AllergyWatch®

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

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Flu Season Is Near – Learn What Is Here!

WITH the spread of avian influenza to humans, among other factors, there is a new focus on preparing to respond to a potential influenza pandemic. In this event, an effective vaccine would likely be unavailable for the first wave of infection with the new influenza virus strain. Dr. Moscona reviews the central role of the neuraminidase inhibitors in responding to influenza epidemics and pandemics.

The four available drug options for influenza prevention or treatment are the adamantane drugs (amantadine and rimantadine) and the neuraminidase inhibitors zanamivir (currently in short supply) and oseltamivir. The potential for resistance limits the therapeutic value of the adamantanes. The neuraminidase inhibitors, by interfering with virus release from infected cells, can limit the spread of the influenza A virus within the respiratory tract. Viral replication peaks 24 to 72 hours after symptom onset, so treatment must start as early as possible.

Therapeutic studies of oseltamivir have shown significant reductions in duration of illness, especially if treatment is started within 12 hours. Treatment benefits have been reported in the elderly and in children as young as 1 year. These drugs also show important prophylactic effects in healthy adults and exposed children, as well as in previously vaccinated elderly or high-risk populations.

In the community, treatment with neuraminidase inhibitors is indicated when rapid laboratory tests confirm influenza infection or when typical symptoms develop--especially fever with cough. Treatment is best started within 12 hours after symptom onset, and not beyond 48 hours. Clinically based treatment may be particularly valuable for high-risk patient groups. Although vaccination remains the main preventive approach, neuraminidase inhibitors provide a useful adjunct. Pending further studies, they should not be used in infants less than 1 year old. These antiviral➤➤

CONTENTS

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

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

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drugs will play an important role in any planned response to an influenza pandemic; however, current supplies are inadequate. Careful surveillance, along with new strategies for drug production and distribution, are needed to lessen the impact of future influenza pandemics.

COMMENT: *It is widely speculated that a pandemic of influenza A is due, and may come from a strain of the avian flu in southeast Asia. There are no vaccines yet for those strains of H5Nl influenza (or for influenza B viruses), so it behooves us to be prepared to use antiviral medications. This article reviews the four licensed drugs currently available and contrasts their usefulness. You should be aware that the 2004 avian H5N1 viruses are resistant to the adamantanes but sensitive to the neuraminidase inhibitors. If that sounds like Greek to you, you'd better read this article.*
R. J. M.
Moscona A: Neuraminidase inhibitors for influenza.
N Engl J Med. 2005;353:1363-1373. ♦♦

To Prescribe or Not to Prescribe?

ONLY recently have studies looked at the morbidity associated with mild persistent asthma, and the potential benefits of treatment. Arguments for and against the use of daily inhaled corticosteroid therapy for mild persistent asthma are presented.

Dr. O'Byrne believes that patients with mild persistent asthma should receive a trial of low-dose ICS, to assess the magnitude of clinical benefit. Two recent trials have focused on this group of patients. In the OPTIMA trial, low-dose budesonide reduced the rate of severe asthma exacerbations to 0.26 per patient per year, compared with 0.77 in the placebo group. In the START trial, early intervention with ICS reduced the need for additional corticosteroid therapy, as well as the rate of severe asthma exacerbations. These studies used very safe, low doses of ICS--no more than 400 µg/d.

Dr. Boushey questions whether the benefits justify the costs of ICS therapy for mild persistent asthma. In the IMPACT study, regular budesonide showed some benefits, including improvement in prebronchodilator FEV_1, reduced bronchial reactivity, and increased symptom-free days. However, there was no advantage in exacerbation rate or disease control, compared with symptom-based treatment. The author calculates that routine daily ICS treatment for mild persistent asthma would carry costs of over $2 billion per year.

In a rebuttal, Dr. O'Byrne points out that regular ICS treatment yields consistent benefits in pulmonary function, symptoms and functioning, and inflammation. He questions the IMPACT trial's ability to show an effect on exacerbation rate. Dr. Boushey counters that the assembled data strongly support a symptom-based approach to anti-inflammatory treatment.

The question of whether regular ICS treatment is justified for patients with mild persistent asthma remains open to debate. A large clinical trial is needed to compare daily low-dose ICS with as-needed corticosteroid treatment under "real-world" conditions, focusing on patients managed in primary care.

COMMENT: *This excellent "pro/con" debate between Drs. O'Byrne and Boushey highlights the issues associated with the regular use of ICS: cost to the individual patient for drugs and potential side effects vs cost to society of potential progression to more severe asthma exacerbations with a more expensive price tag. Both authors make salient points. The article is extremely provocative for those who see such patients and must make treatment decisions that are in both the short- and long-term interest of patients as well as cost-effective.*
G. D. M.
O'Byrne PM: Daily inhaled corticosteroid treatment should be prescribed for mild persistent asthma. Am J Respir Crit Care Med. 2005; 172:410-➤➤

412; and Boushey HA: Daily inhaled corticosteroid treatment should not be prescribed for mild persistent asthma.
Am J Respir Crit Care Med. 2005;172:412-414 ♦♦
(pro/con editorials, with rebuttals and concluding statement).

MOSAIC Study and the Prescription Debate

CURRENT guidelines for persistent asthma call for long-term anti-inflammatory controller therapy. The leukotriene-modifying agent montelukast is effective in controlling asthma symptoms, and may provide an alternative to inhaled corticosteroids for patients with mild asthma. The randomized, controlled Montelukast Study of Asthma in Children (MOSAIC) compared montelukast with fluticasone for treatment of mild asthma in children.

The study included 994 children, aged 6 to 14 years, meeting Global Initiative for Asthma criteria for mild, persistent asthma. One group received oral montelukast, 5 mg once daily; the other group received inhaled fluticasone, 100 µg twice daily. Treatment continued for 12 months. The main study endpoint was the percentage of asthma rescue-free days (RFDs), with a noninferiority limit of -7%--corresponding to approximately 2 RFDs per month.

Children receiving montelukast had a mean of 84.0% RFDs per month, compared to 86.7% for those receiving fluticasone. The least-squares mean difference of -2.8% was well within the specified noninferiority limit. Average percent of predicted FEV_1 increased from 88.1% to 89.0% with montelukast, compared with an increase from 88.9% to 91.7% in the fluticasone group. Both treatments were associated with significant reductions in days of β-receptor agonist use. The percentage of patients with asthma attacks was 32.2% with montelukast vs 25.6% with fluticasone. Patients in the montelukast group received more systemic corticosteroids, but final height was lower in the fluticasone group. Both treatments were well tolerated.

For children with mild persistent asthma, montelukast offers 1-year treatment outcomes comparable to those of fluticasone. The difference in the main study endpoint is less than 1 asthma RFD per month. Most secondary outcomes favor fluticasone, with the exception of final height. Both treatments are effective, compared with baseline.

COMMENT: *This study examines the option of montelukast as opposed to fluticasone in children with mild persistent asthma in a "real-world" experience. The primary endpoint was the percentage of rescue-free days and was shown to be fairly equal. As expected, the fluticasone group had greater improvements in FEV_1, days without β-receptor agonist use, and overall quality of life. The montelukast group required more oral corticosteroids and had a greater number of patients with an asthma exacerbation. The growth rate was less in the fluticasone group than in the montelukast group. This was true despite the fact that 17.8% of the montelukast group vs 10.5% of the fluticasone group required oral corticosteroids. In light of this negative impact on growth, should we then in the "real world" use montelukast as first-line therapy in children with mild persistent asthma?*
T. L. H.
Garcia MLG, Wahn U, Gilles L, et al: Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: The MOSAIC Study.
Pediatrics. 2005;116:360-369. ♦♦

Exhaled NO Predicts ICS Responsiveness

MANY patients with persistent respiratory symptoms are started on treatment with inhaled corticosteroids (ICS). An alternative to such empiric use of ICS might be some means of identifying patients who have underlying airway inflammation, and thereby are likely to have a good response to ICS therapy. Exhaled nitric oxide (FE_{NO}) was evaluated as a predictor of response to ICS in patients with undiagnosed respiratory symptoms.

The study included 52 patients referred for evaluation of persistent respiratory symptoms. Patients underwent a fixed sequence of tests, including FE_{NO} measurement. They then underwent 4 weeks of treatment with inhaled placebo, followed by a 4-week trial of treatment with inhaled fluticasone, 500 µg/d. Exhaled NO and other test results were compared as predictors of response to fluticasone. Assessment of ICS response was based on international guidelines, using data on symptoms, peak flow measurements, spirometry, and airway responsiveness to adenosine.

Twenty-seven patients met criteria for a diagnosis of asthma. This included 88% of patients in the highest tertile of FE_{NO}, greater than 47 ppb; 39% in the middle tertile, 15 to 47 ppb; and 29% in the lowest tertile, less than 15 ppb. Regardless of diagnosis, patients in the highest tertile of FE_{NO} had a greater response to ICS. As a predictor of ICS response, FE_{NO} had consistently higher area under the curve values than the other pretreatment variables studied: FEV_1% predicted, bronchodilator reversibility, bronchial hyperresponsiveness to methacholine, and peak flow variation.

Exhaled nitric oxide predicts response to ICS in patients with persistent respiratory symptoms. A cut point of 47 ppb offers maximal predictive accuracy. The predictive value of FE_{NO} measurement will depend on the definition of ICS responsiveness.

COMMENT: *Exhaled NO has been touted as a noninvasive indicator of airway inflammation. It has also been proposed that the best responders to ICS use are those with eosinophilic airway inflammation, for which FE_{NO} is used as a surrogate marker. This study sought to determine whether elevated FE_{NO} could also serve as a predictor of ICS responsiveness, defined by both* ➤➤

and subjective measures. In this study, if the baseline FE_{NO} was greater than 47 ppb, the patient had a high likelihood of responding to ICS by many of several measures. Exhaled NO measurement has potential therapeutic value.
G. D. M.
Smith AD, Cowan JO, Brassett KP, et al: Exhaled nitric oxide: a predictor of steroid response.
Am J Respir Crit Care Med. 2005; 172:453-459. ♦♦

Exhaled NO Reflects Severity and Location Too!

MUCH of the inflammation occurring in asthma may be located in the peripheral areas of the lung. Fractional exhaled nitric oxide (FE_{NO}) and 8-isoprostane are molecular markers of airway inflammation and oxidative stress. These two inflammatory markers were evaluated as indicators of inflammatory dysfunction of the small airways in patients with asthma.

The cross-sectional study included 16 nonsmoking patients with mild asthma: mean age 23 years, each with an FEV_1% predicted greater than 80%. Assessments included FE_{NO} measurement by chemiluminescence and measurement of 8-isoprostane concentration in exhaled breath condensates by enzyme-linked immunosorbent assay. The results were evaluated for their ability to predict small airways function, assessed by the single breath nitrogen test.

The patients had a median FE_{NO} level of 30.4 ppb and a median corrected 8-isoprostane concentration of 2.2 pg/mL. On assessment of the single breath washout curve, the mean slope of phase III (δN_2) was 1.1%; mean value for closing volume as a percentage of vital capacity (CV/VC) was 8.6%. The FE_{NO} measurement was significantly and positively correlated with δN_2, although not with FEV_1% predicted. The 8-isoprostane concentration was positively correlated with CV/VC and inversely correlated with FEV_1% predicted.

As markers of airway inflammation and oxidative stress, FE_{NO} and 8-isoprostane are significantly correlated with indicators of small airways function in mild asthma. The findings are consistent with previous reports of changes in peripheral lung function in asthma patients. More study is needed to define associations of FE_{NO} and 8-isoprostane with small airway morphology and inflammation.

COMMENT: *Fractional exhaled NO and 8-isoprostane are considered biomarkers of inflammation and oxidative stress. These investigators examined the relationship of FE_{NO} and 8-isoprostane in exhaled air with small airways function, as measured by the single breath nitrogen test. They found these markers to be associated with small airway involvement in patients with mild asthma. The study highlights the relevance of small airways even in mild asthma, and adds some excellent biomarkers to our armamentarium for evaluation of small airways. It would be interesting to apply these techniques to patients with a history of asthma thought to be in "remission." The tests may also serve as screening studies in healthy workers exposed to industrial pollutants. (See* AllergyWatch *May/June 2005, pg 6.)*
E. J. B.
Battaglia S, den Hertog H, Timmers MC, et al: Small airways function and molecular markers in exhaled air in mild asthma.
Thorax 60:639-644, 2005. ♦♦

Allergic Sensitization Is on the Rise

IN the United States and worldwide, the prevalence of asthma has increased significantly for several years. Allergic sensitization may be an important contributor to this trend. Data from consecutive National Health and Nutrition Examination Surveys (NHANES) were used to analyze trends in the prevalence of positive skin test results in the United States from the mid-1970s to the mid-1990s.

For NHANES III (1988-94), skin test responses to 10 common allergens and 2 controls were assessed in all subjects aged 6 to 19 years and in a random one-half sample of those aged 20 to 59 years. Wheal measurements were used to define positive responses to allergen. Rates and predictors of positive skin test results were analyzed, and compared to those from NHANES II (1976-80).

The prevalence of positive skin test results in NHANES III was 54.3%. Dust mite was the most common allergen, with positive results in 27.5% of patients, followed by rye, 26.9%; ragweed, 26.2; cockroach, 26.1%; grass, 18.1%; cat, 17.0%; thistle, 15.2%; oak, 13.2%; *Alternaria* mold, 12.9%; and peanut, 8.6%.

Median number of positive tests per affected patient was 3.0. Factors associated with positive skin tests included age 20 to 29 years, male sex, minority race/ethnicity, western region, living in an older home, and low serum cotinine. Of the six allergens tested in both surveys (cockroach and peanut were not tested in NHANES II), rates of positive results increased by 2- to 5-fold. The rate of positive responses to at least one of the six allergens increased from 21.8% in NHANES II to 41.9% in NHANES III.

Over 50% of the American population is sensitized to one or more common allergens, NHANES III data suggest. Rates of positive skin test results increased substantially from NHANES II to NHANES III. The NHANES 2005-06 study will include total and specific IgE levels and measurement of indoor allergens.

COMMENT: *The NHANES is conducted periodically here in the United States. This report presents the allergy skin test data from the two most recent surveys: NHANES II, conducted during 1976-80, and NHANES III, during 1988-94. The important findings are that more than half of the population tested positive to at least one allergen and that the prevalence for positive reactions to the most common allergens was 2.1 to 5.5 times higher in the more recent survey. Although there were some methodologic differences, it seems that these data support the premise that the U. S. prevalence* ➤➤

of allergic sensitization is increasing.
S. M. F.
Arbes SJ, Gergen PJ, Elliott L, Zeldin DC: Prevalences of positive skin test responses to 10 common allergens in the US population: results from the Third National Health and Nutrition Examination Survey.
J Allergy Clin Immunol 2005;116:377-383. ♦♦

Skin Test Devices: Which Is Fairest of Them All?

THE results of allergy skin testing have important implications for diagnosis and treatment. Several different skin test devices are available, including newer multiheaded devices that allow simultaneous administration of multiple antigens. A controlled comparison of eight different skin test devices is reported.

The study included four single-headed devices--the Greer Pick, Accuset, Sharptest, and Quintip; and four multiheaded devices--the Quintest, Quantitest, Greer Track, and Multi-Test II. In standardized fashion over 4 test days, each device was used to administer histamine and saline on the arms and backs of 13 volunteers. One trained technician performed all tests, while another technician read the results in blinded fashion. Outcomes included wheal, flare, pain, specificity, and variability.

There were significant differences in performance for all devices across all outcomes. The rate of false-negative histamine wheal reactions ranged from 0.96% to 3.8% for single-headed devices vs 3.4% to 22% for multiheaded devices. Whereas the single-headed devices showed high reproducibility, there was substantial variability between the multiheaded devices. Pain ratings were generally low, but higher for the multiheaded devices, which also produced larger skin reactions on the back. The single-headed devices produced larger reactions on the arm. Sensitivity was similar among the single-headed devices, but higher with the Multi-Test II than with other multiheaded devices.

Direct comparison finds differences in performance between various devices for allergy skin testing. The Greer Track multiheaded device is singled out as having the lowest performance on several outcomes. Otherwise, the clinical significance of the differences is unclear. Allergists should choose a device based on their clinical setting, while ensuring proper training of technicians.

COMMENT: *A chain is only as strong as its weakest link. In allergy skin-prick testing, the results depend on the device used to introduce the allergen into the skin. An assortment of such devices are available to the clinical allergist, some multiheaded and some single-headed. This article reports the advantages and disadvantages of eight skin test devices studied under very standardized conditions.*
R. J. M.
Carr WW, Martin B, Howard RS, et al: Comparison of test devices for skin prick testing.
J Allergy Clin Immunol. 2005;116:341-346. ♦♦

The Evolution of EIB Is Multifactorial

AIRWAY hyperresponsiveness (AHR) to histamine results from direct effects on the airways, while exercise-induced bronchospasm (EIB) is related to release of mediators from inflammatory cells. Although AHR and airway inflammation are both part of asthma, they may also be seen in asymptomatic subjects. The adult outcomes of children with asymptomatic AHR to histamine or EIB were assessed in a long-term follow-up study.

Subjects were identified from a random sample of 281 Danish children, aged 7 to 17 years in 1986. Baseline assessments included skin prick testing, pulmonary function tests, histamine challenge, and exercise testing. Except for exercise testing, the assessments were repeated at a 12-year follow-up evaluation in 1998.

At baseline, 22% of subjects had AHR to histamine, 12% had EIB with a 10% decrease in FEV_1 from baseline (EIB_{10}), and 4% had EIB with a 15% decrease from baseline (EIB_{15}). The overall rate of AHR to histamine and/or EIB was 29%. These conditions were unrelated to skin prick test results, allergic symptoms, or lung function.

The rate of current asthma at follow-up was 22% in subjects who originally had AHR to histamine and 30% in those who had EIB_{15}, compared to 5% in those who originally had EIB_{10}. Asthma was reported sometime during follow-up by 38% of subjects with AHR to histamine, compared to 11% without. The rate of reported asthma was 30% for patients with EIB_{15} vs 15% for those with EIB_{10}. For subjects with AHR to histamine at baseline, independent risk factors for asthma were parental history of asthma, personal history of rhinitis and/or dermatitis, and having pets in childhood. No significant risk factors were identified in the EIB groups.

Children with asymptomatic AHR to histamine or EIB are at increased risk of asthma in adulthood. The association is stronger for AHR to histamine; within this group, parental and personal history of allergic disease and pet ownership are significant risk factors. The lower predictive value of EIB may reflect the perception of bronchoconstriction, the severity of inflammation, and the presence of triggering factors.

COMMENT: *The natural history of EIB and asymptomatic BHR appears to depend on multiple factors. The authors provide further evidence that an atopic genetic background and the presence of other atopic comorbidities are important risk factors for persistent asthma in adulthood. The answer to the question of "Will my child outgrow this?" appears to be a solid "It depends!"*
A. M.
Porsbjerg C, von Linstow M-L, Ulrik CS, et al: Outcome in adulthood of asymptomatic airway hyperresponsiveness to histamine and exercise-induced bronchospasm in childhood.
Ann Allergy Asthma Immunol. 2005;95:137-142. ♦♦

Can We Predict the Severity of Future Peanut Reactions?

THE best way of predicting the severity of allergic reactions to foods remains unclear. The predictive value of reactions to food challenges, and their relationship to the severity of previous reactions in the community, has not been established. A scoring system was developed to predict the response to double-blind placebo-controlled food challenge (DBPCFC) in patients with peanut allergy.

The study included 40 patients with peanut allergy, defined by clinical history and skin prick testing. Clinical reactivity was evaluated using a questionnaire, which included assessment of the severity of the patients' last two allergic reactions, along with an estimate of the allergen dose causing the reactions. Evaluation also included skin prick testing, peanut-specific IgE measurement, and low-dose DBPCFC.

Median wheal diameter was 9 mm and median specific IgE level 71.85 kU/L. The severity of the patient's most recent reaction to peanut exposure in the community, assessed by the questionnaire, was only weakly correlated with the reaction to DBPCFC. The score for community reactions was not significantly related to the results of peanut-specific IgE measurement or skin prick testing. However, the specific IgE level was correlated with the DBPCFC challenge score, which considered the allergen dose.

History of asthma was not directly related to the eliciting dose of allergen or the challenge score. However, both the peanut-specific IgE level and the challenge score were higher in asthmatic patients.

Patient reports of the severity of allergic reactions to peanut in the community are not strongly related to the results of DBPCFC. Peanut-specific IgE levels do predict the severity of reactions to food challenge, when the allergen dose is taken into account. The latter association appears stronger in nonasthmatic patients.

COMMENT: *With the increasing prevalence of peanut allergy, we all struggle with trying to predict the severity of future reactions to peanut. These authors used a new scoring system that combines dosage and symptom grades to give an overall severity score for each peanut reaction. The peanut-specific IgE level, but not the reported historical reaction severity or the peanut skin test wheal diameter, predicted the severity of clinical reactivity in DBPCFC.*
S. A. T.

Hourihane JO'B, Grimshaw KEC, Lewis SA, et al: Does severity of low-dose, double-blind, placebo-controlled food challenges reflect severity of allergic reactions to peanut in the community?
Clin Exp Allergy. 2005;35:1227-1233. ♦♦

"Toxic Mold" Is a Societal Phenomenon!

THE media, the Internet, and other sources have contributed to public concern over reputed adverse health effects of exposure to molds. Meanwhile, the scientific basis of inhalational mold toxicity remains to be demonstrated. The results of evaluation for mold-induced illness in 50 patients are presented.

The retrospective study included 82 consecutive patients referred for evaluation of symptoms attributed to mold exposure at home or work. Fifty patients had complete data for analysis, including laboratory tests, chest imaging studies, and indoor air quality studies.

The patients were 36 females and 14 males, mean age 34 years--15 patients came from 5 families. The average number of symptoms was more than 8 per patient, including upper respiratory symptoms in 80% of patients, lower respiratory symptoms in 94%, systemic symptoms in 74%, and neurocognitive symptoms in 84%.

In 30 patients the symptoms were attributable to causes other than mold exposure, including a wide range of infectious, allergic, psychiatric, and other contributing conditions. Convincing evidence of mold allergy was found in 2 patients. One patient with fear-induced somatic symptoms received a diagnosis of "toxic agoraphobia." In 17 patients, symptoms seemed to be related to mild, transient irritation from mold exposure, with no objective link to mold and no permanent impairment.

Clinical evaluation of patients with symptoms attributed to mold exposure finds no convincing evidence of a toxic mold syndrome. Most patients have other conditions or contributing causes. In other patients with a psychogenic predisposition, transient aeroirritation may gradually transform into chronic symptoms related to nonspecific irritants, similar to those described in "sick building syndrome" or "idiopathic chemical intolerance." The authors propose that toxic mold syndrome represents a "societal phenomenon" rather than a disease.

COMMENT: *The increasing number of patients reporting symptoms or medical conditions related to suspected mold exposure requires that physicians be knowledgeable concerning the effects of mold on human health. The clinical importance is further dramatized by the recent flooding along the Gulf Coast, with concern about mold growth in existing buildings. The authors of this paper have extensive clinical experience in evaluating patients reporting symptoms presumed to result from mold inhalation. The article presents the current state of the art related to toxic mold exposure. Alternative diagnoses were made in the majority of patients. It is proposed that subjects with ill-defined symptoms purported to be mold-related would be better categorized as having a "societal phenomenon" rather than a disease.*
D. K. L.

Khalili B, Montanaro MT, Bardana EJ: Inhalational mold toxicity: fact or fiction? A clinical review of 50 cases.
Ann Allergy Asthma Immunol. 2005;95:239-246. ♦♦

Shared Allergenicity Among Edible Nuts

TREE nuts and peanuts are common causes of serious allergic reactions. Although many patients are sensitized to more than one type of tree nut, questions remain about the degree of cross-reactivity among nut antigens. This study assessed cross-reactivity among different types of tree nuts, and between tree nuts and peanuts.

Serologic cross-reactivities were assessed, controlling for primary nut sensitization, for walnut, pecan, hazelnut, cashew, Brazil nut, pistachio, and almond, and peanut. In addition to human specific IgE enzyme-linked immunosorbent assay inhibition, the investigators used single-nut rabbit antisera techniques, including double immunodiffusion, crossed immunoelectrophoresis (CIE), crossed-line immunoelectrophoresis, and CIE with intermediate gel.

Peanut antigen did not generally cross-react with tree nut antigens, but there was evidence of peanut-pistachio and peanut-walnut cross-reactions. Among the tree nuts, cross-reactivity was strong for walnut, pecan, and hazelnut and moderate for hazelnut, cashew, Brazil nut, pistachio, and almond. On CIE, cashew and pistachio seemed to have the strongest cross-reactivity. There was evidence of weak cross-reactivity between rye grass and tree nuts and between peanut and grass.

Moderate to strong cross-reactivities are noted among tree nuts, mainly within members of botanical families. Cross-reactions do occur between families but are not as strong. Although peanut does not cross-react with most tree nuts, some cross-reactions are observed.

COMMENT: *This report addresses an important clinical problem in both pediatric and adult allergy. The authors confirm previous observations that there is little but definite cross-reactivity between peanut and tree nuts and significant but incomplete cross-reactivity among the tree nuts. The bottom line remains that history and skin testing remain necessary to distinguish relevant sensitivity.*
A. M.

Goetz DW, Whisman BA, Goetz AD: Cross-reactivity among edible nuts: double immunodiffusion, crossed immunoelectrophoresis, and human specific IgE serologic surveys.
Ann Allergy Asthma Immunol. 2005;95:45-52.

The Hygiene Hypothesis Under Siege

ALTHOUGH allergic sensitization generally becomes apparent after age 3, the immunologic process leading to allergic disease probably starts earlier. Studies have suggested that early exposure to endotoxin may protect against the development of allergy. This prospective study examined the effects of endotoxin exposure in high-risk infants on peripheral blood mononuclear cell responses to allergen stimulation at age 2 to 3.

The analysis included 96 children with a parental history of asthma or allergy. All had available data on endotoxin in home dust samples at age 2 to 3 months and on PBMC responses to allergen and mitogen stimulation at age 2 to 3 years. The PBMC measurements included proliferative and cytokine responses to cockroach, dust mite, and cat allergens and to the nonspecific mitogen phytohemagglutinin.

Geometric mean endotoxin level in family room dust was 95 EU/mg. Children with higher exposure to endotoxin in infancy had reduced interleukin (IL)-13 responses to cockroach, dust mite, and cat allergen, but not in response to phytohemagglutinin. The relationship was strongest for cockroach allergen. Endotoxin exposure was unrelated to interferon-γ, tumor necrosis factor-α, or IL-10 responses to allergen or mitogen.

For children with a family history of allergic disease, higher levels of endotoxin exposure in infancy are related to reduced lymphocyte responses to allergenic stimulation. The observed reduction in IL-13 may be an important early event in the protective effect of endotoxin exposure.

COMMENT: *In an effort to test the hygiene hypothesis, these Boston researchers measured dust endotoxin levels in homes of a cohort of infants at age 2 to 3 months and tested a variety of immunologic parameters at age 2 to 3 years. Children with higher dust endotoxin exposure had reduced IL-13 levels in response to various allergens, but not to mitogen stimulation. This suggests a specific endotoxin-related downregulation of the Th2 cytokine IL-13, which can mediate IgE isotype switching. Although there was only a single measure of endotoxin in the children's homes, the data suggest that exposure to endotoxin in infancy decreases the risk of allergic disease in later childhood.*
S. M. F.

Abraham JH, Finn PW, Milton DK, et al: Infant home endotoxin is associated with reduced allergen-stimulated lymphocyte proliferation and IL-13 production in childhood.
J Allergy Clin Immunol. 2005;116:431-437. ♦♦

LONG-term follow-up studies are needed to test the theory that early infections protect against the development of allergic disease. The relationship between respiratory infections during infancy and allergic disease and sensitization later in childhood was assessed in a birth cohort study.

The study included 2,549 children enrolled in the Oslo Birth Cohort at birth in 1992-93. Data on health outcomes, including physician-diagnosed asthma and allergic rhinitis, were gathered at regular intervals up to 10 years of age. Early respiratory infections--including lower respiratory tract infections, otitis media, and croup through the first 12 months of life and colds during the first 6 months--were evaluated as predictors of allergic disease outcomes. Attending child care and having older siblings were evaluated as indirect measures of exposure to infectious pathogens.

At age 10, 11.5% of children had received a physician diagnosis of asthma and 14.1% had been diagnosed ➤➤

with allergic rhinitis. Skin prick tests, performed in 1,740 children, were positive in 24% of children. Of this group, 10.5% were diagnosed with asthma and 14.3% with allergic rhinitis.

Children with lower respiratory infections and croup during the first year were more likely to be diagnosed with asthma: adjusted odds ratios were 2.1 and 2.3, respectively. Asthma rates were also higher for children with early otitis media and colds, although these relationships were not significant. Associations with allergic rhinitis were generally weaker, but there was a significant positive association with otitis media. Birth order and child care attendance had no effect on either form of allergic disease. Positive skin prick test results were associated with a small increase in the risk associated with otitis media during infancy. The link between infections and asthma was stronger for children with more than one type of infection during infancy.

Respiratory infections during infancy are associated with higher rates of asthma by age 10. Early infections may affect the lower respiratory tract in a way that increases the risk of asthma, with differing effects in children with vs without atopy. The results contrast with the suggestion that early-life respiratory infections protect against allergic disease.

COMMENT: *The most recent Norwegian study could not substantiate the hygiene hypothesis. In this study, early-life respiratory infections did not appear to protect against the development of atopic diseases. However, the jury is still out, as this study was done in a country with very few large families and limited entry into a child care settings before age 1. A repeat of this study in the United States might be more conclusive.*
T. L. H.

Nafstad P, Brunekreef B, Skrondal A, Nystad W: Early respiratory infections, asthma, and allergy: 10-year follow-up of the Oslo Birth Cohort.
Pediatrics. 2005;116:e255-262. ♦♦

Toxic MBP Is Implicated in CRS

CHRONIC rhinosinusitis (CRS) is a common condition with a major impact on quality of life and large economic costs. It is associated with persistent eosinophilic inflammation causing epithelial damage. Among the many cytotoxic proteins associated with eosinophil granules is major basic protein (MBP), deposits of which have been shown to localize to areas of epithelial damage. This study examined the contribution of eosinophil MBP to tissue damage in CRS.

The investigators carefully collected samples of mucus attached to tissue from 22 patients, mean age 47 years, undergoing endoscopic sinus surgery for CRS. Immunofluorescence staining with digital analysis was performed to ascertain the area covered by MBP. Staining intensity was assessed as an indicator of MBP concentration.

Intact eosinophils were detected in all surgical specimens. There was little evidence of eosinophil degranulation in the form of diffuse extracellular MBP deposition. However, the mucus component of each specimen showed diffuse distribution of MBP, including extracellular MBP deposits within eosinophil clusters. Concentrations of MBP in mucus were estimated at 11.7 µg/mL--more than sufficient to cause epithelial damage from the luminal side.

Major basic protein is diffusely present in the epithelium of patients with CRS. Release of this cytotoxic protein by eosinophil clusters could account for the epithelial damage associated with CRS, thus predisposing to secondary bacterial infections. Treatments to address the underlying inflammation of CRS might be more effective than treatments directed against the secondary infections.

COMMENT: *Chronic rhinosinusitis is an intensely inflammatory and destructive disease of the paranasal sinuses. Its cause is much debated, and the mediation of the inflammation is the subject of this study. The authors show that MBP is heavily deposited in the mucus adherent to the nasal epithelium, in concentrations above those found in the actual tissues and that are highly toxic to cells. It is likely that the cause of the inflammation and erosion is the eosinophil-derived MBP external to the tissues. This gives support to the clinical indication of nasal lavage in patients with CRS.*
R. J. M.

Ponikau JU, Sherris DA, Kephart GM, et al: Striking deposition of toxic eosinophil major basic protein in mucus: implications for chronic rhinosinusitis.
J Allergy Clin Immunol. 2005;116:362-369. ♦♦

Histamine-Releasing Factors and Chronic Urticaria

MANY patients with idiopathic spontaneous chronic urticaria (CU) have a skin reaction on autologous serum skin testing (ASST), consistent with the presence of histamine-releasing factors (HRFs). About half of patients with a positive ASST show functional autoantibodies on functional basophil assays. Immunoassays show autoantibodies against the IgE or high-affinity IgE receptor (FcεRI), along with basophil and mast cell histamine release (HR). A new basophil HR assay was evaluated in patients with CU, including comparison with the results of ASST.

The HR-Urticaria test was first evaluated in a well-characterized group of 28 patients with CU, 16 of whom had a positive ASST. In this test, healthy donor white blood cells containing 1% to 2% basophils were incubated with patient sera in the presence of interleukin-3, with histamine measured using the glass fiber method. Using the ASST as the gold standard and an HR cutoff value of over 16.5%, the HR-Urticaria test offered sensitivity and specificity of 75%. None of the subjects in three control groups--with atopic dermatitis, birch allergy, or no allergy--had a positive result.

The test was then evaluated in an unselected sample of 873 referral patients with CU. The frequency of positive results was about 35% for both male and female adults. However, the sample included twice as ➤➤

many females as males.

The HR-Urticaria test offers a new cellular assay for the detection of functional endogenous HRFs in patients with CU. It is sensitive and specific, compared with the ASST. Roughly one-third of unselected CU patients show evidence of sera-inducing HR.

COMMENT: *These investigators compare a standardized laboratory test using basophils for HR against ASST as the gold standard of endogenous histamine-releasing activity in unselected patients with chronic urticaria. Their assay was able to distinguish between patients with and without functional HR factors with high sensitivity and specificity. Additional studies will be required to explore whether other factors (besides anti-IgE or anti-FCεR1) are involved in the HR process--eg, cytokines, C3a or C5a, etc.*
E. J. B.

Platzer MH, Grattan CEH, Poulsen LK, Skov PS et al: Validation of basophil histamine release against the autologous serum skin test (ASST) and outcome of serum-included basophil histamine release studies in a large population of chronic urticaria patients.
Allergy. 2005;60:1152-1156. ♦♦

In Vitro Assay for Aspirin Sensitivity

THE diagnosis of aspirin sensitivity poses a clinical challenge. The authors have previously found that nasal polyp epithelial cells and peripheral blood leukocytes (PBLs) from patients with aspirin sensitivity generate 15-hydroxyeicosateraenoic acid (15-HETE). An assay to detect 15-HETE release from PBLs was evaluated as a test for aspirin sensitivity among asthma patients.

The study included 43 aspirin-sensitive and 35 aspirin-tolerant patients with asthma and rhinosinusitis, along with 17 healthy controls. The "aspirin-sensitive patients identification test" (ASPITest) was performed by incubating PBLs with aspirin, 2 to 200 μM and measuring 15-HETE release in cell supernatants using a competitive enzyme-linked immunosorbent assay.

In the absence of aspirin, levels of 15-HETE from unstimulated PBLs were similar across groups. However, when incubated with 200 μM of aspirin, PBLs from aspirin-sensitive patients showed over a 4-fold increase in 15-HETE generation, compared with little or no change among aspirin-tolerant patients or healthy controls. Some but not all of the aspirin-sensitive patients also had a significant increase in 15-HETE on incubation with naproxen. On receiver operating curve analysis, the ASPITest was 83% sensitive in confirming aspirin sensitivity, with positive and negative predictive values of 79% and 86%, respectively.

By detecting 15-HETE generation by PBLs in the presence of aspirin, the ASPITest appears useful in the diagnosis of aspirin sensitivity in asthma patients. Further study is needed to confirm the clinical value of this test.

COMMENT: *The diagnosis of aspirin sensitivity depends on a supportive history and placebo-controlled challenge test. The latter is time-consuming and requires special equipment. These investigators found an assay to measure 15-HETE from PBL to be both sensitive and specific for ASA sensitivity. Naproxen induced a significant increase in 15-HETE in only a portion of aspirin-sensitive asthmatics. Additional studies will be needed to determine the reliability of ASPITest in a larger study group.*
E. J. B.

Kowalski M, Ptasinska A, Jedrzejczak M, et al: Aspirin-triggered 15-HETE generation in peripheral blood leukocytes (PBL) is a specific and sensitive Aspirin-Sensitive Patients Identification Test (ASPITest).
Allergy. 2005;60:1139-1145. ♦♦

Assessing Cephalosporin Allergy

CEPHALOSPORINS induce a significant number of cutaneous reactions, along with a low but rising rate of anaphylactic reactions. In the absence of a specific diagnostic test, skin testing for cephalosporin allergy is commonly done using individual free drugs. A specific approach to diagnosis of immediate reactions to cephalosporin antibiotics is reported.

The study included 76 patients being evaluated for immediate reactions to cephalosporins, most commonly ceftriaxone, cefotaxime, and ceftazidime. Each patient underwent skin tests and specific IgE measurement for the implicated drugs plus cefaclor; testing for penicillins was performed as well. Challenges and retests were performed, including tests for responses to other cephalosporins, in some patients.

Initial skin tests or specific IgE measurement led to a diagnosis of IgE-mediated penicillin and/or cephalosporin allergy in 83% of patients. Further tests in 8 of 13 patients increased the rate of positive skin test results from 76% to 86% and the rate of sepharose-radioimmunoassay positivity from 67% to 74%. A final diagnosis of IgE-mediated hypersensitivity was made in 70 patients, after retesting in 7.

Through the combination of skin tests and CAP-FEIA, 3 patients were classified as testing positive for penicillin allergy only, 17 to both cephalosporin and penicillin, 24 to multiple cephalosporins, and 21 to just the suspected cephalosporin. The remaining 11 patients had negative results on skin tests and CEP-FEIA, including 5 with positive results on sepharose-radioimmunoassay.

Most patients with immediate reactions to cephalosporins have IgE-mediated allergy. Diagnostic workup should include cephalosporin skin tests and sepharose-radioimmunoassay. Since cephalosporin hypersensitivity may be transient, further testing including challenge studies should be performed in patients with initially negative results.

COMMENT: *To date only the penicillin skin test reagent panel is well validated for confirming or ruling out IgE-mediated drug allergy. This study explores the utility of testing in patients with a reported history of cephalosporin reactions. In addition to* ➤➤

cephalosporin skin tests using nonirritant concentrations of the drugs in question, serologic tests using both ImmunoCap and sepharose-radioimmunoassay techniques were also helpful. This work may help pave the way for establishing validated methods for assessing cephalosporin allergy.
S. A. T.
Romano A, Guéant-Rodriguez R-M, Viola M, et al: Diagnosis immediate reactions to cephalosporins.
Clin Exp Allergy. 2005;35:1234-1242. ♦♦

SLIT Found Safe in 3-Year-Olds

SUBLINGUAL-swallow immunotherapy (SLIT) has been suggested as an attractive option for pediatric use, but few studies have examined the safety of SLIT in children. The minimum age for starting immunotherapy in children is unclear--some reports have discouraged its use before age 5 years. This pilot study assessed the safety of SLIT in young children.

The Italian study included 65 children, median age 60 months, receiving SLIT for asthma, rhinoconjunctivitis, or both. Patients went through an 11-day buildup phase to achieve a peak dose of 300 IR (index of reactivity), followed by a maintenance phase dose of 300 IR three times weekly. House dust mite and grass pollen were the most common allergens administered. Adverse reactions and treatment changes were monitored, including comparison of differences between age groups: 38 to 60 months vs 61 to 80 months.

Eleven children had a total of 13 adverse reactions: 6 during the buildup phase and 7 during the maintenance phase. Urticaria was the most common symptom; others included orolabial itching and gastrointestinal symptoms. All reactions were mild to moderate, and none required stopping SLIT. More than three-fourths of the reactions occurred in children receiving dust mite SLIT. Risk of adverse events was similar in the two age groups.

This experience supports the safety of high-dose SLIT in young children. The risk of adverse reactions appears no different for children aged 3 to 5 years vs those aged 5 to 7 years. The authors call for efficacy trials of SLIT in children aged 5 years or younger.

COMMENT: *This observational study shows that sublingual immunotherapy is safe even in subjects less than 5 years of age. Safety and acceptability make SLIT very attractive to parents of young children. However, until we have data on efficacy and long-term benefits in young children, SLIT remains an unproven treatment modality.*
D. K. L.
Fiocchi A, Pajno G, La Grutta S, et al: Safety of sublingual-swallow immunotherapy in children aged 3 to 7 years.
Ann Allergy Asthma Immunol. 2005;95:254-258. ♦♦

CLINICAL TIDBITS

Sodium Hypochlorite Kills Mold

THERE is a need for some economical approach to remediating mold contamination in buildings. Two solutions containing sodium hypochlorite--a 1:16 dilution of bleach and the household cleaner Tilex--were evaluated as treatments for mold-contaminated building materials. Both solutions effectively killed *Aspergillus fumigatus* in culture and on contaminated materials (eg, drywall and plywood). The solutions also reduced the allergenicity of *A. fumigatus*, not only on enzyme-linked immunosorbent assay but also on skin prick testing of allergic subjects. Sodium hypochlorite solutions can be a useful aid to mold remediation.

COMMENT: *Household bleach containing sodium hypochlorite has been used to disinfect surfaces and kill molds for over a century. These researchers found that sodium hypochlorite sprayed on common building construction materials contaminated with mold not only effectively killed the mold, but also reduced its allergenicity. With increasing concerns about mold contamination in buildings, it is helpful to have proven methods to advise our patients in remediating indoor mold.*
S. M. F.
Martyny J, Harbeck RJ, Pacheco K, et al: Aerosolized sodium hypochlorite inhibits viability and allergenicity of mold on building materials.
J Allergy Clin Immunol. 2005;116:630-635. ♦♦

Saline Rinse Found Effective for SAR

NASAL lavage with hypertonic saline solution has been suggested as a helpful treatment for chronic sinusitis. This randomized trial evaluated the use of nasal rinsing with hypertonic saline solution in 44 children with seasonal allergic rhinoconjunctivitis (SAR) from grass pollen, mean age 9 years. Treated patients used a spray bottle to perform intranasal rinsing three times daily; controls received no treatment. The treatment group had reductions in mean weekly symptom score, significant by the sixth week. Oral antihistamine use was markedly reduced. Nasal rinsing with hypertonic saline is a well-tolerated and effective adjunct for treatment of pediatric SAR.

COMMENT: *With rising costs associated with prescription medications and our patients' interest in "natural" treatments, nonpharmaceutical approaches are increasingly gaining favor. Nasal saline irrigation is a safe, inexpensive, and simple treatment that in this study was effective for children with SAR. There was no placebo arm for the study, although placebo controls are not practical when evaluating nasal saline efficacy. Future studies comparing the efficacy of saline irrigation to regularly dosed rhinitis medications would be helpful.*
S. A. T.
Garavello W, Di Berardino F, Romagnoli M, et al: ➤➤

Nasal rinsing with hypertonic solution: an adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis.
Int Arch Allergy Immunol. 2005;137:310-314.

Consider Diaper Dye Dermatitis!

MOST babies with diaper dermatitis have a simple irritant contact dermatitis. The authors report 5 infants with persistent diaper rash. Some of the patients had a history of atopic dermatitis. In all 5 reported cases, the location of diaper rash corresponded to an area of dye on disposable diapers or training pants. All patients improved after switching to dye-free diapers. Patch testing performed in 2 patients showed positive responses to various dyes. The authors conclude that these cases likely represent sensitization reactions to disperse dyes used in disposable diapers.

COMMENT: *I must admit in my clinical practice I have seen an increase in referrals for diaper dermatitis. These patients are referred for evaluation of possible atopic dermatitis or immunodeficiency manifested as presumed recurrent candidiasis. Often I have concluded that it is neither condition, but offered no plausible explanation. This study enlightened me as to the possibility of allergic contact dermatitis caused by the overuse of blue, pink, and green dyes in diapers. The authors used patch testing to confirm the diagnosis. In clinical practice, the use of dye-free diapers may be more practical when one suspects diaper dye dermatitis.*
T. L. H.
Alberta L, Sweeney SM, Wiss K: Diaper dye dermatitis.
Pediatrics. 2005;116:e450-e452.

Aggregated Vaccine Exposure Found to Be Safe

THERE is concern over the possibility that multiple-antigen vaccines or aggregated vaccine exposure could cause immune system "overload," leading to an increased risk of infections other than those targeted by the vaccines. Rates of such nontargeted infections were evaluated in a cohort of more than 805,000 Danish children born from 1990 through 2001. Of more than 84,000 hospitalizations for infectious disease, 42 possible associations were identified. Just one association was significant: between *Haemophilus influenzae* type b vaccine and acute upper respiratory infection, rate ratio 1.05. Children receiving a higher number of vaccines showed no increase in infectious diseases. Multiple-antigen vaccines and aggregated vaccine exposure do not appear to increase the risk of nontargeted infectious diseases in children.

COMMENT: *Allergists/immunologists should be able to provide the latest information and best advice to patients concerning a variety of immunologic therapies, including the original immunomodulator--vaccination. We should be well-versed on all potential adverse effects and be able and willing to handle questions from patients who are influenced by misinformation. This very large cohort study demonstrates that there are no adverse immunologic effects of multiple vaccinations.*
D. K. L.
Hviid A, Wohlfahrt J, Stellfeld M, Melbye M: Childhood vaccination and nontargeted infectious disease hospitalization.
JAMA. 2005:294:699-705. ♦♦

Vaccination Protects Adults from Pertussis

EARLIER this year, two tetanus toxoid, reduced diphtheria toxoid, reduced acellular pertussis, adsorbed (Tdap) vaccines were approved by the U.S. Food and Drug Administration. One vaccine, Adacel, is approved for adolescents and adults, aged 11 through 64; the other, Boostrix, is approved for children and adolescents aged 10 through 18. These vaccines play a central role in new recommendations for global control of pertussis. The author believes that a program of Tdap immunization--beginning in the preteen years and continuing every 10 years in adulthood--is the most promising approach not only to controlling *Bordetella pertussis* in adolescents and adults, but also to preventing transmission to unvaccinated infants.

COMMENT: *For those who are concerned about the risk of pertussis infection in adults, as I am, this commentary by a well-known pediatric infectious disease specialist is worth reading! We now have safe, FDA-approved diphtheria-tetanus-acellular pertussis vaccines available for use in adolescents and adults. Since* B. pertussis *infection is endemic in the United States, I hope that patients will take advantage of this opportunity to be protected--adults for themselves and parents for their adolescents or younger children.*
J. A. A.
Cherry JD: Pertussis vaccines for adolescents and adults.
Pediatrics. 2005;116:755-756.

Open Sesame!

SESAME is listed among the top allergenic foods in Europe and Canada, but not in the United States. A literature search suggested that reports of sesame allergy have increased since the 1950s, with most reports coming from the developed world. Some studies described immediate hypersensitivity, often in the form of anaphylaxis. These patients had positive results on skin prick testing and/or IgE measurement, with some cross-reactivity to other foods. Some patients with negative allergy test results reacted on oral challenge ➤➤

testing. Other studies mentioned delayed hypersensitivity reactions to lignin-like compounds in sesame oil, often appearing as contact allergic dermatitis. Sesame is notable for its ability to trigger immediate, IgE-mediated reactions as well as delayed, cell-mediated responses.

COMMENT: *This is a brief but meaningful review of an emerging problem that is unlikely to be on most practitioners' radar. The authors have reviewed the importance of systemic and cutaneous exposure and hypersensitivity.*
A. M.
Gangur V, Kelly C, Navuluri L: Sesame allergy: a growing food allergy of global proportions?
Ann Allergy Asthma Immunol. 2005;95:4-11. ♦♦

REVIEWS OF NOTE

COMMENT: *Everyone knows that the common cold, caused by rhinoviruses, can trigger bronchial hyperresponsiveness--even in nonasthmatics. Allergists at the University of Wisconsin have taken a leading role in elucidating the details of this phenomenon. This article is a brief review of the known, and postulated, mechanisms of an all-too-common clinical problem.*
R. J. M.
Friedlander SL, Busse WW: The role of rhinovirus in asthma exacerbations.
J Allergy Clin Immunol. 2005;116:267-273. ♦♦

COMMENT: *The inability to perform controlled trials of human anaphylaxis requires that we rely on well-done literature reviews, as well as consensus opinion. This review discusses the issue of late-phase anaphylaxis, offering the recommendation that an observation period of 8 hours is probably sufficient, although some authors recommend 24 hours. The factors associated with late-phase anaphylaxis are discussed in detail.*
D. K. L.
Lieberman P: Biphasic anaphylactic reactions.
Ann Allergy Asthma Immunol. 2005;95:217-226. ♦♦

COMMENT: *This comprehensive review covers the biologic mechanism involved in the interruption of the allergic pathway by anti-IgE antibodies. Basically these antibodies are felt to block IgE-mediated cell activation and inhibition of new IgE production by IgE-switched B cells without affecting the production of other antibody classes.*
E. J. B.
Inführ D, Crameri R, Lamers R, Achatz G: Molecular and cellular targets of anti-IgE antibodies.
Allergy. 2005;60:977-985. ♦♦

COMMENT: *This is an outstanding update on the pathophysiology of allergic bronchopulmonary aspergillosis, emphasizing the role of genetic factors in its development. The recent evolution of treatment using corticosteroids and itraconazole is reviewed in detail.*
E. J. B.
Tillie-Leblond I, Tonnel A-B: Allergic bronchopulmonary aspergillosis.
Allergy. 2005;60:1004-1013. ♦♦

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