AllergyWatch®

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

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Fatal Anaphylaxis: Findings of a Registry Study

In severe cases, anaphylaxis may progress so rapidly that no treatment is possible before the patient goes into respiratory or cardiac arrest. Randomized trials of treatment are impractical; other means must be sought to make management recommendations. Toward this end, the investigators analyzed 164 deaths from anaphylaxis, identified from a British registry.

The deaths occurred over a 6-year period; anaphylaxis was certified as the cause of death in each case. Twenty-five additional cases were excluded, including 2 deaths from adrenaline overdose in the absence of anaphylaxis; 2 fatal myocardial infarctions occurring after adrenaline treatment; and 14 cases involving complex circumstances around the time of death.

Overall, about one-half of the deaths were iatrogenic, one-fourth were caused by foods, and one-fourth by venom. Fatal reactions to food commonly involved respiratory arrest, while shock was more likely in patients with iatrogenic and venom reactions. Respiratory or cardiac arrest occurred in a median of 30 minutes for food reactions, 15 minutes for venom reactions, and 5 minutes for iatrogenic cases. Resuscitation was successfully carried out in 28% of cases. However, the patients died 3 hours to 30 days later, most often from hypoxic brain damage. Only 14% of patients received adrenaline before going into arrest.

The findings have important implications for the treatment of anaphylaxis, especially early use of adrenaline. However, some reactions are so severe that treatment could not be successful; allergen avoidance is key to preventing such reactions. Some deaths in patients with previous reactions might be prevented by recognizing the potential for cross-reactivity. Adrenaline overdose can also be fatal, and must be avoided.

COMMENT: *Using a U.K. national registry, the authors analyzed 164 fatal anaphylaxis cases. The cause in the largest proportion was "iatrogenic," with a median time to respiratory or cardiac arrest of 5 minutes. In contrast, the median time to food allergy-induced respiratory or cardiac arrests was 30* ➤➤

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
- 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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minutes. In almost one-third of fatal cases, the patient was temporarily revived. Delayed use of epinephrine probably contributed to the majority of the fatalities reported, and several patients died from an overdose of epinephrine. This article provides valuable insights for counseling patients at risk and may also help us avoid this dreaded outcome in our offices.
S. A. T.
Pumphrey RSH: Lessons for management of anaphylaxis from a study of fatal reactions. **Clin Exp Allergy** 30:1144-1150, 2000. ♦♦

Patient "Dumping" of Inhalers Confounds Clinical Trials

COMPLIANCE with prescribed metered-dose inhaler (MDI) use is an important issue in clinical trials of treatment for respiratory diseases. Simply weighing the MDI canisters provides no information on when the medication was administered. Studies using the Nebulizer Chronolog electronic medication monitor suggest that some patients intentionally "dump" the medication immediately before clinic visits in order to conceal their lack of inhaler use. This study sought to identify characteristics associated with dumping behavior.

The analysis included 101 patients participating in the Lung Health Study, a 5-year trial assessing the effects of inhaled bronchodilator use on progression of chronic obstructive pulmonary disease. All patients were smokers, aged 35 to 60 years. They were not informed of the purpose of the Chronolog device on their inhalers.

During the first year of the trial, the patients completed 81% of potential follow-up visits. During this time, 30% of patients "dumped" their medication—ie, actuated their inhalers more than 100 times within a 3-hour period—on at least one occasion. These episodes usually occurred just before a scheduled clinic visit. Patients who did and did not dump their medications were not significantly different in self-reported medication use or in MDI canister weights. The Chronolog data showed lower compliance among the "dumpers." No demographic or clinical predictors of dumping behavior could be found, although "dumpers" were less likely to lie about their smoking status.

A high percentage of clinical trial participants surreptitiously empty the contents of their inhalers to cover up noncompliance with their assigned medication. The findings underscore the importance of using electronic monitors to gather data on actual use of study medication.

COMMENT: *We are all well aware that our patients typically take significantly fewer doses of medication than we have prescribed. Despite financial incentives, study patients also have difficulties adhering to dosing required by protocols. This study used the Chronolog device to record the exact time at which a bronchodilator metered-dose inhaler was actuated. Almost one-third of the patients were guilty of dramatic "dumping" of their inhalers before an office visit. While we might assume that patients innocently forget to take medication, many are clearly guilty of willful protocol violations to "cover up" their missed doses. This phenomenon should be considered when interpreting clinical research data.*
S. A. T.
Simmons MS, Nides MA, Rand CS, et al: Unpredictability of deception in compliance with physician-prescribed bronchodilator inhaler use in a clinical trial. **Chest** 118:290-295, 2000. ♦♦

Airway Inflammation Persists After Asthma Remission in Adolescents

SYMPTOMS of childhood asthma commonly resolve or lessen as the patient enters puberty. However, many of these patients will have recurrent asthma symptoms later in life. This study examined measures of ➤➤

airway inflammation—including exhaled nitric oxide (eNO) and bronchial responsiveness to methacholine (MCh) and adenosine 5´-monophosphate (AMP) —among young patients in clinical remission of asthma.

The study included 21 patients, aged 18 to 25 years, who had been in clinical remission from atopic asthma for at least 1 year. During this time, they had been completely free from symptoms and had used no asthma medications. Each patient underwent spirometry and measurement of peak expiratory flow rate, in addition to measurement of eNO and bronchial responsiveness to MCh and AMP. The findings were compared with those of 21 patients with current asthma and 18 healthy controls.

Geometric mean values for eNO were significantly higher for the patients in asthma remission than in the healthy controls. The PD_{20}MCh dose was less than 1,000 μg in 55% of the remission group, compared with 90% of the patients with current asthma and none of the healthy controls. The patients in clinical remission also had a significant reduction in baseline FEV_1 as a percentage of predicted normal.

This study documents signs of ongoing airway inflammation among young patients in clinical remission of atopic asthma. Some of these measures, such as eNO, are similar to those of patients with current asthma. The measures of inflammation do not appear to be related to the duration of remission; their relationship to later asthma relapse remains to be defined.

COMMENT: *As a pediatrician, I have always been told that children outgrow their asthma. Years of clinical experience with children going through adolescence have tended to support that belief. These investigators measured markers of airways inflammation, including exhaled nitric oxide, and measured airways hyperresponsiveness using methacholine and cAMP challenges in adolescents who have gone into clinical asthma remission. Interestingly, they found that inflammation remains even after symptoms have remitted, and this may predict later recurrence of asthma as adolescents turn into adults. It is not clear whether ongoing anti-inflammatory treatment of adolescents who are in clinical remission would prevent relapse even if it were possible—which, given adolescents' tendency to noncompliance, is doubtful. Even so, we need to keep this study in mind the next time we tell teenaged patients that they have outgrown their asthma. (Also see "Relapsed Childhood Asthma Is More Severe Than Adult-Onset Asthma,"* AllergyWatch *Sept-Oct 2000, p 9.)*

J. M. P.

ven den Toorn LM, Prins J-B, Overbeek SE, et al: Adolescents in clinical remission of atopic asthma have elevated exhaled nitric oxide levels and bronchial hyperresponsiveness.

Am J Respir Crit Care Med 162:953-957, 2000. ♦♦

History Is Often Vague in Patients with Penicillin Allergy

SKIN testing for penicillin-specific IgE antibodies accurately predicts which patients can safely be treated with this antibiotic. Reported rates of skin-test positivity in patients with a positive history of penicillin allergy vary widely, from 7% to 76%. This rate is lower among patients with only a vague history of penicillin allergy, compared to those with a more convincing history. Published studies were reviewed to estimate the percentage of patients with a positive skin test who had only a vague history of penicillin allergy.

Through a MEDLINE search and other means, the investigators identified 30 studies that described patients with a positive history and positive skin test for penicillin allergy, and also provided information on the type of the previous reaction. The study definition of a vague history was one deemed unlikely to be IgE mediated, such as maculopapular rash, GI symptoms, or unknown reaction.

The studies identified a total of 1,063 patients with a positive skin test to penicillin. Of these, 33% had only a vague history of penicillin allergy. In individual studies, the percentage of patients with a vague history ranged from 0% to 70%.

The findings suggest that a vague history of penicillin allergy is quite common among skin-test-positive patients. Patient selection seems to have a major impact on reported rates of penicillin skin test positivity. Physicians tend to follow a less-cautious approach to patients with a vague history of penicillin allergy than for those with a convincing history. Such a policy is likely to miss a significant number of patients with penicillin-specific IgE antibodies.

COMMENT: *Allergists and primary care physicians are constantly challenged by the patient with a "vague" history of penicillin allergy. Previous studies have highlighted that many or indeed most of these patients do not have penicillin-specific IgE. This retrospective study emphasizes that approximately 33% of over 1,000 patients with penicillin-specific IgE had a vague history of suspected penicillin allergy. Fortunately, reasonable alternatives to β-lactam antibiotics can be found in most patients.*

A. M.

Solensky R, Earl SH, Gruchalla RS: Penicillin allergy: prevalence of vague history in skin test-positive patients.

Ann Allergy Asthma Immunol 85:195-199, 2000. ♦♦

β_2 Adrenoreceptor Polymorphism Affects Response to Salbutamol in Asthma Patients

POLYMORPHISMS of the β_2 adrenoreceptor are a frequent finding, the most common being substitution of glycine for arginine at position 16 and of glutamic acid for glutamine at position 27. There is evidence to suggest that β_2 adrenoreceptor genotype may influence the effects of inhaled β agonist treatment. Data from a randomized trial of asthma treatment were analyzed to assess the impact of β_2 adrenoreceptor polymorphisms on the response to salbutamol and salmeterol.

The analysis included 115 patients with mild to moderate asthma who were subjects in a randomized, crossover trial of regular treatment with inhaled ➤➤

salbutamol and salmeterol. Asthma control was scored in terms of changes in peak flow rates, asthma symptoms, and rescue bronchodilator use. Genetic tests were performed to determine genotype at codons 16 and 27 of the β_2 adrenoreceptor.

Patients homozygous for arginine at position 16 had the highest rate of major exacerbations while taking salbutamol—more than twice as high as with placebo. In contrast, patients heterozygous for arginine and glycine or homozygous for glycine at position 16 showed no significant differences in response to salbutamol. Genotype at position 16 had no significant effect on the response to salmeterol. Position 27 genotype had no significant effect on the response to either β agonist.

Asthma patients who are homozygous for arginine at position 16 of the β_2 adrenoreceptor have an elevated rate of major exacerbations during treatment with salbutamol. This genotype is present in a significant proportion of patients—16% in the present study. Although confirmatory studies are needed, the results suggest the possibility of targeting patients with the implicated genotype for alternative treatments. The study finds no adverse outcomes during salbutamol treatment in patients homozygous for glycine at position 16.

COMMENT: *Asthma has long been recognized as a heterogeneous disorder. This is especially true in individual response to drugs. This study provides insight into some genetic variations which account for this variability. Approximately 1 in 6 patients with asthma is homozygous for the arginine-16 β_2-adrenoreceptor allele. These individuals were found to be susceptible to clinically important increases in asthma exacerbations during chronic dosing with short-acting β_2-agonists, but not with long-acting agonists. If this can be confirmed, it would be prudent to identify such patients early on and offer them alternative treatment.*
E. J. B.
Taylor DR, Drazen JM, Herbison GP, et al: Asthma exacerbations during long term β agonist use: influence of β_2 adrenoreceptor polymorphism.
Thorax 55:762-767, 2000. ♦♦

Figures Show Drop in U.S. Mortality from Asthma

FROM the late 1970s to the late 1980s, mortality from asthma in the United States increased significantly. Since that time, asthma mortality has stabilized for most of the population. The author reviews trends in U.S. asthma mortality through 1997, the most recent year for which complete data are available.

Data on deaths from asthma were obtained from the National Center for Health Statistics. The total number of asthma deaths increased from 1,674 in 1977 to 5,667 in 1996. This figure decreased somewhat in 1997, to 5,434. Rates of death from asthma were 0.8 per 100,000 population in 1977 to 1978, 2.1 per 100,000 in 1994 through 1996, and 2.0 per 100,000 in 1997. Black females have had somewhat higher asthma mortality than black males, although rates decreased in both groups during 1997. Asthma continued to be a relatively infrequent cause of death overall.

Among children less than 15 years old, the number of asthma deaths increased from 54 in 1977 to 191 in 1996, then decreasing to 154 in 1997. Most of these deaths occurred in the 5- to 14-year age group, in which chronic obstructive pulmonary disease—mainly asthma—was the eighth-leading cause of death.

The most recent data suggest that asthma mortality in the United States has stabilized and may be on the decline. The probable explanation for this trend is improvements in treatment prompted by that National Asthma Education Program guidelines. The author discusses the need for new efforts to disseminate these guidelines in a form that will promote their use by clinicians.

COMMENT: *Deaths due to asthma continue to haunt all of us who care for asthmatic patients. In this important paper, Dr. Sly reviews updated data from the National Center for Health Statistics. It appears that the troubling increases in mortality that occurred throughout the 1980s have stabilized, and actually decreased slightly in 1997. While this is encouraging information, clinicians, educators, and researchers must remain vigilant. Since improvement in asthma management appears to explain the stabilization, we must continue to develop better management plans for the future.*
A. M.
Sly RM: Decreases in asthma mortality in the United States.
Ann Allergy Asthma Immunol 85:121-127, 2000. ♦♦

Nasal Polyposis Is a Persistent Problem for Most Patients

PREVIOUS studies have linked nasal polyposis to various clinical conditions, among them acetylsalicylic acid (ASA) intolerance. Debate continues over the role of allergy. There is evidence that long-term treatment with topical corticosteroids may reduce the risk of recurrent polyps. This study reviewed the long-term clinical course of 41 patients with nasal polyps.

The patients had all undergone polypectomy or ethmoidectomy for nasal polyps in 1977-78. Clinical evaluations revealed ASA intolerance, based on definite clinical history or positive response to aspirin provocation, in 11 patients; a history of atopy in 11 patients; and intrinsic allergic disease, with no specific etiologic factors, in 19 patients. The patients were re-examined at 20-year follow-up, including a sinus CT scan and a biopsy from polyp or middle turbinate mucosa. In biopsy specimens, an eosinophil count of 20 or more per 100 inflammatory cells was considered to indicate tissue eosinophilia.

On clinical review, 78% of patients reported continuous nasal symptoms; for 69% of patients, the most troublesome symptom was nasal blockage. Ninety percent of patients had undergone additional surgery during follow-up, and 3 of the remaining 4 patients had polyps at re-examination. Eight patients had had at least 11 additional nasal surgeries; 7 of these 8 were ➤➤

ASA intolerant. Sixty-one percent of patients, most of them with numerous additional surgeries, reported decreased or absent sense of smell. All of the patients with ASA intolerance had bronchial asthma, as did 36% of those with atopy and 16% of those with intrinsic allergic disease. Tissue and secretion eosinophilia were most common among patients with ASA intolerance.

This long-term follow-up study documents a high recurrence rate among patients undergoing surgery for nasal polyps. Even patients who report decreased symptoms may still have significant pathology requiring treatment. Patients with ASA intolerance have the most active nasal polyposis, in terms of degree of sinus involvement, number of additional operations, and use of medications. The authors recommend lifelong follow-up for patients with nasal polyposis.

COMMENT: *Nasal polyps continue to provide a challenge to the allergist. Despite the availability of potent corticosteroids and leukotriene modifiers, nasal polyposis appears to be a lifelong disease associated with significant morbidity. This paper provides additional insight into the almost universal association of nasal polyps and paranasal sinus mucosal disease, as well as the universal association of sensitivity to nonsteroidal anti-inflammatory drugs and asthma.*
A. M.
Vento SI, Ertama L, Hytönen ML, et al: Nasal polyposis: clinical course during 20 years.
Ann Allergy Asthma Immunol 85:209-214, 2000. ♦♦

Specific Bronchial Reactivity to Occupational Allergens Usually Persists

FOR some workers with occupational asthma, elimination of the offending exposure results in normalization of nonspecific bronchial reactivity (NSBR) and resolution of asthmatic symptoms. However, such patients may have further reactions if the exposure resumes. This study examined long-term persistence of specific bronchial reactivity (SBR) in 16 workers with a history of occupational asthma caused by high-molecular-weight agents. Seven workers had reacted to flour, 5 to psyllium, and 4 to guar gum. The offending exposure had been eliminated a mean of 5.7 years previously. Since then, all workers had been free of asthma symptoms, with normal lung function and NSBR.

At follow-up, the workers were re-exposed to the offending allergens by specific inhalation challenges, just as when the initial diagnosis was made. The challenge produced an asthmatic reaction in 11 of 16 patients, with exposure times similar to those recorded at initial diagnosis: 3.5 vs 4.2 min, respectively. Specific IgE levels to allergen decreased from 31.2% to 21.6% binding in patients who reacted to the second challenge, vs 24.2% to 16.9% binding in those who did not react to the second challenge. However, the decrease was significant in both groups.

Most workers with occupational asthma to high-molecular-weight agents still show asthmatic reactions when rechallenged with the offending agent. This is so despite symptom-free status and normal NSBR for several years after withdrawal of the exposure. Workers without such reactions have a significantly greater decrease in specific IgE than those who show continued SBR. The persistence of SBR in these cases appears to involve persistent immunologic sensitization.

COMMENT: *The investigators challenged 16 workers who had previously had asthma in response to flour, psyllium, and guar gum exposure a mean of 5 years after the exposure had stopped. In 11 workers, specific bronchial reactivity persisted even though nonspecific bronchial reactivity had resolved. This seemed to be related to a persistence of atopic sensitivity over this prolonged period of time. The implication is that workers who become sensitized to occupational agents may be prevented from ever working in that occupation again. Preventing such sensitization is therefore more critical than has been appreciated.*
J. M. P.
Lemière C, Cartier A, Malo J-L, Lehrer SB: Persistent specific bronchial reactivity to occupational agents in workers with normal nonspecific bronchial reactivity.
Am J Respir Crit Care Med 162:976-980, 2000. ♦♦

Horse Allergy Occurs Even Without Direct Exposure

PET allergy is a well-known cause of morbidity in children, but physicians may be less familiar with horse allergy. The authors believe that allergy to horses is an important cause of symptoms in children, even in urban environments and often without obvious exposure to horses. They review three illustrative cases of horse allergy in children.

The cases were selected from among 28 encountered at a London clinic. The children were 3 boys aged 5 to 9 years. One patient developed angioedema and respiratory distress within a few minutes after a pony ride. His symptoms improved with treatment in the emergency department. Skin prick testing showed a 6 mm wheal in response to horse dander.

The second patient had recurring asthma exacerbations over the weekends. The cause of the symptoms was unknown; psychosocial issues were considered. One weekend when the boy's sister was away, he remained symptom free. His sister rode horses every Friday evening, storing her riding gear in the home. Further history revealed the patient had a history of reactions to horses; skin prick testing showed an 8 mm wheal in response to horse dander. Once his sister stopped riding, the patient's asthma was controlled to the point where he no longer needed inhaled steroids. In the third case, summertime exacerbations of asthma—initially ascribed to nut allergy—proved to be associated with exposure to horses.

Horse dander may be a "hidden" allergen causing symptoms in children. As with cat allergy, horse allergen may be readily carried on clothing. Diagnosis relies on a careful clinical history. Recognizing the ➤➤

cause of the allergy may be particularly difficult when, as in the second case, late-phase symptoms develop many hours after allergen exposure.

COMMENT: *Recent studies have clearly demonstrated that cat allergen can be found on clothing and be transmitted to homes, offices, and schools. Thus symptoms may develop in cat-allergic patients even though there is no cat in the environment. These case studies from Roberts and Lack document that horse allergen can also bind to clothing and trigger allergic reactions in sensitive patients indoors. Just as we are recognizing cat-induced symptoms in allergic children and adults even without direct cat exposure, we should add horse allergy as another "hidden" indoor allergen that can exacerbate symptoms.*
M. S. B.
Roberts G, Lack G: Horse allergy in children.
BMJ 321:286-287, 2000. ♦♦

β_2-Agonist Treatment Linked to Increased Serum Tryptase Levels

PREVIOUS studies have suggested that regular users of β_2-agonists may develop increased asthmatic responses to allergen. This effect, occurring after as little as 7 days of use, may involve desensitization of β_2-adrenergic receptors on airway mast cells. This study examined the response of serum tryptase—a marker of mast cell degranulation—in asthmatic patients taking salbutamol.

The randomized, crossover study included 16 patients with asthma. In 10-day treatment periods, they received salbutamol, 100 µg, 2 puffs 4 times daily via metered-dose inhaler, or placebo. There was a 7-day washout period between treatments. Bronchial allergen challenge studies were performed after each treatment. The early and late asthmatic responses were assessed, and serum tryptase levels were measured. Sputum samples were obtained for measurement of tryptase content.

The early asthmatic response was significantly greater after salbutamol treatment than placebo: 20% vs 15%. One-hour serum tryptase levels were also higher after salbutamol, 9.09 vs 7.52 µg/L, respectively.

Asthma patients treated with salbutamol show an increased early asthmatic response and increased serum tryptase level in response to allergen challenge, compared with placebo-treated patients. The results are consistent with the hypothesis that regular salbutamol has a potentiating effect on allergic inflammation. The mechanism of this effect may involve increased mast cell mediator release. With concomitant increases in release of inflammatory mediators, this could increase eosinophil infiltration and survival in the lung.

COMMENT: *The debate over whether the use of chronic β_2-agonist therapy in asthma leads to worsening of the disease continues. This study by Swystun et al documents that inhaled albuterol four times daily over a 10-day period will increase both the early- and late-phase response to inhaled allergen challenge and increase serum tryptase levels in some patients. These findings suggest enhanced mast cell degranulation. The results were the same in a subgroup of subjects on chronic inhaled corticosteroids. As physicians prescribe more dual therapy with inhaled corticosteroids and long-acting β-agonists, it is important to determine whether this controlled allergen-challenge study is relevant to the real world of asthma management.*
M. S. B.
Swystun VA, Gordon JR, Davis EB, et al: Mast cell tryptase release and asthmatic responses to allergen increase with regular use of salbutamol.
J Allergy Clin Immunol 106:57-64, 2000. ♦♦

Controlled Trial Supports Effectiveness of Zinc for the Common Cold

SOME studies have shown that zinc acetate lozenges can reduce the duration of the common cold, although others have given conflicting results. The efficacy of zinc was studied in a randomized, controlled trial including 48 volunteers recruited within 24 hours of initial symptoms of the common cold. They were assigned to take either zinc—one lozenge containing zinc acetate 12.8 mg every 2 to 3 hours while awake—or placebo. Treatment continued for as long as the patients had cold symptoms. In addition to subjective symptom scores, plasma zinc and proinflammatory cytokine levels were measured on the first day of the study and after the symptoms had resolved.

Cold symptoms lasted for an average of 4.5 days in the zinc group vs 8.1 days in the placebo group. Zinc was associated with specific reductions in the duration of cough, 6.3 vs 3.1 days; and nasal discharge, 4.1 vs 5.8 days. Mean soluble interleukin-1 receptor antagonist level was higher in the zinc group, but the difference was not significant.

Taking zinc acetate lozenges as soon as symptoms develop can reduce the duration and severity of the common cold. The mechanism of this effect, including whether zinc has an antiviral effect, is unknown. This study used a high dose of zinc: about 80 mg of elemental zinc/d over 4 to 5 days, compared with a recommended daily allowance of 15 mg.

COMMENT: *Previous clinical trials of zinc lozenge therapy for the common cold have inconsistent results, with flaws in most of the studies. This is a well-done, double-blind, placebo-controlled trial demonstrating that zinc lozenges shorten the duration of a cold. The symptoms of rhinitis and cough were particularly affected. Treatment with high-dose zinc for less than a week is safe and is a current, viable therapeutic option. Zinc may have a direct antiviral effect, modulate inflammatory mediators, or affect symptoms directly. Regardless of how zinc does it, this news is just in time for the winter cold season.*
D. K. L.
Prasad AS, Fitzgerald JT, Bao B, et al: Duration of symptoms and plasma cytokine levels in patients with the common cold treated with zinc acetate.
Ann Intern Med 133:245-252, 2000. ♦♦

Daily Budesonide Inhibits Responses to Repeated, Low-Dose Allergen Challenge

IN patients with atopic asthma, repeated exposure to low doses of allergen causes increased airway hyperresponsiveness and sputum eosinophilia. Studies using high-dose allergen challenge have shown that inhaled corticosteroids reduce the ensuing airway response. However, their effects on the response to repeated, low-dose allergen challenge have not been studied.

Eight patients with mild atopic asthma were randomized to receive once-daily treatment with inhaled budesonide, 100 or 400 µg, or placebo. For 4 consecutive days, the patients underwent a low-dose allergen challenge 30 minutes after taking their assigned treatment. The airway response to methacholine and sputum eosinophilia were also measured at intervals. With 1-week washout periods, the patients were then crossed over to the other treatments.

Sputum eosinophil percentage increased from 2.0% at baseline to 16.6% on placebo after 4 consecutive days of low-dose allergen challenges. This value decreased significantly on both doses of budesonide: 5.6% on 100 µg and 3.1% on 400 µg. The higher dose of budesonide also inhibited allergen-induced methacholine airway hyperresponsiveness by day 4.

In patients with mild allergic asthma, daily inhaled budesonide—either 100 or 400 µg—significantly reduces sputum eosinophilia in response to repeated low-dose allergen challenge. The 400 µg dose also reduces allergen-induced airway hyperresponsiveness. The low-dose allergen challenge protocol followed in this study is designed to mimic the natural conditions of atopic asthma. The new results confirm the relationship between airway eosinophils and airway hyperresponsiveness.

COMMENT: *The authors designed the low-dose allergen inhalation to stimulate natural allergen exposure. The results help validate budesonide's indication for once-daily inhalation by Turbuhaler. Of note, even the 100 µg once-daily dose inhibited allergen-induced sputum eosinophilia by the fourth day of therapy.*
S. A. T.
Gauvreau GM, Sulakvelidze I, Watson RM, et al: Effects of once-daily dosing with inhaled budesonide on airway hyperresponsiveness and airway inflammation following repeated low-dose allergen challenge in atopic asthmatics. **Clin Exp Allergy** 30:1235-1243, 2000. ♦♦

Salmeterol/Fluticasone Combination is Safe and Effective for Pediatric Asthma

MORE and more children with asthma are being treated with salmeterol plus an inhaled corticosteroid. Seretide is a new product containing salmeterol and fluticasone propionate. This product, given via Diskus inhaler, was compared with the same drugs given separately in children with poorly controlled asthma.

The randomized trial included 257 children with reversible airways obstruction who had poor disease control with inhaled corticosteroids alone, 200 to 500 µg/d. Both groups received salmeterol 50 µg twice daily and fluticasone propionate 100 µg twice daily for 12 weeks. One group received the two drugs in combination, in a single Diskus inhaler, while the other group received the drugs concurrently but in separate inhalers.

Both groups had significant increases in mean morning peak expiratory flow. Adjusted mean change in this variable was 33 L/min in the combination therapy group vs 28 L/min in the concurrent therapy group. Both treatments brought significant improvement in secondary outcome variables as well—including pulmonary function, symptom score, and rescue salbutamol use—with no significant differences between groups. The two regimens were similarly safe and well-tolerated; adverse event rates were 10% with combination therapy and 5% with concurrent therapy.

In children with poorly controlled asthma, combination therapy with salmeterol and fluticasone propionate, given in a single inhaler, is as effective as concurrent therapy with the same drugs, given in separate inhalers. The product may be given via Diskus inhaler, which provides consistent drug delivery to the lungs across a wide range of inspiratory flow rates. Providing asthmatic children with just one inhaler may improve compliance with therapy.

COMMENT: *Several articles have appeared in the literature over the last 2 months reviewing the use of salmeterol/fluticasone propionate combination. For several reasons, it is important to review its use in children aged 4 to 11 years. This formulation has the potential advantages of improved compliance, improved control of daily symptoms (including exercise-induced bronchoconstriction, which is often a major issue for young children), and potentially improved use of inhaled steroids to "heal" young lungs. Furthermore, these children are able to generate adequate inspiratory flow rates using the Diskus™ device.*
J. B.-M.
Van den Berg NJ, Ossip MS, Hederos CA, et al: Salmeterol/fluticasone propionate (50/100µg) in combination in a Diskus™ Inhaler (Seretide™) is effective and safe in children with asthma.
Pediatr Pulmonol 30:97-105, 2000. ♦♦

Budesonide Inhalation Suspension for Young Children: Face Mask vs Mouthpiece

FOR asthmatic children under 4 years old, inhaled budesonide using a pressurized metered-dose inhaler (pMDI) with a spacer and face mask is an effective treatment. Budesonide inhalation suspension is a new, nebulized formulation designed for use in infants and young children with persistent asthma. Data from a randomized trial of this preparation were analyzed to compare efficacy with two routes of administration: face mask vs mouthpiece.

The analysis included 471 children, aged 6 months to 8 years, with moderate, persistent asthma. Budesonide inhalation suspension or placebo was ➤➤

delivered via face mask in 211 patients and via mouthpiece in 260. Mean age in these two groups was 36.4 and 70.0 months, respectively. Compared with placebo groups, patients receiving budesonide via either device showed clinical improvement in nighttime and daytime asthma symptoms. With the face mask, statistically significant improvements in nighttime symptoms were achieved at budesonide doses of 0.25 mg/d, 0.25 mg twice daily, and 0.5 mg twice daily. In the mouthpiece groups, significant improvement in nighttime symptoms were achieved with doses of 0.25 mg twice daily and 1.0 mg/d. Daytime symptoms improved significantly with budesonide 0.5 mg twice daily via face mask. With both devices, the need for breakthrough medication was significantly lower for patients receiving budesonide vs placebo.

At the doses studied, budesonide inhalation suspension improves symptoms in infants and young children with moderate, persistent asthma. Similar results are achieved whether the patient uses a face mask or mouthpiece. Nebulized bronchodilators offer a significant advantage for patients who are unable to use dry powder devices or pMDIs.

COMMENT: *This retrospective analysis compares the face mask versus mouthpiece administration of budesonide in 481 children aged 6 months to 8 years at 37 U.S. centers. The mode of administration did not affect the efficacy of budesonide treatment. Larger studies will be required to confirm the equivalent efficacy of these delivery devices.*
J. B.-M.

Mellon M, Leflein J, Walton-Bowen K, et al: Comparable efficacy of administration with face mask or mouthpiece of nebulized budesonide inhalation suspension for infants and young children with persistent asthma.
Am J Respir Crit Care Med 162:593-598, 2000. ♦♦

Conjugated Allergen Has High Immunogenicity and Low Allergenicity

ATTEMPTS at reducing the allergenicity of immunotherapy have been hampered by reduced immunogenicity. Recent studies suggest that bacterial DNA or immunostimulatory oligodeoxynucleotides (ISS-ODNs), both of which contain CpG motifs, can induce a strong T_H1 response. The authors coupled a 22-mer ISS-ODN to the major short ragweed allergen Amb a 1.

Immunization studies in mice showed that the Amb a 1-ISS conjugate induced interferon-γ secretion—a T_H1 response—while a nonconjugated form of Amb a 1 induced interleukin-5 secretion—a T_H2 response. Injection with the Amb a 1-ISS conjugate induced a T_H1 response and suppressed IgE antibody formation even in mice primed for a T_H2 response. Studies in rabbits and cynomolgus monkeys also showed increased immunogenicity of Amb a 1-ISS conjugate, with an enhanced IgG antibody response. Injection of Amb a 1 alone or of mixed Amb a 1 and ISS-ODN did not produce the same response. In basophils from humans with ragweed allergy, histamine release was 30 times lower with the Amb a 1-ISS conjugate than with Amb a 1 alone.

Chemically conjugating ISS-ODN to allergen results in new allergenic properties that are highly promising for use in immunotherapy. The allergen-ISS conjugate offers enhanced immunogenicity, inducing strong T_H1 and IgG responses. At the same time, allergenicity is reduced, which should lower the risk of anaphylaxis or other serious adverse events of immunotherapy.

COMMENT: *There is a need for development of immunotherapy, which improves its immunogenicity and decreases allergenicity and risk of anaphylaxis. Many modifications of immunotherapy—such as alum-precipitated and polymerized extracts—have been suggested, without clear benefit. Tighe et al. demonstrate that the addition of immunostimulatory DNA sequences or CpG motifs to ragweed allergen elicits a T_H1 response with high IgG formation and decreased histamine release from basophils. This additional moiety may be the key to a safer, more effective allergy vaccination. Of course further work is needed, especially in documenting the long-term safety in humans.*
M. S. B.

Tighe H, Takabayashi K, Schwartz D, et al: Conjugation of immunostimulatory DNA to the short ragweed allergen Amb a 1 enhances its immunogenicity and reduces its allergenicity.
J Allergy Clin Immunol 106:124-134, 2000. ♦♦

Montelukast Plus Loratadine Improves Asthma Control

THE leukotriene receptor antagonist montelukast sodium is an effective treatment for chronic asthma. The selective histamine type 1 (H_1)-receptor antagonist loratadine has known antiallergic effects. This study compared the combination of montelukast and loratadine with montelukast alone for the treatment of chronic asthma.

The randomized, double-blind, crossover trial included 125 patients with chronic asthma, all with an FEV_1 of 50% to 80% of predicted and an increase in FEV_1 of at least 15% after β-agonist inhalation. After a 2-week placebo run-in period, the patients were randomized to receive montelukast sodium 10 mg plus loratadine 20 mg, or montelukast 10 mg plus placebo. After 2 weeks of treatment, and another 2-week washout period, the patients were crossed over to the other treatment.

The montelukast-loratadine group had a significantly greater improvement in percentage of change in FEV_1 than the montelukast-placebo group: 13.86% vs 9.72%. The combination treatment also produced significant improvement in daily β-agonist use, daytime and nighttime symptom scores, morning and evening peak expiratory flow rate, and a patient global evaluation.

Adding loratadine to montelukast sodium treatment for patients with chronic asthma offers sig- ➤➤

nificant added benefit over montelukast alone. This is a well-tolerated and effective therapeutic option for patients whose asthma is not well controlled with montelukast alone.

COMMENT: *The results of this study are surprising in view of the minimal benefits of antihistamines used alone in the treatment of asthma. Of note, the added efficacy of giving montelukast concomitantly with loratadine was seen in patients with and without a history of allergic rhinitis. The dose of loratadine was 20 mg/d, which has been associated with sedation. However, in this study only 2 patients in the montelukast plus loratadine group experienced somnolence. Merck and Schering have plans for marketing a combination drug.*
J. R. B.
Reicin A, White R, Weinstein SF, et al: Montelukast, a leukotriene receptor antagonist, in combination with loratadine, a histamine receptor antagonist, in the treatment of chronic asthma.
Arch Intern Med 160:2481-2488, 2000. ♦♦

Allergy Care for Older Adults: ACAAI Member Survey

BY the year 2020, 17% of the U.S. population will be over 65 years old. As in other areas of health care, the aging of the population has important implications for allergy/immunology care. Members of the American College of Allergy, Asthma and Immunology (ACAAI) were surveyed regarding care provided to older adults.

A survey regarding certifications, training, and practice patterns was mailed to 2,857 members and fellows of the ACAAI. The response rate was 32%. More than three-fourths of respondents were certified by the American Board of Allergy and Immunology. The respondents indicated that 20% of their patients were aged 55 years or older. Even for respondents certified in pediatrics and allergy/immunology, 17% of their patients fell into this age group. Nearly all respondents said they provided inhalant allergen immunotherapy to patients in the 40- to 54-year age group with asthma and/or allergic rhinitis. Even for patients in 55- to 69-year age group, and even the 70 and older group, most practitioners continued to provide these services.

The findings suggest that nearly all allergists/immunologists provide care for older adults. With the aging of the population, it is important for the speciality of allergy/immunology to make plans for providing care to this age group.

COMMENT: *As our population ages, allergy care for older adults will assume greater significance. In this important survey of ACAAI members, the authors point out that regardless of the clinician's training, essentially all members provide care for older adults. The survey highlights the importance of future educational and research initiatives in the area of allergy and immunology care for older adults.*
A. M.
Lang DM, Visintainer PF, Howland WC III, et al: Survey of the extent and nature of care for adults and older adults by allergy/immunology practitioners.
Ann Allergy Asthma Immunol 85:106-110, 2000. ♦♦

Safety of Oral Food Challenges in Children Assessed

FOOD allergy is a common condition in children, and is diagnosed using double-blind, placebo-controlled food challenge. These challenges carry a risk of life-threatening reactions. However, there is no way of predicting which children will develop severe symptoms requiring systemic treatment. This study sought to identify predictors of severe reactions to oral food challenges in children, and thus which patients should have intravenous access established before food challenge.

The retrospective analysis included a total of 349 oral challenges in 204 children: 115 boys and 89 girls, median age 33 months. Thirty-eight percent of children had a clinical history of immediate or late-type reactions; the rest were atopic but had no such history. Seventy-nine percent of patients had a specific IgE level of greater than 0.35 kU/L to cow's milk, hen's egg, wheat, or soy. The challenge was performed in double-blind fashion in 210 cases and open fashion in 139. Full emergency equipment was available before each challenge. Medications were given if symptoms occurred, ie, nausea, dyspnea or tachycardia with pruritus, urticaria, flushing, angioedema, or beginning centralization.

Fifty-one percent of challenges gave clinically positive results. Of the positive challenges, 70% were associated with cutaneous symptoms. Overall, 34% of children required medical intervention; 17% had a positive challenge but required no intervention. About two-thirds of the patients requiring treatment received only oral medication. The need for medical intervention was strongly and positively correlated with the patient's specific IgE level—17.7 kU/L or greater for milk and wheat and 3.5 kU/L or greater for egg—together with a positive history for food allergy.

In children undergoing oral food challenges for milk, wheat, or soy, a previous history of food allergy is a reliable predictor of the need for medical intervention. For those undergoing egg challenges, the combination of a positive history plus a high specific IgE level is associated with the need for parenteral medication. Based on their findings, the authors recommend intravenous access before food challenge for children with high specific IgE levels.

COMMENT: *The gold standard for diagnosis of food allergy is a double-blind, placebo-controlled oral provocation. This study analyzed 349 food challenges in 204 children with cow's milk, egg, wheat, and soy. Positive reactions occurred in 178 (51%), and 70% of these were limited to the skin. A history of food allergy was a reliable indicator that medical treatment of the resultant reaction would be necessary. An intravenous access was recommended in children with a specific IgE level of 17.5 kU/L or greater (CAP class 4) to milk and wheat, and in those with specific IgE of 3.5 kU/L or* ➤➤

greater (CAP class 3) to egg.
E. J. B.
Reibel S, Ruöhr C, Ziegert M, et al: What safety measures need to be taken in oral food challenges in children? **Allergy** 55:940-944, 2000. ♦♦

Adding Salmeterol to Inhaled Steroid Improves Asthma Control in Children

BRITISH guidelines suggest adding a long-acting inhaled β_2-agonist for asthmatic children who fail to respond to inhaled corticosteroids. However, one recent trial found no benefit of adding inhaled salmeterol. This randomized trial compared the effects of salmeterol 50 µg bid, salmeterol 100 µg bid, and salbutamol 200 µg qds in asthmatic children who did not respond adequately to inhaled corticosteroid.

The study included 45 children, aged 5 to 14 years, who had continued asthma symptoms despite an inhaled corticosteroid dose of at least 400 µg/d. Clinical characteristics included a family history of asthma in 82% of children, seasonal rhinitis in 80%, and positive skin tests in 60%. In double-blind, crossover fashion, the children were assigned to receive salmeterol 50 µg bid, salmeterol 100 µg bid, and salbutamol 200 µg qds for 4 weeks. Inhaled corticosteroid therapy continued throughout.

Asthma control, morning and evening peak expiratory flow (PEF), and spirometric variables improved significantly with all 3 treatments. Bronchial hyperreactivity was unchanged. Salmeterol brought a greater improvement in mean morning PEF than salbutamol. Estimated treatment difference in mean morning PEF, compared with salbutamol 200 µg qds, was 9.6 L/min for salmeterol 50 µg bid and 13.8 L/min for salmeterol 100 µg bid. There was no significant difference between the two doses of salmeterol. All treatments were well tolerated, although salbutamol had a somewhat higher overall incidence of adverse events.

This study supports the use of the long-acting β_2-agonist salmeterol in children whose asthma is inadequately controlled despite inhaled corticosteroid therapy. β_2-Agonists should not be used as monotherapy in asthmatic children; rather, they should be used in addition to inhaled corticosteroids. This study included a more symptomatic group of patients than the previous study that found no benefit of salmeterol in asthmatic children.

COMMENT: *The role of long-acting β_2-agonists in children with mild, well-controlled asthma has been contested in previous studies. This study focuses on moderate to severe asthma in children for whom inhaled corticosteroids have not completely controlled the disease. Salmeterol in a dose of either 50 µg bid or 100 µg bid was found significantly more effective at increasing morning PEF rate over a 1-month period than salbutamol 200 µg qds. β_2-Agonists should never be used as monotherapy. However, when added to corticosteroids they result in improved asthma control and better lung function. There is no deterioration in bronchial hyperreactivity, at least in the short term.*
E. J. B.
Byrnes C, Shrewsbury S, Barnes PJ, Bush A: Salmeterol in paediatric asthma.
Thorax 55:780-784, 2000. ♦♦

Protective Effects of Deep Inspirations: New Findings

IN a previous study, the authors found that deep inspirations (DIs) have a bronchoprotective effect in healthy subjects that is lacking in asthmatic subjects. The available evidence suggests that the bronchoprotective effect of DIs is stronger than the bronchodilator effect. An experimental study was performed to test this hypothesis, as well as the likely involvement of airway smooth muscle stretch in both effects.

Ten healthy subjects underwent challenges with methacholine at doses previously shown to reduce FEV_1 by 10% to 20% (dose 1) and by 20 to 40% (dose 2). To measure the bronchodilator effect, a set of DIs were performed immediately after the first post-methacholine spirometry, after which another lung function test was performed. To measured the bronchoprotective effect, the subjects performed DIs before a single dose of methacholine. The post-methacholine FEV_1 was compared with and without DIs.

In response to dose 1, DIs had an equal ability to reverse and prevent methacholine-induced airway obstruction. In response to dose 2, both the bronchodilating and bronchoprotective effects of DIs were stronger. However, the bronchoprotective effect showed a continued increase, while the bronchodilator effect plateaued.

In healthy subjects, DIs have a comparable bronchodilator and bronchoprotective effect at low levels of bronchoconstriction. Both effects become relatively stronger at higher doses of methacholine; however, the increase in the bronchoprotective effect is more pronounced. The greater potency of the bronchoprotective effect appears to reflect a limitation on the effects of airway stretch. The 2 effects of DIs are only weakly related to each other, suggesting that they involve different physiologic mechanisms

COMMENT: *The reflex to breathe deeply, as during a yawn, has recently been shown to have a beneficial effect on pulmonary function. In this study, the authors have improved our understanding of that benefit by demonstrating that a deep breath protects against bronchoconstriction induced by methacholine better than it bronchodilates airways that are already constricted. The effect is greater with increased degrees of constriction. The lesson here is that deep breathing—such as when one participates in exercise—is intrinsically beneficial in that it helps to prevent bronchoconstriction. In other words, prevention is the way we evolved to maintain our airway function, rather than treating constriction after it has already occurred.*
J. M. P.
Scichilone N, Kapsali T, Permutt S, Togias A: Deep inspiration-induced bronchoprotection is ➤➤

stronger than bronchodilation.
Am J Respir Crit Care Med 162:910-916, 2000. ♦♦

Does Menstrual Phase Affect Asthma Exacerbations?

PREVIOUS reports have suggested that hormonal changes during the menstrual cycle may affect the likelihood of asthma exacerbations. One study found that nearly one-half of emergency department (ED) visits occurred when women were in the perimenstrual phase of the cycle. The relationship between phase of the menstrual cycle and acute asthma was evaluated in a prospective cohort study. The analysis included 288 women seen at 64 EDs for acute asthma attacks. Information on stage of the menstrual cycle and other variables was collected by a standardized interview.

Thirty-three percent of visits occurred during the preovulatory phase, days 5 to 11; 25% during the periovulatory phase, days 12 to 18; 21% during the postovulatory phase, days 19 to 25; and 21% during the perimenstrual phase, days 26 to 4. Menstrual cycle phase was not significantly related to measures of asthma severity. Just 13% of women said that reproductive factors were a trigger for their asthma attacks.

The results cast doubt on the hypothesis that menstrual cycle phase affects the occurrence of asthma exacerbations in women. Previous survey studies of this issue have been subject to recall bias. This study is larger than the previous study showing a higher rate of asthma attacks during the perimenstrual phase. The findings are limited by the reliance on self-reported menstrual and asthma histories.

COMMENT: *In this large study, emergency department visits for asthma were most frequent in the preovulatory phase (days 5 to 11) of the menstrual cycle rather than the perimenstrual phase, as has been previously reported. Thirty-three percent of the ED visits occurred during the preovulatory phase, compared with 21% in the perimenstrual phase. The results cast doubt on the importance of hormonal changes as a factor in exacerbations of asthma in women.*
J. R. B.
Zimmerman JL, Woodruff PG, Clark S, et al: Relation between phase of menstrual cycle and emergency department visits for acute asthma.
Am J Respir Crit Care Med 162:512-515, 2000. ♦♦

Fluticasone Has Reduced Systemic Availability in Asthma Patients

INHALED corticosteroids are the mainstay of asthma treatment. Fluticasone propionate has low oral bioavailability, so any systemic activity results from absorption of the proportion of drug dose deposited in the lungs. However, studies in normal subjects suggest that this agent may be associated with significant systemic absorption. In patients with more severe asthma receiving high corticosteroid doses, many different factors could influence lung deposition and thus systemic absorption. To evaluate the safety of high-dose fluticasone, the investigators compared the drug's pharmacokinetics and pharmacodynamics in patients with moderate to severe asthma vs healthy controls.

The randomized, double-blind, crossover study included 11 patients with asthma and 13 matched, healthy subjects. The asthma patients all had an FEV_1 of less than 75% and history of bronchodilator use, and were in stable condition on high-dose inhaled corticosteroids. All subjects received training in optimal inhalation technique, then completed a 1-week run-in period. They were randomized to receive 1 week of treatment with either fluticasone propionate 1,000 µg/d or beclomethasone dipropionate 2,000 µg/d (a therapeutically equivalent dose). Plasma fluticasone propionate and cortisol concentrations were monitored for 12 hours after dosing.

The two groups showed significant differences in the pharmacokinetics of inhaled fluticasone propionate. Values for plasma area-under-curve, systemic availability, and peak fluticasone propionate concentration were all significantly higher in the control group. Because systemic availability was lower in the asthma patients, hypothalamic-pituitary-adrenal suppression was lower as well. There were no significant differences in intravenous pharmacokinetic parameters, including dose clearance, distribution volume at steady-state, plasma half-life, and mean residence time.

High-dose inhaled fluticasone propionate has significantly lower systemic availability in patients with asthma than in healthy matched controls. A number of factors make it very difficult to assess the risk-benefit ratio of high-dose corticosteroids. Accurate assessments of the pharmacokinetics and pharmacodynamics of inhaled corticosteroids with minimum oral bioavailability can only be made if the dose is appropriate to the severity of the patient's asthma. The findings emphasize the importance of using the minimum inhaled corticosteroid dose for asthma control.

COMMENT: *A number of previous studies have stressed that systemic absorption is best assessed in nonasthmatic subjects. This is based on the assumption that systemic absorption profiles for an inhalational agent would be similar in both groups. Brutsche et al. provide data demonstrating that this assumption is invalid. They show that nonasthmatic individuals absorbed twice as much fluticasone as did patients with asthma. The study demonstrates that—apart from several pharmacodynamic properties of a drug—the characteristics of the host airways are a critical factor in determining absorption profiles.*
E. J. B.
Brutsche MH, Brutsche IC, Munavvar M, et al: Comparison of pharmacokinetics and systemic effects of inhaled fluticasone propionate in patients with asthma and healthy volunteers: a randomised crossover study.
Lancet 356:555-561, 2000. ♦♦

Why Do Some CIU Patients Have Skin Reactions to Their Own Serum?

THE pathogenesis of chronic idiopathic urticaria is unknown, but about 60% of affected patients show a wheal-and-flare response to intradermal injection of autologous serum. This suggests the patients may have IgG autoantibodies against IgE or the α-chain of the high-affinity IgE receptor (FcεRIα) on basophils and mast cells. Patients with a positive skin test result to autologous serum were tested for the presence of anti-IgE or anti-FcεRI antibodies.

The study included 15 patients with a positive skin response to native serum. All but 1 of 15 native sera showed anti-FcεRIα antibodies on enzyme-linked immunosorbent assay. Just 2 of these sera induced basophil degranulation in vitro. None of the sera showed detectable levels of anti-IgE antibodies. When sera were depleted of IgG by protein G, anti-FcεRIα antibodies were eliminated completely in 10 of 14 samples and largely in the other 4. Heating and protein G adsorption eliminated the capacity to trigger histamine release in the 2 sera with functional activity. However, even with heating and IgG depletion, the sera still caused wheal-and-flare reactions similar to those of untreated sera.

This study demonstrates anti-FcεRIα IgG antibodies in sera from CIU patients with a positive skin response to autologous serum. Even with heat decomplementation and IgG depletion, these sera still cause wheal-and-flare reactions. Some unknown, non-immunoglobulin reactant appears to be responsible for the skin reaction to autologous serum in this group of CIU patients.

COMMENT: *Chronic idiopathic urticaria is a vexing disorder, the cause(s) of which remains obscure. Some evidence implicates IgG autoantibodies against IgE or the IgE receptor on mast cells. In this study of 15 patients with CIU, 14 had anti-IgE receptor antibodies, but only two of them had histamine-releasing activity. Removing complement and IgG from the sera did not abrogate their autologous wheal-and-flare sensitivity. This suggests that there are non-IgG reactants in the sera of CIU patients.*
R. J. M.

Fagiolo U, Kricak F, Ruf C, et al: Effects of complement inactivation and IgG depletion on skin reactivity to autologous serum in chronic idiopathic urticaria.
J Allergy Clin Immunol 106:567-572, 2000. ♦♦

REVIEWS OF NOTE

Schubert MS: Medical treatment of allergic fungal sinusitis. Ann Allergy Asthma Immunol 85:90-101, 2000.

COMMENT: *Allergic fungal sinusitis is a recently described allergic disease that is increasingly recognized in the medical and popular press. Since these patients frequently present to the allergist/immunologist, it is critical that practitioners be aware of the current medical and surgical treatment options. In this review, Dr. Schubert details his significant experience and reviews the literature on medical treatment. He points out that further controlled studies are needed to clarify the role of therapies, including fungal immunotherapy.*
A. M.

Anzueto A, Angel L: Update in pulmonary disease.
Ann Intern Med 133:360-366, 2000.

COMMENT: *This paper is a summary of the state-of-the-art lecture on pulmonary medicine presented at the 2000 American College of Physicians meeting. The review presents highlighted literature on relevant subjects to the clinical allergist, such as asthma, chronic obstructive pulmonary disease, chronic bronchitis, and pneumonia. It is extremely well written and well referenced, and may provide an excellent up-to-date resource.*
A. M.

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