose of methacholine at the inflection point of $tcPO_2$, or minimal dose of methacholine (Dmin)-PO_2.

The Dmin-PO_2 was similar between the first and second methacholine challenges for the children without asthma and for those with atopic asthma. However, in the children diagnosed with asthma at follow-up, the Dmin-PO_2 decreased significantly from the first challenge to the second.

In most children who go on to develop asthma, BHR is undetectable before the initial asthma attack, but can be detected after at least the second attack. Thus BHR does not appear to be a prerequisite for the first attack of childhood asthma. The findings suggest a possible predisposition to developing BHR, which appears especially common in the presence of atopy. ➤➤

COMMENT: *A great deal of controversy surrounds the question of how asthma develops in infants. One hypothesis is that infants are genetically programmed to be asthmatic, while another is that exposure to environmental factors causes the asthma. In this study, some infants who did not initially have bronchial hyperreactivity developed it after several asthma episodes, supporting the latter hypothesis. What the authors failed to determine is why some infants developed asthma while others with the same viral infections did not. Since recent evidence suggests that viral infections may protect some infants with asthma while others seem to develop asthma from those same infections, it seems likely that genetics is at work. How one would test this hypothesis is unclear.*
J. M. P.

Mochizuki H, Shigeta M, Arakawa H, et al: Bronchial hyperresponsiveness before and after the diagnosis of bronchial asthma in children.
Pediatrics 106:1442-1446, 2000. ♦♦

Immunotherapy Can Reduce Airway Responsiveness in Patients with Allergic Rhinitis

AMONG patients with allergic rhinitis, the presence of bronchial hyperresponsiveness (BHR) is associated with an increased risk of asthma. There is ongoing debate over the effectiveness of specific immunotherapy (SIT) in asthma. However, it is possible that giving SIT on a prophylactic basis to susceptible patients might prevent the development of asthma. The ability of SIT to prevent progression to asthma and increased BHR in patients with allergic rhinitis was studied.

The double-blind trial included 44 subjects with perennial rhinitis who were sensitized to house dust mite only and who had BHR in response to methacholine challenge. All were free of asthma symptoms and had normal results on lung function testing. They were randomized to receive 2 years of treatment with either SIT or placebo. For patients in the SIT group, the maximal dose tolerated was identified and given monthly for the duration of the study. The 2 groups were compared in terms of airway responsiveness, disease activity, and serum IgE levels.

The 2 groups were comparable at baseline, including similar values for the provocative dose of methacholine necessary to produce a 20% decrease in FEV_1 ($PD_{20}FEV_1$). However, by the end of the first year of treatment, the SIT group had a 2.88-fold increase (95% confidence interval, 2.9- to 5.7-fold) in $PD_{20}FEV_1$. By the end of the second year, there was a 4.1-fold increase (95% confidence interval 2.9- to 5.7-fold). After 2 years, one-half of patients in the SIT group had a methacholine $PD_{20}FEV_1$ within the normal range, ie, greater than 8 µmol. In contrast, all patients in the placebo group had continued BHR. Serum IgE levels did not change significantly during treatment in either group, and were unrelated to the change in methacholine $PD_{20}FEV_1$ for patients in the SIT group.

In some monosensitized patients with perennial allergic rhinitis, SIT can significantly reduce airway responsiveness and may eliminate BHR. The authors propose testing of bronchial reactivity in such patients to identify those with BHR, who may then be candidates for SIT to prevent progression to asthma. Starting SIT at an early phase, when bronchial reactivity is mild, may increase the likelihood of benefit. Compared with early corticosteroid treatment--which is unproven in any case--SIT may have the advantage of modifying airway sensitivity in allergen-specific fashion.

COMMENT: *The authors suggest that patients with allergic rhinitis caused by house dust mite undergo tests for bronchial hyperreactivity to identify individuals particularly likely to benefit from immunotherapy. This might be a good idea, at least for patients who have symptoms compatible with asthma but normal spirometry results. The information obtained could help patients decide whether to commit to a course of immunotherapy.*
J. R. B.

Grembiale RD, Camporota L, Naty S, et al: Effects of specific immunotherapy in allergic rhinitic individuals with bronchial hyperresponsiveness.
Am J Respir Crit Care Med 162:2048-2052, 2000. ♦♦

Ventolin HFA Performs Just as Well as Ventolin CFC in Asthmatic Children

BECAUSE of the adverse effects of chlorofluorocarbons (CFCs) on the environment, the CFC propellants widely used in asthma inhalers are being phased out. In their place, new propellants such as hydrofluoroalkane-134a (HFA) are being introduced. The clinical comparability of albuterol products formulated with CFC vs HFA propellants was assessed.

The randomized trial included 135 asthmatic children, aged 4 to 11 years. During a run-in period, all children took conventional CFC-containing Ventolin Inhalation Aerosol (Ventolin CFC) as needed. They were then randomized to 2 weeks of treatment with placebo; Ventolin CFC; or Ventolin HFA Inhalation Aerosol (Ventolin HFA). Each treatment was given 4 times daily via metered-dose inhaler. Rescue albuterol was available as needed. The groups were compared in terms of mean percentage of predicted peak expiratory flow (PEF) after the morning dose on the first and last days of treatment.

The postdose increase in mean percentage of predicted PEF on day 1 was 14% with Ventolin HFA and 13% with Ventolin CFC, compared to 6% with placebo. Values at the end of treatment were 11% in both Ventolin groups vs 5% with placebo. The 2 Ventolin groups were similar in their effects on pulmonary function, time to onset of response, duration of response, and peak effects. Safety characteristics were similar to those of placebo.

In asthmatic children, the newer Ventolin HFA products offer clinical performance similar to that of conventional Ventolin CFC products. The 2 products provide similar increases in bronchodilation, compared with placebo, and similar safety profiles. To date, ➤➤

no non-CFC albuterol products have been approved for pediatric use in the United States.

COMMENT: *With the approval of the Montreal protocol, we have been forced to change the fluorocarbon propellants in the inhaler devices available for our asthmatic patients. This study confirms that the new hydrofluroalkane (HFA) propellant can be just as efficacious as the previously used CFC propellent for Ventolin in children aged 4 to 11 years. Although the issue was not specifically addressed in the data analysis, the graph in the results section appears to show a slightly better improvement in PEF after a dose with HFA compared to CFC. Other HFA products have been shown to have improved drug deposition compared to CFCs. Should we be seeing more significance in the differences in the effect of HFA compared to CFC products?*
S. M. F.
Shapiro G, Bronsky E, Murray A, et al: Clinical comparability of Ventolin formulated with hydrofluoroalkane or conventional chlorofluorocarbon propellants in children with asthma.
Arch Pediatr Adolesc Med 154:1219-1225, 2000. ♦♦

Follow-up Study of Latex-Allergic Children

CHILDREN with spina bifida or other conditions requiring multiple surgeries are at risk of developing sensitization to natural rubber latex (NRL). However, some atopic children may become sensitized to NRL even if they have not undergone surgery. The outcomes of NRL allergy--including children with and without a history of multiple operations--were examined.
The follow-up study included 24 children with NRL allergy who had not undergone surgery, as well as 8 children with NRL allergy and a history of multiple operations. At a mean follow-up of 2.8 years, the children underwent skin-prick testing using the same NRL allergens as at initial diagnosis (Stallergenes SPT reagent and Triflex glove extract). At the same time, SPT for banana, kiwi fruit, and avocado were performed, with histamine dihydrochloride used as a positive control and physiologic saline as a negative control. Clinical symptoms and NRL exposure during follow-up were assessed as well.

Of the 24 children with NRL allergy who had not undergone surgery, 19 had occasional contact with balloons and other NRL-containing products at home. Ten of these children experienced symptoms during follow-up, ranging from contact urticaria to systemic reactions. Overall, symptoms developed during follow-up in 62% of children who had been symptomatic at baseline as well as 22% of those who had been asymptomatic. Of the 8 children with a history of multiple operations, 8 had had contact with rubber balloons without experiencing symptoms. Five had undergone further operations in a latex-free environment, without adverse effects. Skin-prick test reactivity was unchanged, as were mean latex RAST levels.

Even with NRL precautions in place, about two-thirds of children with NRL allergy come into contact with rubber products--especially balloons--during follow-up. Even among children with no history of operations, symptomatic reactions may occur. Symptoms occur in the absence of changes in SPT reactivity or latex RAST levels. The findings underscore the difficulty of completely avoiding exposure to NRL products in the home.

COMMENT: *The children in this study exercised reasonable latex avoidance measures, yet both their sensitization to natural rubber latex and their capacity for latex-induced symptoms persisted. The findings contrast with previous report in occupationally sensitized adults, in whom latex-specific IgE declined with avoidance. These observations remind us that we are only just beginning to understand the natural history of latex allergy.*
S. A. T.
Ylitalo L, Alenius H, Turjanmaa K, et al: Natural rubber latex allergy in children: a follow-up study.
Clin Exp Allergy 30:1611-1617, 2000. ♦♦

A Successful Management Program for Peanut/Tree Nut Allergy

THIS prospective study assessed the effectiveness of a management plant for patients with peanut and nut allergy, one of the major causes of severe or fatal food-related anaphylaxis. The experience included 567 unselected referral patients with confirmed allergy to peanut or tree nuts. Based on severity grading, the patients were assigned to varying levels of emergency medication, which consisted of oral antihistamine with or without inhaled or injected epinephrine. All patients received advice on nut avoidance, including verbal and written instructions for patients, parents, and school staff; training in recognition and self-treatment of reactions; and a written treatment plan. At follow-up of greater than 13,610 patient-months, the impact of the program on subsequent reactions was assessed.

During follow-up, 15% of patients had a reaction of reduced severity. Most of these reactions were classified as mild and mainly cutaneous. Medications used for these reactions included oral antihistamine in 49 patients, inhaled adrenaline in 6, and no treatment in 10. Moderate reactions occurred in 12 patients, all of which responded to inhaled epinephrine. Just 3 patients had severe reactions--the rate of such reactions decreased from 12% at baseline to 0.5% during follow-up. Just 1 patient with a mild index reaction developed a severe reaction during follow-up.

An effective management program for patients with allergy to peanut or tree nuts is reported. The plan depends on assessment of allergy severity to determine the effective self-treatment measures: inhaled epinephrine for early laryngeal edema, epinephrine injector for severe reactions. To ensure optimal management, patients with this type of allergy should be referred to a specialist allergy center.

COMMENT: *In the United States, up to 7.6 cases of food anaphylaxis occur per 100,000 person-years, an incidence approximating 29,000 episodes of food* ➤➤

anaphylaxis causing 150 deaths per year. These authors evaluated 567 patients to assess the value of a management program. They determined that allergy to peanuts is common with a prevalence that is increasing. It is commonly associated with sensitivity to tree nuts and some seeds. They showed that an aggressive management program was effective. Patients with nut allergy should be referred to an allergy specialist for evaluation.
E. J. B.
Ewan PW, Clark AT: Long-term prospective observational study of patients with peanut and nut allergy after participation in a management plan.
Lancet 357:111-115, 2001. ♦♦

REVIEWS OF NOTE

Campbell D, DeKryuff RH, Umetsu DT: Allergen immunotherapy: novel approaches in the management of allergic diseases and asthma. **Clin Immunol** 97:193-202, 2000.

COMMENT: *This short analytical review contrasts conventional allergen immunotherapy--and its ability to attenuate prevailing detrimental allergic inflammatory responses--with future modalities of immunotherapy involving immunization with modified allergen, peptides of allergen, cDNA of allergen, adjuvants, cytokines, and bacterial products. Future immunotherapy may provide a long-lasting cure for allergic disease without the need for continuous treatment.*
E. J. B.

Kurup VP, Fink JN: The spectrum of immunologic sensitization in latex allergy. **Allergy** 56:2-12, 2001.

COMMENT: *Latex sensitization continues to challenge all allergists because. It's diagnosis is hampered by the lack of a standardized allergen that can be used for both skin testing and in vitro testing. The authors review the clinical spectrum of latex sensitization, its prevalence, and currently available purified allergens. The review is well-referenced and should be a very useful resource.*
E. J. B.

Gonzales R, Sande MA: Uncomplicated acute bronchitis. **Ann Intern Med** 133:981-991, 2000.

COMMENT: *This outstanding review highlights several important clinical issues for the allergist. Among the most important is that bronchial hyperresponsiveness appears to be the most important mechanism is the cough of acute bronchitis and that patients respond to inhaled albuterol. The authors also highlight the observation in most clinical trials that antibiotic use for uncomplicated bronchitis does not alter the natural history in most patients. It appears that conservative management serves our patients well in this setting.*
A. M.

Kay AB: Allergy and allergic diseases. First of two parts. **N Engl J Med** 344:30-37, 2001.
Kay AB: Allergy and allergic diseases. Second of two parts. **N Engl J Med** 344:109-113, 2001.

COMMENT: *If a textbook of allergy can be reduced to 12 pithy pages and four figures, this is it. Dr. Kay succinctly covers the array of genetic, molecular, and clinical aspects of atopic disease. For medical students, primary care residents, and even certified specialists, this is the immunology of allergy in a thoroughly digestible nutshell.*
R. J. M.

Neugut AI, Ghatak AT, Miller RL: Anaphylaxis in the United States: an investigation into its epidemiology. **Arch Intern Med** 161:15-21, 2001.

COMMENT: *This article provides an overview of published information on the incidence of anaphylaxis, emphasizing the magnitude and importance of the problem. There is a good discussion of the difficulties encountered in epidemiologic studies of anaphylaxis, which are reflected in the widely varying estimates of incidence.*
J. R. B.

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