AllergyWatch®

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

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Inhaled Budesonide for Asthmatic Children: Good Disease Control, Minor Growth Effects

THERE is concern that asthma in children may cause impairment of lung growth and progressive declines in pulmonary function throughout the child's life. Anti-inflammatory treatments are recommended for asthmatic children, but few studies have assessed the long-term outcomes of anti-inflammatory therapy. This placebo-controlled trial assessed the effects of long-term treatment with inhaled budesonide or inhaled nedocromil on lung growth in asthmatic children, compared to symptomatic treatment only.

The multicenter trial included 1,041 children with mild to moderate asthma, aged 5 to 12 years. They were randomized to receive inhaled budesonide, 200 µg twice daily; inhaled nedocromil, 8 mg twice daily; or placebo. During 4 to 6 years of treatment, all children received albuterol as needed for asthma symptoms. Outcome measures included changes in lung function studies, symptoms and other measures of disease control, and height and growth measures.

The three groups were similar in their baseline characteristics, with slightly more boys in the nedocromil group. The budesonide group showed initial improvement in FEV_1 after bronchodilator administration, from 103% predicted to 107% predicted within the first 2 months. However, this measure gradually decreased to the point where there was no significant difference between treatment groups. The budesonide group had a significant increase in the prebronchodilator FEV_1 compared with the other two groups, and a lesser decline in the ratio of FEV_1 to forced vital capacity. Budesonide treatment was also associated with a 43% reduction in hospitalizations, a 45% reduction in urgent-care visits, and a 43% reduction in courses of prednisone, compared with placebo. Lesser reductions in these outcomes were noted in the nedocromil group. The budesonide group had other evidence of superior asthma control, including lower airway responsiveness to methacholine, fewer asthma symptoms, less ➤➤

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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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albuterol use, and more episode-free days. Children in the budesonide group gained about 1 cm less in height than the other two groups, mainly in the first treatment year. By the end of treatment, all three groups had similar growth velocity.

In children with mild to moderate asthma, neither inhaled budesonide nor nedocromil improves lung function compared with symptomatic treatment only. However, inhaled budesonide provides better disease control without any lasting effects on growth. The results highlight the need for long-term, controlled trials of asthma treatments.

COMMENT: *Previous research from Finland suggested that as little as a two-year delay in instituting anti-inflammatory therapy in asthmatic children could irreversibly impair lung function. This multicenter North American study of 1,041 asthmatic 5- to 12-year-old children who received 4 to 6 years of treatment with inhaled budesonide, nedocromil, or placebo reached some surprising conclusions. There were no differences in* FEV_1 *after 4 years. There was no evidence of a decline in lung function even in the placebo group. However,* clinical *control was best with budesonide. Budesonide impaired growth velocity only in the first 1 to 2 years, after which it was the same in all groups. Extrapolation from 1-year growth studies may not be appropriate.*
R. J. M.
The Childhood Asthma Management Program Research Group: Long-term effects of budesonide or nedocromil in children with asthma.
N Engl J Med 343:1054-1063, 2000. ♦♦

Inhaled Budesonide Does Not Reduce Final Height in Children

THERE is concern about the potential effects of long-term inhaled corticosteroid therapy on growth in children. However, few long-term studies have addressed this issue. This study examined the impact of inhaled budesonide for children with persistent asthma on final adult height.

The analysis was part of a long-term, prospective study of growth, lung function, and hospitalizations in children with persistent asthma. It included data on 211 children who had achieved adult height: 142 asthmatic children treated with inhaled budesonide for a mean of 9 years, mean dose 412 µg/d; 18 asthmatic children who did not receive inhaled budesonide; and 51 healthy siblings of children in the budesonide group. The main outcome was measured adult height compared with target adult height.

Budesonide-treated children were just as likely to reach their target adult height as untreated asthmatic or healthy children. Mean difference between measured and target adult height was +0.3 cm in the budesonide group vs -0.2 cm in the asthmatic controls and +0.9 cm in the healthy controls. The difference was unrelated to sex, age at the start of budesonide therapy, age at which adult height was reached, and duration of asthma before budesonide therapy. Growth was significantly reduced during the first few years of budesonide treatment, but there was no lasting impact on final adult height. This transient growth effect was more pronounced in younger children.

For children with asthma, long-term treatment with inhaled budesonide does not appear to interfere with final adult height. The first year of budesonide treatment is associated with an average 1 cm reduction in growth rate. However, this reduction does not persist and does not adversely affect adult height.

COMMENT: *It has been debated whether short-term impairment of growth by inhaled corticosteroids will or will not affect final adult height. These Danish researchers present data on 142 children treated with budesonide for a mean of 9.2 years, with a mean daily dose of 412 mg. The children's growth* velocity *was reduced by about 15% during the first year of treatment, but the reduction did not persist. Final adult height was not* ➤➤

adversely affected, regardless of total cumulative dose or duration. These findings should not be extrapolated to other inhaled corticosteroids.
R. J. M.
Agertoft L, Pedersen S: Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. **N Engl J Med** 343:1064-1069, 2000. ♦♦

Is Inhaled Epinephrine Appropriate for Children At Risk of Anaphylaxis?

INJECTED epinephrine is the treatment of choice for out-of-hospital anaphylaxis, providing prompt peak plasma concentrations and systemic effects. In recent years, inhaled epinephrine has been recommended as a noninvasive alternative to injected epinephrine. This study examined the adequacy of epinephrine dose when administered via metered-dose inhaler in children at risk of anaphylaxis.

The prospective, randomized trial included 19 children with severe allergies and systemic anaphylaxis, for which they carried injectable epinephrine. Most were allergic to peanut or tree nut. In a clinical research center under closely supervised conditions, the children received 10 to 20 inhalations of epinephrine (using the Bronkaid Mistometer) or placebo via pressurized metered-dose inhalers. Before and at frequent intervals after the inhalations, blood samples were obtained for measurement of plasma epinephrine. The study hypothesis was that inhaled epinephrine would achieve a prompt, adequate increase in plasma epinephrine levels.

Just 18% of children in the epinephrine group and 25% in the placebo group were able to take the full number of inhalations needed to reach a significant increase in plasma epinephrine. Compared with those in the placebo group, children in the epinephrine group never attained a significant increase in mean plasma epinephrine concentrations. Epinephrine treatment was also associated with a significant rise in mean blood glucose concentration, but no differences in mean heart rate or blood pressure. Nearly all children in the epinephrine group complained of a bad taste. Some children in both groups developed coughing or dizziness.

Inhaled epinephrine does not appear to be an acceptable substitute for injected epinephrine in children at risk of anaphylaxis. Too many inhalations would be required to reach an adequate dose of epinephrine, and the bad taste of the medication would be a serious limiting factor. In this study, the mean dose of epinephrine inhaled was 2.64 mg, nearly 10 times higher than the maximum dose recommended for injection.

COMMENT: *Injected epinephrine is the gold standard for treatment of anaphylaxis. However, there is an increasing tendency for physicians to recommend inhaled epinephrine instead because it is less expensive and felt to be easier to use. To test the validity of this practice, the investigators compared plasma epinephrine concentrations and physiologic changes in a group of children who received injected and inhaled epinephrine. They concluded that the bad taste and large number of inhalations required to achieve a therapeutic effect make inhaled epinephrine a poor substitute for the injected form. Thus the gold standard remains just that: a standard from which one should be reluctant to deviate.*
J. M. P.
Simons FER, Gu X, Johnston LM, Simons KJ: Can epinephrine inhalations be substituted for epinephrine injection in children at risk for systemic anaphylaxis? **Pediatrics** 106:1040-1044, 2000. ♦♦

Inflammation and Response to Steroids Are Similar in Recent vs Long-standing Asthma

EVIDENCE of airway inflammation and mucosal remodeling is found even in patients with mild or recently diagnosed asthma. Irreversible structural damage appears to be present even before symptoms develop, and does not improve with inhaled corticosteroid therapy. This study compared measures of airway inflammation and airway remodeling in patients with recently diagnosed vs long-standing asthma (RDA vs LSA), including the effects of high-dose inhaled corticosteroid therapy.

The study included 32 adult asthma patients who were receiving inhaled β_2-agonist therapy only. The asthma was classified as recently diagnosed—present for 2 years or less—in 13 patients, and as long-standing—present for 13 years or longer—in 16 patients. Assessment included a respiratory questionnaire, symptom diary, skin-prick testing, spirometry and methacholine challenge, and bronchial biopsy. Patients were studied before and after 8 weeks of treatment with inhaled fluticasone propionate, 1,000 μg/d. Before and after treatment, the RDA and LSA groups were compared for airway inflammatory cell counts and subepithelial collagen deposition, a measure of airway remodeling.

At baseline, geometric mean methacholine PC_{20} was 0.44 mg/mL in the RDA group vs 3.37 mg/mL in the LSA group. Both groups showed similar improvement—by 1.85 and 1.86 double concentrations—with fluticasone therapy. Two patients in the LSA group and 5 in the RDA group had normalization of methacholine PC_{20}. Bronchial inflammatory cell counts were similar in the 2 groups at baseline and, for most cell types, decreased to a similar extent in both groups. There was no difference in the LSA vs RDA groups in terms of type 1 and type 3 collagen deposition beneath the basement membrane, and neither group showed a significant change after fluticasone therapy.

Among patients with mild asthma, the extent of airway inflammation and subepithelial fibrosis is similar, irrespective of how long the asthma has been present. Patients with RDA and LSA have similar improvement in airway hyperresponsiveness on high-dose inhaled corticosteroids. Even with such treatment, most patients cannot achieve normal airway responsiveness once they have developed asthma symptoms.

COMMENT: *The results of this carefully done study suggest that when asthma patients first become* ➤➤

symptomatic, there is already considerable airway inflammation and structural change. Contrary to the investigators' expectations, patients with recently diagnosed asthma did not have less inflammation and were not more responsive to inhaled corticosteroids than those with longstanding asthma. The use of inhaled corticosteroids may improve pulmonary function and symptom control, but may not change the long-term course of asthma. It should be noted that study subjects were mild asthmatics and the investigators did not examine other possible parameters of airway remodeling, such as changes in bronchial smooth muscle.
J. R. B.
Boulet L-P, Turcotte H, Laviolette M, et al: Airway hyperresponsiveness, inflammation, and subepithelial collagen deposition in recently diagnosed versus longstanding mild asthma.
Am J Respir Crit Care Med 162:1308-1313, 2000. ♦♦

High Rate of Biphasic Reactions in Children with Anaphylaxis

IN biphasic anaphylactic reactions, symptoms of anaphylaxis recur after an initial remission. The reported rate of biphasic reactions in adults ranges from 5% to 20%, but no studies have addressed this issue in children. This study examined the incidence of biphasic reactions in children with anaphylaxis, risk factors for this occurrence, and the need for inpatient observation after apparent resolution of an anaphylactic episode.

The 14-year retrospective study included a total of 108 anaphylactic episodes in 106 pediatric inpatients. The study definition of episode resolution was cessation of all symptoms of anaphylaxis with no need for therapy for at least 1 hour. If resolution was followed by worsening of symptoms requiring new treatment, a biphasic reaction was said to be present. Biphasic reactions requiring oxygen, vasopressors, intubation, subcutaneous epinephrine, or unscheduled bronchodilator administrations were considered significant.

There was a 2% rate of fatal anaphylaxis and a 1% rate of protracted anaphylactic reactions. Nearly two-thirds of patients had clinical evidence of atopy; the median age was 8 years. Food was the most common trigger, usually peanuts, tree nuts, or seafood. Seventy-eight percent of patients had upper airway symptoms and 30% had cardiovascular symptoms. The mean time from symptom onset to first treatment with subcutaneous epinephrine in 75 patients was 113 minutes. Of 105 episodes with documented resolution, 6% were classified as biphasic. The biphasic reactions occurred 6 to 48 hours after initial symptom onset, with an asymptomatic interval ranging from 1 to 28 hours. In addition to subcutaneous epinephrine, 5 of the 6 patients with biphasic reactions had received steroids during the initial episode. In each case, the biphasic reaction involved the same organ system as the initial reaction; in 1 case, the biphasic reaction was more severe than the initial reaction. The patients with biphasic reactions had a longer interval between symptom onset and epinephrine treatment than those without biphasic reactions.

For children admitted with anaphylactic reactions, the incidence of significant biphasic reactions is about 3%. Such reactions appear more common when initial epinephrine treatment is delayed, and they are not prevented by steroids. The results suggest that a 24-hour period of observation after resolution of the initial anaphylactic episode will be beneficial for about 2% of children.

COMMENT: *This retrospective analysis of anaphylaxis in a pediatric population is the first study to address biphasic reactions in this age group. Of 105 anaphylactic episodes that resolved, 6% went on to exhibit a biphasic reaction. Three percent of biphasic reactions were considered significant, with symptom onset ranging between 1.3 to 28.4 hours. Delayed administration of epinephrine was associated with an increased incidence of biphasic reactions. Administration of corticosteroids did not appear to suppress onset of biphasic reactions.*
J. B.-M.
Lee JM, Greenes DS: Biphasic anaphylactic reactions in pediatrics.
Pediatrics 106:762-766, 2000. ♦♦

Study Finds 0.12% Rate of Systemic Reactions to Penicillin Skin Tests

SKIN testing for penicillin allergy is generally regarded as a safe procedure. This study examined the rate of systemic reactions to penicillin skin tests performed in 1,710 patients from 1992 to 1999. All patients had a history of penicillin allergy. Testing began with a skin prick; if negative, intradermal tests were performed.

Penicillin skin tests were positive in 86 patients. Two had systemic reactions. Thus the systemic reaction rate was 0.12% overall and 2.3% for patients with positive skin-test results. Both systemic reactions were managed successfully; neither patient died.

In patients with a history of penicillin allergy undergoing penicillin skin tests, the risk of systemic reactions is low. Testing should always start with a skin prick. If the patient's previous reaction to penicillin was a serious one, testing should start with a dilute solution, if performed at all. Clinicians performing penicillin skin testing should be prepared to manage systemic reactions.

COMMENT: *Penicillin allergy remains a diagnostic and therapeutic challenge for all physicians. Skin testing has been demonstrated in multiple studies to have high diagnostic sensitivity and specificity for predicting severe anaphylactic responses. In this study, the authors peer-review their experience with 1,710 patients who were skin-tested over 7 years. Although the frequency of systemic reactions was 0.12%, the authors point out the need for testing to be done in settings in which systemic reactions can be adequately recognized and treated.*
A. M.
Valyasevi MA, Van Dellen RG: Frequency of systematic reactions to penicillin skin tests.
Ann Allergy Asthma Immunol 85:363-365, 2000. ♦♦

Influenza Vaccination of Day Care Children Also Prevents Illness in Family Members

THE growing number of children in day care are at increased risk of various forms of illness, notably influenza. These young children are likely to transmit respiratory illnesses to other members of their household, so measures to reduce or prevent such transmission would be beneficial. The effects of influenza vaccination of day care children on the rate of household transmission of influenza-related morbidity were analyzed.

The analysis was based on a randomized, controlled trial of 149 children, aged 24 to 60 months, who were attending day care. All were children of U.S. Navy personnel, who were required to receive influenza vaccine. Sixty children received inactivated influenza vaccine; the remaining 67 children received hepatitis A vaccine as a control. Information on febrile respiratory illnesses and related morbidity among other members of the household was gathered in telephone interviews.

As reported previously, vaccination effectively reduced the risk of serologically confirmed influenza virus infection. The rate of febrile respiratory illnesses was reduced by 42% among nonvaccinated contacts of influenza-vaccinated children, compared with unvaccinated contacts of control children. For school-aged contacts of the vaccinated children, the rate of febrile respiratory illnesses was reduced by 80%. Reductions of greater than 70% were noted in missed school days, earaches, physician visits, antibiotic prescriptions, and missed work days due to caring for sick children.

Influenza vaccination of day care children prevents morbidity not only in the children themselves but also in their household contacts. The benefits in terms of reduced morbidity are particularly noteworthy for school-aged contacts. Programs of vaccination for children attending day care might significantly reduce the burden of respiratory illness and exposure to antibiotics among their family members at home.

COMMENT: *The importance of influenza vaccination in older adults and asthmatics is frequently emphasized. Previous studies show a reduction in antibiotic use and otitis media in day care-attending children who are vaccinated for influenza. This paper demonstrates a reduction in febrile respiratory illness in household contacts—particularly 5- to 17-year-old siblings—of vaccinated day care attendees. Although the study is small, these statistically significant beneficial effects were achieved in military families in which at least one adult in each household also received the influenza vaccine. The benefits of administering influenza vaccine to day care children would likely be greater if the adults were not vaccinated. This point is particularly important if any of the family members are at increased risk for otitis media, pneumonia, or asthma.*

D. K. L.

Hurwitz ES, Haber M, Chang A, et al: Effectiveness of influenza vaccination of day care children in reducing influenza-related morbidity among household contacts.
JAMA 284:1677-1682, 2000. ♦♦

Effects of Disease Duration Studied in Elderly Asthma Patients

IN patients with chronic asthma, persistent airway inflammation leading to recurrent injury and repair is thought to result in distortion and remodeling of the bronchial architecture. Elderly patients with asthma may have durations of disease ranging from months to decades, providing an ideal population for study of the effects of asthma duration on remodeling of the airway or parenchyma. The impact of duration of asthma on airflow limitation and hyperinflation was studied in a group of elderly, nonsmoking patients with asthma.

The study included 75 asthma patients who were older than 60 years and were lifetime nonsmokers. Thirty-eight patients had long-duration asthma (LDA), present for 26 years or longer (median 40 years); 37 had short-duration asthma (SDA), present for less than 26 years (median 9 years). Age at onset varied significantly, with a median of 40 years. Most patients in both groups were classified as having severe, persistent asthma. Airflow and lung volumes were measured in all subjects, and correlated with duration of asthma.

Mean FEV_1% predicted was 59.5% in the LDA group vs 73.8% in the SDA group. Patients with LDA continued to have obstructed airflow even after bronchodilator treatment, with a mean FEV_1% predicted of 65.4%. Postbronchodilator FEV_1 was normal in just 18% of the LDA group vs 50% of the SDA group. Percentage of predicted functional residual capacity was also significantly higher in LDA patients, an association that was independent of the degree of limitation of airflow.

In elderly patients with chronic asthma and no history of smoking, the duration of asthma is directly related to the extent of airflow limitation and hyperinflation. The findings support the hypothesis that long-standing asthma causes irreversible airway changes, and that remodeling of the distal airways or parenchyma is involved in this process. Elderly asthma patients also show significant loss of elastic recoil, the mechanisms of which are uncertain. Years of persistent airway inflammation lead to airway remodeling and thus to fixed airway obstruction.

COMMENT: *However, results here don't tell us how often this occurs in the general population of asthmatics. Most patients in this study had severe persistent asthma. It is notable that the patients with onset of asthma early in life were no more likely to be atopic than individuals with late-onset disease.*

J. R. B.

Cassino C, Berger KI, Goldring RM, et al: Duration of asthma and physiologic outcomes in elderly nonsmokers.
Am J Respir Crit Care Med *162:1423-1428, 2000.* ♦♦

Exercise-Induced Bronchoconstriction Does Not Cause Airway Inflammation

THE cysteinyl leukotrienes C_4, D_4, and E_4 may play an important role in asthmatic airway inflammation. Leukotriene production plays a role in the development of exercise-induced bronchoconstriction in asthma patients, but it is unclear whether this leads to airway inflammation. The effects of exercise-induced bronchoconstriction on inflammatory cells were studied.

The randomized study included 10 nonsmoking patients with mild asthma, with a methacholine PC_{20} of less than 2 mg/ml or a history of exercise-induced bronchoconstriction. On 2 occasions 1 week apart, the patients performed an exercise challenge and underwent a methacholine challenge. On both occasions, spirometry was measured for 2 hours after the challenges and airway hyperresponsiveness was assessed the day before and after. In addition, inflammatory cells were measured in blood and sputum samples. The response to a separate allergen challenge was assessed in 9 patients.

The peak percentage decline in FEV_1 was 21.3% after exercise challenge, 29.9% after methacholine challenge, and 28.9% after allergen challenge. Airway hyperresponsiveness and sputum eosinophils increased significantly after allergen exposure. In contrast, exercise challenge caused no changes in airway responsiveness or blood or sputum inflammatory cells.

This study finds no evidence of airway inflammation in response to exercise bronchoconstriction in patients with mild asthma. This is despite the fact that the same subjects show significant inflammation in response to a similar extent of bronchoconstriction induced by allergen.

COMMENT: *Exercise has no effect on methacholine sensitivity, the total number of cells in sputum, or the portion of cells identified as eosinophils or metachromatic (mast cells or basophils). This is good news. If exercise caused airway inflammation, the implication would be that regular exercise might make asthma worse.*
J. R. B.

Gauvreau GM, Ronnen GM, Watson RM, O'Byrne PM : Exercise-induced bronchoconstriction does not cause eosinophilic airway inflammation or airway hyperresponsiveness in subjects with asthma.
Am J Respir Crit Care Med 162:1302-1307, 2000. ♦♦

Is Indoor Allergen Exposure Related to Childhood Asthma?

ENVIRONMENTAL factors, such as increased exposure to indoor allergens, may play a role in the rising prevalence of asthma and atopy. However, at least one retrospective study found no significant association between cat exposure and asthma. A prospective birth cohort study was performed to evaluate the relationship between exposure to mite and cat allergen and development of childhood asthma.

The study included 939 children from a German 1990 birth cohort who were available for follow-up at age 7 years. In regular evaluations starting at 1 month of age, the children underwent measurement of specific IgE to food and inhalant allergens. Indoor allergen levels were measured at 6 months, 18 months, and 3 years. Parents were interviewed regarding symptoms of asthma or atopy. Six hundred forty-five children underwent tests of pulmonary function and bronchial hyperresponsiveness.

Children available for follow-up were more likely to have nonsmoking and better-educated parents. At age 7, 10% percent of children had a history of wheezing in the past 12 months and 6% had a physician diagnosis of asthma. Mite and cat allergen levels were similar for families with and without a history of asthma or atopy. Cat ownership was not related to the 12-month prevalence of wheezing or to bronchial hyperresponsiveness. Children who were sensitized in indoor allergens were more likely to have asthma, wheezing, and bronchial hyperresponsiveness. However, exposure to indoor allergens during early childhood was unrelated to any of these outcomes.

Added to previous epidemiologic studies, the findings do not support the hypothesis that cat and mite allergen exposure play a role in the development of childhood asthma. Other factors are probably responsible for the induction of specific IgE responses and development of wheezing and asthma during childhood. The authors note that the indoor allergen levels measured in this study were relatively low, compared to areas with higher levels of mite infestation and asthma.

COMMENT: *Allergic sensitization has been identified as a risk factor for persistent asthma. However, it remains unclear whether the onset of asthma is increased by exposure to allergens early in life or prevented by avoidance. Lau et al. selected a cohort in which 62% of the subjects were not at high risk for atopy. They found that exposure to indoor allergens was related to sensitization, but not to an increased prevalence of asthma.*
E. J. B.

Lau S, Illi S, Sommerfeld C, et al: Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study.
Lancet 356:1392-1397, 2000. ♦♦

Chronic Rhinosinusitis Linked to Cystic Fibrosis Gene

CHRONIC rhinosinusitis (CRS) is a very common chronic disease of uncertain cause. Patients with the autosomal recessive disease cystic fibrosis (CF) almost always have CRS. This study assessed the presence of mutations in the cystic fibrosis transmembrane regular (CFTR) gene—the causative mutation of CF—among patients with CRS.

The study included 147 consecutive white, adult patients meeting strict diagnostic criteria for CRS, including nasal or sinus symptoms present for ➤➤

longer than 8 weeks. Genomic DNA samples were tested for the presence of 16 mutations representing 85% of CF alleles in the general population. One hundred twenty-three matched volunteers without CRS were studied for comparison.

A CF allele was identified in 11 patients with CRS, mainly the ΔF508 mutations. On further testing, the diagnosis of CF was excluded in 10 of these patients. The remaining patient was diagnosed as having CF. Excluding this patient, the prevalence of a CF mutation was 7% in the CRS patients vs 2% in controls. In addition, most CRS patients with CF mutations also had variants in their other CFTR gene.

The CFTR gene is found with increased frequency among patients with CRS. The findings provide a possible genetic basis for a very common clinical condition. The CFTR gene plays a key role in the normal function of the sinus epithelium, which accounts for the chronic sinus disease seen in patients with CF.

COMMENT: *The challenge of caring for many subjects with chronic or recurrent rhinosinusitis is compounded by the frequent lack of explanation for the condition's cause. Generally, if allergy, humoral immunodeficiency, cigarette smoke exposure, and structural abnormalities are excluded, the clinician proffers the idiopathic, or "bad luck," hypothesis. This paper describes the increased prevalence for carrying a cystic fibrosis gene in chronic rhinosinusitis subjects. The odds ratio of having a cystic fibrosis allele for patients with chronic rhinosinusitis compared with normals is 4.9. The mechanism by which a recessive, single gene results in clinical disease is unknown. However, a novel molecular insight into such a common clinical condition will suggest other strategies of investigation.*
D. K. L.
Wang X, Moylan B, Leopold DA, et al: Mutation in the gene responsible for cystic fibrosis and predisposition to chronic rhinosinusitis in the general population.
JAMA 284:1814-1819, 2000. ♦♦

Study Finds High Rates of Steroid Side Effects in Children with Severe, Persistent Asthma

CHILDREN with severe, persistent asthma are treated with high-dose inhaled glucocorticoids (GCs), sometimes in addition to regular oral GCs. Few studies have addressed the rate of steroid side effects in this group of patients. The investigators assessed GC-induced adverse effects in a group of 163 consecutive children with severe, persistent asthma. All were at least 9 years old, median age 14 years. They were receiving inhaled GCs at a mean dose of 1,675 μg/d, plus an average of 6 systemic GC bursts per year. About half of the patients were receiving chronic oral GC therapy. Mean age at starting systemic GC therapy was 7 years.

Adverse effects of GC therapy were very common, including hypertension in 88% of patients, cushingoid features in 66%, adrenal suppression in 56%, myopathy in 50%, osteopenia in 46%, growth suppression in 39%, and obesity and hypercholesterolemia in 30%. Adverse effects were frequent in patients who were and were not receiving chronic oral CGs. The use of alternative-day dosing did not appear to reduce the rate of adverse effects compared with daily GC therapy. The subjects' mean height corresponded to the 37th percentile for males and the 33rd for females, and osteopenia was strongly associated with growth suppression. Patients with growth suppression and delayed bone age were more likely to develop cataracts.

Children and adolescents with severe, persistent asthma have unacceptably high rates of GC-induced adverse effects. Osteopenia is a major problem, especially in girls. Growth suppression remains common, though the magnitude of suppression is less than a few decades ago. This finding suggests that the use of high-dose inhaled GCs, by improving asthma control, has reduced the adverse effects of poorly controlled asthma on growth.

COMMENT: *This retrospective review of the most severe cases of steroid-dependent asthma in children admitted to National Jewish Medical and Research Center over a 5-year period examined the incidence of steroid-associated side effects. The prevalence of side effects—including hypertension, cushingoid features, adrenal suppression, osteopenia, growth suppression, and cataracts—was high in children treated with high-dose inhaled GCs, with or without regular use of oral GCs. There was a suggestion that patients with significant growth suppression also had delayed bone age and cataracts. These data emphasize the importance of closely monitoring corticosteroid side effects in young asthmatic patients who require this therapy.*
S. M. F.
Covar RA, Leung DYM, McCormick D, et al: Risk factors associated with glucocorticoid-induced adverse effects in children with severe asthma.
J Allergy Clin Immunol 106:651-659, 2000. ♦♦

Clinical Pathway Improves Outcomes for Hospitalized Children with Asthma

CLINICAL pathways offer a promising approach to enhancing compliance with current guidelines for asthma treatment. However, few studies have assessed how clinical pathways affect patient outcomes. The authors recently developed a pathway to improve compliance with treatment recommendations for inpatients with asthma. Main features included nurse-driven guidelines for weaning from bronchodilators, regular peak flow measurement, and measures to enhance asthma education, home therapy, and coordination of care. This study evaluated the effects of the clinical pathway on various outcomes for pediatric inpatients with asthma.

The randomized, controlled trial included 110 children and adolescents who were hospitalized for treatment of an asthma exacerbation and were not currently under the care of an asthma specialist. Patients assigned to one ward received care according to ➤➤

the clinical pathway, while patients assigned to another ward received usual care. The two groups had similar demographic characteristics and asthma severity profiles. Outcomes compared included length of hospital stay, amount of bronchodilator therapy, and frequency of readmission within 2 weeks after discharge.

Mean duration of hospitalization was 40 hours for patients managed according to the clinical pathway vs 54 hours for those receiving usual care. Thirty-eight percent of patients on the clinical pathway were discharged within 24 hours after admission, compared with 15% in the control group. At each dosing interval, patients on the clinical pathway received less nebulized β-agonist therapy. There were no deaths and no readmissions within 2 weeks.

This study documents improved patient outcomes with a clinical pathway for inpatient pediatric asthma care. The pathway safely reduces length of hospital stay, overall nebulized β-agonist use, and overall cost of care. The study—the first to show the effect of an asthma clinical pathway on length of stay—underscores the value of following current asthma treatment guidelines, customized for the care setting.

COMMENT: *Clinical pathways have been developed for a number of diseases including asthma. Evaluation of such pathways generally is confined to measurement of compliance, without considering whether or not the patient actually benefits from the treatment. Last summer an article in* Pediatrics *(105:767-773, 2000) demonstrated that when one pathway for treating asthmatics in the ED was actually followed, the outcomes were worse than when it was not followed. The current study evaluates an inpatient pathway and demonstrates that when it is followed, length of stay and the number of nebulizer treatments are decreased. Though this is what one would hope to observe in such studies, it should not be summarily assumed that clinical pathways improve patient outcomes until they have been subjected to rigorous testing.*
J. M. P.

Johnson KB, Blaisdell CJ, Walker A, Eggleston P: Effectiveness of a clinical pathway for inpatient asthma management. **Pediatrics** 106:1006-1012, 2000. ♦♦

Combined Mediator Blockade vs Topical Budesonide for Allergic Rhinitis and Asthma

In patients with persistent asthma, combined mediator blockade—including both histamine and leukotriene receptor antagonists—improved symptom control compared with a leukotriene receptor antagonist alone. However, combined mediator blockade has never been compared with topical steroid therapy. This study compared combined histamine and leukotriene receptor antagonists with combined inhaled and intranasal corticosteroids in patients with seasonal allergic rhinitis (SAR) and asthma.

The placebo-controlled, double-dummy, single-blind study included 14 patients with SAR and asthma with bronchial hyperreactivity. They were randomized to receive orally inhaled budesonide, 400 μg, with intranasal budesonide, 200 μg; or oral montelukast, 10 mg, plus oral cetirizine, 10 mg. All treatments were given once daily in the morning for 2 weeks; the study was conducted during pollen season. At the end of the treatment, there was a 1-week washout period, after which patients were crossed over to the other treatment. Laboratory and domiciliary measures were compared between groups.

Mean peak expiratory flow was 478 L/min with budesonide and 483 L/min with combined mediator blockade, compared with 463 L/min with placebo. Geometric mean adenosine monophosphate PC_{20} was 133 mg/mL with mediator blockade, compared with 51 mg/mL with budesonide and 47 mg/mL with placebo. Exhaled nitric oxide was reduced to 7.6 ppb with budesonide vs 11.5 ppb for combined mediator blockade and 13.6 ppb for placebo. Both active treatments brought significant improvement in symptoms and rescue inhaler use.

For patients with SAR and asthma, topical corticosteroids and combined histamine and leukotriene receptor antagonists are equally effective antiasthma therapy. Topical budesonide suppresses exhaled NO but does not offer bronchoprotection in response to adenosine monophosphate challenge, whereas combined mediator blockade has the opposite effects. A wide range of variables will affect the choice between these two forms of antiasthma therapy.

COMMENT: *Corticosteroids are considered to be the ultimate anti-inflammatory agents for treatment of asthma and allergic rhinitis. This is believed to be because they block a large number of inflammatory mediators. Because steroids may be associated with significant adverse effects, more specific mediator blockade using presumably safer agents, if equally effective, could offer substantial benefits. This study compared inhaled and nasal budesonide with montelukast combined with cetirizine. The combination improved adenosine PC_{20}, while budesonide reduced exhaled nitric oxide. Both regimens improved physiologic parameters of asthma and rhinitis. Since the long-term outcomes of mediator blockade are unknown, corticosteroids must still be considered the most effective treatment. However, further investigation of combination treatment may eventually remove corticosteroids from their pedestal.*
J. M. P.

Wilson AM, Orr LC, Sims EJ, et al: Antiasthmatic effects of mediator blockade versus topical corticosteroids in allergic rhinitis and asthma.
Am J Respir Crit Care Med 162:1297-1301, 2000. ♦♦

"Artificial Season" Model Shows Dose-Response Effect of Budesonide for Allergic Rhinitis

ALTHOUGH the clinical efficacy of topical glucocorticoids for allergic rhinitis is well demonstrated, it has been difficult to show any dose-response relationship. Part of the problem is the variability in onset, duration, and intensity that is characteristic of seasonal allergic rhinitis. Using nasal allergen challenges to create an artificial "allergy season," the authors compared the efficacy of two different doses of topical budesonide.

The study, performed outside of allergy ➤➤

season, included 25 patients with seasonal allergic rhinitis. Patients were randomized to receive the lowest and highest clinically recommended doses of budesonide aqueous nasal spray—64 and 256 µg/d, respectively—for 2 weeks. After 1 week, the patients received individually titrated nasal allergen challenges once daily for 8 days. The challenges consisted of birch or timothy allergen, given in increasing doses to produce a specified symptom response. The patients recorded nasal symptoms in diary cards, with analysis of symptoms on challenge days 6 to 8. The patients were studied on all three treatments in crossover fashion, with a 4 week washout period between treatments.

The allergen challenges induced clinically relevant, tolerable rhinitis symptoms. Within several days, a transient allergic condition similar to allergic rhinitis was established. Both doses of budesonide reduced nasal symptoms. Total nasal symptom score decreased from 5.19 to 4.23 with budesonide 64 µg, and to 3.41 with budesonide 256 µg, demonstrating a dose-dependent effect.

This model of artificial seasonal rhinitis demonstrates a dose-dependent effect of intranasal budesonide at clinically relevant doses. The model may be useful in examining the pharmacology of mucosal inflammation in allergic rhinitis. Although both high-dose and low-dose budesonide are effective, the higher dose offers greater symptom-reducing effects.

COMMENT: *The majority of clinical trials using inhaled or intranasal corticosteroids cannot demonstrate a dose-response relationship. Comparisons among the various corticosteroids are consequently limited by the inability to define clearly the equivalent efficacy dose or clinical potency. A reproducible model in which a dose-response to corticosteroids could be demonstrated would make it possible to compare and more accurately titrate the dose of inhaled/nasal corticosteroid. The authors of this paper describe a daily, allergen-challenge nasal model that demonstrates a dose-response for intranasal corticosteroid. If this model performs similarly for other investigators, it could provide a relatively straightforward means of comparing a variety of therapies and dosages in the management of allergic respiratory disease.*
D. K. L.
Andersson M, Svensson C, Persson C, et al: Dose-dependent effects of budesonide aqueous spray on symptoms in a daily nasal allergen challenge model. **Ann Allergy Asthma Immunol** 85:279-283, 2000. ♦♦

Patients Can't Predict Positive Skin Test Results

THERE are few data on the accuracy of the medical history—including the patient's perception of the problem—in diagnosing allergic disease. This contributes to the difficulty of making a clinical diagnosis of allergy. Eighty-six patients with chronic rhinitis or asthma were studied for their ability to predict the results of skin testing to aeroallergens. Before testing, the patients were asked which allergens they expected to give positive results. Seventy-three patients provided usable responses for comparison with the actual skin test results.

Fifty-six percent of patients with a positive skin test for cat allergen correctly predicted this result. For other allergens, the percentage of correct predictions was lower: 29% for tree, 27% for weeds, 22% for dust mite, 17% for grass, and 12% for mold. The patients were much better able to predict negative results of skin testing for the same allergens, ranging from 94% for dust mite to 81% for weeds.

Allergy patients can accurately predict those allergens to which they will have a negative result, but not a positive result. Asking patients what they think they are allergic to may be a useful screening question. However, allergy testing is needed to confirm the diagnosis.

COMMENT: *In this brief report the authors reinforce the value of skin testing in establishing the diagnosis of allergic disease. It appears that while patients are reasonably accurate in predicting negative results, they have limited ability to predict positive results to aeroallergens.*
A. M.
Li JTC, Andrist D, Bamlet WR, Wolter TD: Accuracy of patient prediction of allergy skin test results. Ann **Allergy Asthma Immunol** 85:382-384, 2000. ♦♦

Powdered Latex Gloves Cause Allergen Dispersion in Health Care Settings

ALLERGIC sensitization to natural rubber latex is an important occupational health problem in health care workers. Personal avoidance of latex has been recommended for affected workers. The authors recently encountered a dental assistant who experienced worsening asthma despite following personal avoidance measures. They sought to identify the source of latex aeroallergen in this case, including the effects of switching to a nonpowdered, low-aeroallergen latex glove at the study site.

In a small dental practice, volumetric air sampling was performed to measure baseline latex aeroallergen levels in rooms where the latex-allergic patient did and did not work, as well as in common areas. Samples of upholstery fabric, dust from ventilation ducts, and latex gloves were studied as well. During the work day, the patient's work areas had latex aeroallergen levels of 6 to 25 ng/m^3, while other rooms had levels of 29 to 90 ng/m^3. Latex antigen was identified in various brands of powdered latex gloves used in other rooms, as well as in upholstery fabric and carpet dust. When the entire practice switched over to using nonpowdered latex gloves—without any other control measures—the airborne latex level become undetectable.

Powdered latex gloves appear to be the major source of latex aeroallergen in health care settings. The allergen can disperse from areas in which such gloves are used to other areas, including nonpatient care areas and rooms in which latex precautions are observed. Exclusive use of nonpowdered latex gloves can promptly eliminate latex aerosol. ➤➤

COMMENT: *This study illustrates the importance of eliminating the use of powdered latex gloves. Volumetric air sampling verified clinically significant, airborne latex concentrations in work areas of a dental office building in which latex was not used. The allergen was transferred from work areas in which powdered latex gloves were used. Carpet and upholstered furniture also may be a repository for the latex allergen. Latex continues to be an important clinical problem.*
D. K. L.
Charous BL, Schuenemann PJ, Swanson MC: Passive dispersion of latex aeroallergen in a healthcare facility. **Ann Allergy Asthma Immunol** 85:285-290, 2000. ♦♦

Inhaled Zanamivir Prevents Influenza in Family Members

AMANTADINE and rimantadine have been tried for postexposure prevention of influenza for family members of an affected patient. However, studies have shown inconsistent protective effects, partly because of drug-resistant influenza virus variants. Zanamivir, a selective inhibitor of influenza A and B virus neuraminidases, was studied for use in the treatment and prevention of influenza in households with an affected member.

Seven hundred ninety-nine families were entered into a prospective influenza surveillance protocol. If any family member developed an influenza-like illness, all members of that family were randomized to receive either inhaled zanamivir or placebo. The zanamivir dosage was 10 mg twice daily for 5 days in affected patients, and 10 mg once daily for 10 days in the other family members. One hundred sixty-three index patients received zanamivir and 158 placebo; in both groups, more than 400 family members were treated.

The two groups of families were similar in their baseline characteristics. Influenza developed in 1 or more previously healthy members of the household in 4% of families assigned to zanamivir vs 19% of families assigned to placebo. Zanamivir appeared to be effective against both influenza A and B. For index patients, zanamivir shorted the time to symptom relief by 2.5 days.

Inhaled zanamivir appears effective in preventing influenza in initially healthy family members of index patients. Treatment reduces the risk of spreading influenza by 79% and is well tolerated. There are no apparent problems with emergence of resistant strains.

COMMENT: *The supply of influenza vaccine and its delivery date have been suboptimal this season. Other strategies may be needed if there is an epidemic. Secondary spread may cause 25% to 50% of household members to acquire the infection. In this placebo-controlled study, chemoprophylaxis with inhaled zanamivir provided a 79% rate of protection. No resistant strains emerged. Treatment of household members was started within 36 hours after the onset of symptoms in the index patient.*
R. J. M.
Hayden FG, Gubareva LV, Monto S, et al: Inhaled zanamivir for the prevention of influenza in families. **N Engl J Med** 343:1282-1289, 2000. ♦♦

Do Antiasthma Medications Affect the Response to Inhaled Endotoxin?

BACTERIAL endotoxin is a proinflammatory contaminant of dust, and has been linked to the development of chronic obstructive pulmonary disease and atopic asthma. Inhaled endotoxin produces bronchial hyperresponsiveness in humans, among other effects. The authors examined the impact of giving antiasthma medications on the responses to inhaled endotoxin.

The study included 12 patients with mild asthma, who underwent a weekly bronchial challenge with endotoxin, 20 μg. This challenge produced a significant drop in FEV_1 and in luminol-enhanced chemiluminescence, a measure of neutrophil activation. Significant increases occurred in blood neutrophil count, C-reactive protein, and haptoglobin. The response to endotoxin challenge was unchanged by pretreatment with beclomethasone dipropionate. The reduction in FEV_1 was completely prevented by the bronchodilators salbutamol and salmeterol.

Pretreatment with β_2-agonists prevents reductions in lung function caused by endotoxin inhalation in patients with asthma. However, inhaled corticosteroid does not alter the endotoxin-induced inflammatory response. The results may have important implications for occupational settings with high levels of endotoxin contamination.

COMMENT: *Endotoxin is a substance in inhaled dust potentially contributing to respiratory symptoms, particularly lower-airway disease. This small asthma study shows that a single, moderate dose of inhaled corticosteroid, administered prior to challenge, does not affect the peripheral blood neutrophil activation or airway obstruction resulting from inhaled endotoxin. One could postulate that endotoxin-induced inflammation may amplify airway inflammation in asthma, and this inflammatory augmentation may be corticosteroid resistant. However, multiple doses of inhaled corticosteroid may have beneficial effects. As usual, more questions arise from more information.*
D. K. L.
Michel O, Olbrecht J, Moulard D, Sergysels R: Effect of anti-asthmatic drugs on the response to inhaled endotoxin. **Ann Allergy Asthma Immunol** 85:305-310, 2000. ♦♦

Airway Hyperresponsiveness Linked to COPD Mortality

THIS study examined the relationship between airway hyperresponsiveness and all-cause and cause-specific mortality, including the effects of smoking and reduced lung function. It used histamine challenge ➤➤

test data on 2,008 residents of three Dutch communities, followed up for 30 years starting in 1964-72. Follow-up was 99% complete.

At baseline, 31% of subjects had histamine airway hyperresponsiveness, a finding that was associated with older age, heavier smoking, lower lung function, higher body mass index, and more respiratory symptoms. Mortality from chronic obstructive pulmonary disease (COPD) was higher for subjects with higher levels of airway hyperresponsiveness, in dose-dependent fashion. This relationship was stronger among subjects who smoked. However, even among never-smokers, COPD mortality was higher at higher levels of hyperresponsiveness. Relative risks of COPD mortality at differing histamine thresholds were 3.83 at 32 g/L, 4.40 at 16 g/L, 4.78 at 8 g/L, 6.69 at 4 g/L, and 15.8 at 1 g/L.

These long-term follow-up data suggest that airway hyperresponsiveness plays a significant role in mortality from COPD, even in nonsmokers. Given the high population prevalence of hyperresponsiveness, the results have important implications for COPD mortality. More research is needed to identify determinants of histamine airway hyperresponsiveness and its prevention.

COMMENT: *This large Dutch study followed over 2,000 inhabitants of three communities with histamine challenge data for 30 years. It found airway hyperresponsiveness was a risk factor for the development of respiratory symptoms (asthma and COPD) and decline of FEV_1, independent of other risk factors such as smoking or low lung function. Of special import was the observation that airway hyperresponsiveness was associated with increased mortality from chronic obstructive pulmonary disease.*
E. J. B.

Hospers JJ, Postma DS, Rijcken B, et al: Histamine airway hyper-responsiveness and mortality from chronic obstructive pulmonary disease:a cohort study.
Lancet 356:1313-1317, 2000. ♦♦

Exhaled NO Does Not Reflect Sputum Eosinophilia

EXHALED nitric oxide (eNO) has been investigated as a marker of airway inflammation in asthma and other airway diseases. Few studies have addressed the relationship between eNO and more direct measures of airway inflammation. Exhaled nitric oxide was compared with sputum eosinophils and airway function in patients with asthma, atopy, and eosinophilic bronchitis.

The study included two groups of healthy subjects, 28 with and 22 without atopy; two groups of asthma patients, 38 of whom were taking inhaled steroids and 35 who were not; and 8 nonasthmatic patients with eosinophilic bronchitis. The association between eNO and sputum eosinophil count was assessed, along with the ability of these 2 measurements to distinguish healthy subjects from the disease groups.

The non-steroid-treated asthma patients and healthy atopic controls showed a weak but significant correlation between eNO and eosinophil differential counts. Among asthma patients, eNO was significantly lower in the steroid-treated group, even though there was no difference in sputum cell counts. Exhaled nitric oxide and sputum eosinophils performed equally well in distinguishing steroid-naive asthma patients from healthy controls. The patients with eosinophilic bronchitis had consistently high levels of eNO.

In steroid-treated asthma patients, eNO is poorly correlated with sputum eosinophil count. Exhaled NO does not appear to be a useful clinical marker of the presence or severity of eosinophilic airway inflammation. A high eNO level appears to reflect other components of airway inflammation that are not indicated by sputum cell counts or physiologic measures.

COMMENT: *We are confident that we have effective "anti-inflammatory" medication for asthma. But how do we know which patients are "inflamed," and by how much. How can we measure the anti-inflammatory activity of the medication? When can we cut back? It would be convenient to have a noninvasive marker of airway inflammation. This study found only a weak correlation of exhaled nitric oxide (eNO) with sputum eosinophilia. Exhaled nitric oxide did not correlate with methacholine responsiveness. It was lower in patients on inhaled corticosteroid treatment, but at the same time they had worse FEV_1. Atopy had no effect on eNO levels in nonasthmatic subjects. The search for a good noninvasive marker of airway inflammation must go on.*
R. J. M.

Berlyne GS, Parameswaran K, Kamada D, et al: A comparison of exhaled nitric oxide and induced sputum as markers of airway inflammation.
J Allergy Clin Immunol 106:638-644, 2000. ♦♦

Adjunctive Steroid Nasal Spray Is Beneficial in Acute Sinusitis

INTRANASAL glucocorticoids are an established therapy for allergic rhinitis and are commonly recommended as an adjunctive treatment for sinusitis. However, few controlled trials have examined the effectiveness of nasal corticosteroids for acute sinusitis. The effects of adding intranasal corticosteroids to oral antibiotics for the treatment of acute sinusitis were investigated.

The randomized trial included 407 patients, aged 12 years or older, with a history of acute recurrent sinusitis and a new episode of acute sinusitis. All received 21 days of treatment with oral amoxicillin clavulanate potassium. In addition, they were randomized to receive mometasone furoate nasal spray (MFNS), 400 µg twice daily, or placebo spray. Symptom scores were recorded at baseline and throughout treatment.

At baseline, both groups had a similar and moderately severe level of symptoms. Patients receiving adjunctive MFNS had a significantly greater reduction in total symptom score. Analysis of individual symptoms suggested that the added steroid was effective ➤➤

mainly in reducing inflammatory symptoms related to the obstructive process: headache, congestion, and facial pain. In contrast, MFNS had relatively little effect on symptoms related to secretory processes: rhinorrhea, postnasal drip, and cough. The addition of MFNS did not significantly increase the rate of local adverse events.

In patients with acute sinusitis, adding MFNS to oral antibiotic therapy has significant benefit in reducing symptoms. The findings support current recommendations regarding the adjunctive use of intranasal corticosteroids for acute episodes of sinusitis.

COMMENT: *This multicenter randomized, double-blind, placebo-controlled trial showed significant additional benefit with the intranasal corticosteroid mometasone for patients treated for acute sinusitis. They all received three weeks of amoxicillin clavulanate but no decongestants were permitted. Patients receiving the intranasal corticosteroid reported significantly better symptom relief, particularly in those symptoms relating to swelling such as congestion, headache, and facial pain. Symptoms associated with secretion processes—such as rhinorrhea, postnasal drip, and cough—improved similarly with both placebo and corticosteroid treatment.*
S. M. F.

Meltzer EO, Charous L, Busse WW, et al: Added relief in the treatment of acute recurrent sinusitis with adjunctive mometasone furoate nasal spray.
J Allergy Clin Immunol 106:630-637, 2000. ♦♦

REVIEWS OF NOTE

Ziment I, Tashkin DP: Alternative medicine for allergy and asthma. **J Allergy Clin Immunol** 106:603-614, 2000.

COMMENT: *It is well documented that a sizable segment of the American population has a fascination with "alternative" therapies. Many of these rely on substances (herbs and the like) that may have pharmacologic properties; others are likely to have appeal through purely psychologic mechanisms. This 10-page review nicely covers the therapies, and appropriately recommends that all physicians be familiar with them. I am still waiting for the explanation why any rational being would choose a "crocodile bile pill for asthma" over proven orthodox drug therapy.*
R. J. M.

von Andrian UH, Mackay CR: T-cell function and migration: two sides of the same coin.
N Engl J Med 343:1020-1034, 2000.

COMMENT: *T-lymphocytes are like automobiles: very powerful agents of help or harm, depending on the directions provided by the driver. How do T-cells know where to go? The answer lies in the molecular immunology of T-cell recruitment via chemoattraction and adhesion molecules. This 12-page summary of T-cell migration is a wonderful summary of a most complicated topic. Don't miss it.*
R. J. M.

Thompson AK, Juniper E, Meltzer EO: Quality of life in patients with allergic rhinitis.
Ann Allergy Asthma Immunol 85:338-348, 2000.

COMMENT: *All too often attempts are made to trivialize the impact of allergic rhinitis. In this well-written review article, the authors detail not only the impact of this common illness in multiple domains, but more importantly, document the beneficial effects of therapy in these domains.*
A. M.

van der Vliet A, Cross CE: Oxidants, nitrosants, and the lung. **Am J Med** 109:398-421, 2000.

COMMENT: *This excellent review discusses the current state of knowledge regarding extracellular antioxidant defenses in the lung, their proposed involvement in respiratory disease, and current concepts of the cellular responses underlying involvement of oxidative/nitrosative stress in lung dysfunction. The authors conclude that there remains only circumstantial evidence that oxidant/nitrosative species are causally related in injury, inflammation, and the reparative stages of many lung diseases.*
E. J. B.

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