

ALLERGYWATCH®

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

A Publication of The American College of Allergy, Asthma & Immunology

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Study Defines Distinct Inflammatory Subtypes of Severe Asthma

A number of different mechanisms may contribute to the development of severe, corticosteroid (CS)-dependent asthma. Postulated factors include increased neutrophil numbers and airway remodeling. This study sought to identify distinct subtypes of severe asthma, including their structural, physiologic, and clinical characteristics. Thirty-four patients with severe, refractory, CS-dependent asthma were studied. All underwent a thorough evaluation, including endobronchial biopsy and lavage with assays for tryptase and histamine, pulmonary function testing, allergy testing, clinical history, and immunohistochemical assays of tissue cell types and subbasement membrane thickness.

Two inflammatory groups were identified, based on the presence or absence of eosinophils. Eosinophils were nearly absent in 14 patients, classified as eosinophil negative. The remaining 20 patients, clas-

sified as eosinophil positive, also had increased levels of CD3+, CD4+, and CD8+ lymphocytes, mast cells, and macrophages. Subbasement membrane thickness was also greater in the eosinophil-positive group, who had been intubated significantly more times than the eosinophil-negative group. Both groups had persistently high neutrophil levels.

This study is the first to demonstrate two distinct pathologic types of severe, refractory asthma: eosinophil-positive and eosinophil-negative phenotypes. The eosinophil-positive group not only has high levels of "classic" eosinophilic inflammation, but also elevated numbers of CD3+, CD4+, and CD8+ T cells. Although lacking the classic inflammatory features, the eosinophil-negative group has very similar clinical and physiologic characteristics. The structural changes associated with these pathologic subtypes may lead to differences in physiology and patient clinical status.

COMMENT: *This unique study is the first to define two distinct pathologic subtypes within the phenotype* ►►

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- 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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of severe asthma based on the presence or absence of eosinophils. The eosinophil-positive group display high levels of eosinophilic asthmatic inflammation with increased numbers of CD3+, CD4+, and CD8+ T cells. The eosinophil-negative group are best described by the absence of features seen in the eosinophil-positive group. These observations will likely have significant repercussions in future therapeutic interventions.

J. B.-M.

Wenzel SE, Schwartz LB, Langmack EL, et al: Evidence that severe asthma can be divided pathologically into two inflammatory subtypes with distinct physiologic and clinical characteristics. *Am J Respir Crit Care Med* 160:1001-1008, 1999. ♦♦

Breast-Feeding Reduces Asthma and Atopy Risk in Young Children

PREVIOUS prospective studies have suggested that exclusive breast-feeding of infants has a protective effect against atopic disease throughout childhood and into adolescence. A larger prospective cohort study was performed to assess the effects of breast-feeding on asthma-related outcomes at age 6. A total of 2,187 infants seen at an Australian tertiary obstetric hospital were followed up through 6 years of age. Associations between the duration of exclusive breast-feeding and outcomes related to asthma or atopy were evaluated.

With adjustment for potential confounders, infants in whom non-breast milk was introduced before the age of 4 months were significantly more likely to have asthma- and atopy-related outcomes by age 6. Associations with asthma and wheezing held across a wide range of ages at which other milk was introduced. The association with positive skin-prick testing was significant only at age 4 months.

Breast-feeding exclusively through the first 4 months of life significantly reduces the risk of asthma and atopy through age 6 years. This large prospective study has a high response rate, although its power may be limited by random nonresponse. Breast-feeding reduces a wide range of asthma- and atopy-related outcomes, including skin-prick test positivity.

COMMENT: Controversy exists as to the benefit of breast-feeding for the prevention of allergic disorders in the infant. This large-scale prospective study from Australia supplies important information for physicians to provide to pregnant women. The researchers found that exclusive breast-feeding for at least 4 months may reduce the risk of asthma and atopy at the age of 6. With the incidence of asthma increasing in the pediatric population, this study should lead to increased endorsement of breast-feeding for all infants.

M. S. B.

Oddy WH, Holt PG, Sly PD, et al: Association between breast feeding and asthma in 6 year old children: findings of a prospective birth cohort study. *BMJ* 319:815-819, 1999. ♦♦

Are Fungi Really Playing A Pathogenetic Role in Chronic Sinusitis?

REFINED criteria for the diagnosis of allergic fungal sinusitis (AFS) include chronic rhinosinusitis (CRS), allergic mucin, ie, clusters of eosinophils and their by-products; and fungal organisms within the mucin, confirmed by histology and/or culture. Nevertheless, some patients with "AFS-like" disease do not show evidence of fungi, despite the presence of allergic mucin. Using improved test methods, the authors re-evaluated the diagnostic criteria for AFS. The study included 210 consecutive patients with a clinical diagnosis of CRS, with or without nasal polyps. Fourteen controls without nasal or sinus disease were studied for comparison. One hundred one patients underwent surgery, providing a specimen for >>

histologic analysis. In all subjects, careful collection and culture methods were used to identify fungi.

Ninety-six percent of patients with CRS had positive cultures for fungi, averaging 2.7 organisms per patient. All subjects in the control group were positive for fungi, with numbers and types of organisms similar to those found in the patients. Eighty-one percent of the surgical specimens showed fungal elements. Ninety-three percent of the CRS patients met the diagnostic criteria for AFS. Specific and total IgE levels were similar in the CRS patients and controls.

More than 90% of patients with CRS, with or without polyposis, meet current diagnostic criteria for AFS. The results suggest that fungal colonization of the nasal secretions is universal, and that IgE mediation cannot be the primary mechanism of AFS-related tissue damage. In recognition of the key role of eosinophils—possibly triggered by extramucosal fungi—the authors propose changing the name of this condition from AFS to “eosinophilic fungal rhinosinusitis.”

COMMENT: *In this study, the great majority of patients with chronic sinusitis were found to have eosinophilic mucin and fungal elements in their sinus cavities, thus meeting the usual criteria for the diagnosis of allergic fungal sinusitis. However, the investigators could not confirm the importance of type I hypersensitivity mechanisms and suggest that this disease entity be renamed “eosinophilic fungal rhinosinusitis.” With the use of meticulous culture techniques, fungi were isolated from 96% of the patients as well as from 100% of normal control subjects. The findings cast doubt on the importance of fungi in the etiopathogenesis of this disease. Perhaps the term should just be “eosinophilic sinusitis.”*

J. R. B.

Ponikau JU, Sherris DA, Kern EB, et al: *The diagnosis and incidence of allergic fungal sinusitis.* *Mayo Clin Proc* 74:877-884, 1999. ◆◆

Immunotherapy Reduces Skin Mast Cell Numbers

DESPITE its long history of clinical use, little is known about the mechanisms of immunotherapy. Respiratory and skin mast cells play a key role in allergic disease. Patients undergoing immunotherapy were studied to determine the effects of treatment on skin mast cell numbers. Forty patients with summer hay fever were randomized to receive 9 months of active grass pollen immunotherapy or placebo injections. Clinical responses were assessed in double-blind fashion. Skin biopsy specimens were obtained for immunohistochemical assessment of total mast cells and mast cell subtypes in the dermis.

Patients in the active treatment group showed a significant reduction in seasonal symptoms, along with more than a 10-fold reduction in immediate cutaneous response to grass pollen. Immunotherapy also yielded a 7-fold reduction in skin mast cell numbers. The reduction in mast cells was significantly correlated with the

clinical response, based on either symptom scores or use of rescue medications.

In patients with hay fever, the clinical benefits of immunotherapy may be at least partially explained by reduction of mast cell numbers. This leads to a reduction in the immediate response to allergen exposure. In addition, the reduction in mast cells may remove the “priming” mechanism for development of late responses to allergen.

COMMENT: *The mechanism responsible for the efficacy of immunotherapy has eluded us for decades. In this study, Durham and colleagues show an impressive reduction in cutaneous mast cells following immunotherapy. Perhaps this effect is a critical adjunct to the known immunologically specific effects of immunotherapy on both T and B lymphocyte responses.* S. A. T.

Durham SR, Varney VA, Gaga M, et al: *Grass pollen immunotherapy decreases the number of mast cells in the skin.* *Clin Exp Allerg* 29:1490-1496, 1999. ◆◆

Studies Show Efficacy of Asthma Medications with Non-CFC Propellants

TWO recent studies demonstrate the therapeutic value of inhaled asthma medications using hydrofluoroalkane (HFA) instead of chlorofluorocarbon (CFC) propellant. Juniper et al randomized 347 adult patients with moderate asthma to receive 12 weeks of beclomethasone dipropionate (BDP) with HFA propellant (HFA-BDP), 400 µg/d; BDP with CFC propellant, 800 µg/d; or placebo. The patients stopped all other oral or inhaled steroids.

Thirty-three of forty-three withdrawals for worsening asthma occurred in the placebo group, which also showed a significant reduction in asthma-related quality-of-life score. In contrast, quality-of-life scores were stable in both the HFA-BDP and CFC-BDP groups. Thus the two active treatments were similarly effective in maintaining asthma-related quality of life.

Welch et al randomized 514 adult patients with persistent asthma to receive triamcinolone acetonide (TAA) with either HFA propellant or CFC propellant or placebo. Treatments lasted 8 weeks. Patients in the TAA groups received doses of 150, 300, or 600 µg/d. At all doses, both forms of TAA produced significant improvements in spirometry, symptom scores, albuterol use, and peak expiratory flow.

Asthma medications using HFA propellant have been developed in response to the mandate to replace CFC propellants. These new studies confirm the efficacy of BDP and TAA formulations using HFA propellant. Efficacy and safety outcomes are equivalent to formulations using CFC propellants.

COMMENT: *While originally intended to have been completed by the year 2000, the CFC phase-out is only just beginning to impact asthma patient care. Dry powder inhalers have begun to gain worldwide acceptance for a variety of reasons. However, as these two studies argue, metered-dose inhalers using HFA propel- ➤➤*

lants are therapeutically equivalent to their CFC-containing counterparts. As always, a practical knowledge regarding the correct use of new products will be essential to ensure that patients receive optimal benefit from therapy.

S. A. T.

Juniper EF, Buist AS, and The Study Group: Health-Related Quality of Life in Moderate Asthma: 400 µg hydrofluoroalkane beclomethasone dipropionate vs 300 µg chlorofluorocarbon beclomethasone dipropionate. *Chest* 116:1297-1303, 1999.

Welch M, Bernstein D, Gross G, et al: A controlled trial of chlorofluorocarbon-free triamcinolone acetonide inhalation aerosol in the treatment of adult patients with persistent asthma. *Chest* 116:1304-1312, 1999. ♦♦

Updated Review on Asthma Immunotherapy

PREVIOUS reports, reviewing the scientific literature through 1997, concluded that immunotherapy for asthma reduces symptoms, medication requirements, and nonspecific and allergen-specific bronchial hyperreactivity (BHR), compared with placebo. Recent years have seen the development of new allergen vaccines and new techniques of immunotherapy delivery. The authors updated their review of randomized controlled trials of allergen-specific immunotherapy for allergic asthma. A total of 67 studies published from 1954 through 1998 met inclusion criteria, including 10 trials not included in the previous review.

Meta-analysis reconfirmed the benefits of allergen-specific immunotherapy in reducing asthma symptoms and medication requirements. There is some heterogeneity in the responses, probably the result of different scoring systems. The effects of immunotherapy on lung function were inconsistent, even after stratification for different parameters. Immunotherapy reduced the likelihood of developing increased nonspecific BHR somewhat. Allergen-specific BHR was improved significantly and homogeneously, a finding that has important implications for the management of patients with brittle allergic asthma.

Recent studies further strengthen the conclusion that immunotherapy reduces medication requirement and improves allergen-specific BHR in patients with allergic asthma. These are clinically relevant effects with the potential to improve asthma control. Additional studies are needed to answer key questions about the clinical use of allergen immunotherapy.

COMMENT: *The authors update their previous meta-analyses on this subject. They include 10 randomized controlled trials not covered in their 1997 review. This meta-analysis confirms that allergen-specific immunotherapy significantly reduces asthma symptoms and medication requirements. No consistent effect was observed on lung function, but modest improvement was observed in nonspecific bronchial hyperreactivity (BHR), and significant improvement noted in allergen-specific BHR.*

E. J. B.

Abramson M, Puy R, Weiner J: *Immunotherapy in*

asthma: an updated systematic review.
Allergy 54:1022-1041, 1999. ♦♦

ACAAI Issues Minimum Standards for Skin Test Results and Immunotherapy Labeling

ALLERGIST-immunologists differ in the way they label allergy extracts and report the results of skin tests. In an era of managed care and patient mobility, some type labeling standards are needed. The American College of Allergy, Asthma and Immunology has developed minimal requirements for labeling of allergy extracts and reporting the results of skin tests.

Labeling of allergy extracts must include patient identifiers and the name of the prescribing physician. The source and dilution should be indicated, along with the way the dilution was made. The suggested schedule, an expiration date, and a telephone number for questions should be included. The bottle should include the same labeling as the instruction page. The peak flow reading for asthma patients should be indicated, along with the time the shot was given and the time the patient was examined before leaving.

Skin test reports should include patient and physician identifiers and the type and location of tests. Testing materials should be indicated, including positive and negative diluent controls, concentration and source of antigens, diluent, and contents of mixture. The report should include the grading key and name of the physician interpreting the test data.

COMMENT: *This document is a useful consensus opinion from the ACAAI Board of Regents. While there are obvious clinical benefits for all physicians providing immunotherapy services, this document is likely to provide a medicolegal basis for standard of practice issues in the future.*

A. M.

ACAAI Board of Regents: *Minimal requirements for adequate labeling of allergy extracts and skin test report forms.*

Ann Allergy Asthma Immunol 83:201, 1999. ♦♦

Brief Updates in Pulmonary Disease Presented

THIS article presents brief summaries of key research in areas including asthma and chronic obstructive pulmonary disease, pulmonary infection, and interstitial and occupational lung disease. One study examined the role of S-nitrosothiols, which are very potent endogenous bronchodilators, in severe outflow obstruction. Evaluations of 8 asthmatic children with respiratory failure suggested accelerated breakdown of S-nitrosothiols, leading to high concentrations of expired nitric oxide and to bronchospasm. In another study, fluticasone propionate proved to be a safe and effective treatment for chronic obstructive pulmonary disease over a 6-month period. Although the absolute improvement in pulmonary function was small, it was associated with significant improvements in symp- ➤➤

toms, exercise capacity, and exacerbation severity.

New studies in the area of pulmonary infection clarified the necessary length of hospital stay for patients with community-acquired pneumonia and highlighted the importance of pneumococcal vaccine in preventing outbreaks of pneumococcal pneumonia in nursing homes. An occupational medicine study evaluated the potential drug causes of cryptogenic fibrosing alveolitis or idiopathic pulmonary fibrosis. The findings suggested that this condition is strongly associated with the use of tricyclic antidepressants, especially imipramine, dothiepin, and mianserin. Another study reported a new occupational disease called flock worker's lung, caused by exposure to nylon fiber. This study—performed by a research team hired by a textile company—raises important questions about conflict of interest and academic freedom.

COMMENT: *This is a clinically relevant update for practicing allergists from the 1999 Annual Meeting of the American College of Physicians. Dr. Karnik has reviewed articles on asthma therapy, pulmonary infections, and occupational lung disease that should be of interest to all allergists who care for adults. Since many of the cited articles are from journals that allergists do not routinely read, this article can be a very useful resource.*

A. M.

Karnik AM: Update in pulmonary diseases. *Ann Intern Med* 131:596-604, 1999. ◆◆

Salmeterol Reduces Bronchial Eosinophils in Asthma

THERE is continued concern over the long-term use of inhaled β_2 -agonists by patients with asthma. It has been suggested that long-acting β_2 -agonists may have anti-inflammatory activity in addition to their bronchodilating effect. The effects of adding salmeterol to low-dose inhaled corticosteroids (ICS) in symptomatic patients with asthma were assessed. Fifty patients, ICS dosage 100 to 500 $\mu\text{g}/\text{d}$, were randomized to receive 12 weeks of supplementary salmeterol, 50 μg twice daily; fluticasone, 100 μg twice daily; or placebo. Background ICS treatment continued throughout. Pretreatment and posttreatment bronchial biopsy and bronchoalveolar lavage (BAL) specimens were available in 45 patients. The analysis included immunohistochemical assays for inflammatory cells, using antibodies against the preformed and cleaved form of eosinophil cationic protein: anti-EG1 and anti-EG2, respectively.

Both active treatment groups showed significant physiologic improvement, but especially the salmeterol group. None of the treatments produced a significant change in BAL profiles, although lymphocyte activation was significantly reduced in the fluticasone group. Bronchial biopsies showed no significant posttreatment changes in inflammatory cells in the bronchial lamina propria. However, patients taking supplementary salmeterol showed a significant reduction in EG1-positive cells. This group also had a nonsignificant reduction in EG2-positive cells.

Adding salmeterol to ICS in patients with asthma appears to have little impact on allergic inflammation. However, it does appear to reduce airway eosinophilic infiltrate in bronchial biopsy specimens. This effect is not noted when increasing the dose of ICS with fluticasone, although lymphocyte activation in BAL is reduced. In contrast to concerns over deterioration in airway eosinophilia, this study documents an anti-inflammatory effect of long-acting β_2 -agonist therapy in patients with asthma who are already taking ICS.

COMMENT: *As in previous studies the group receiving salmeterol had the best clinical response, as determined by symptom scores and bronchodilator use. The use of salmeterol was also associated with a decrease in tissue eosinophilia, as determined by immunohistochemical studies employing antibody against eosinophilic cationic protein. However, the salmeterol group had more tissue eosinophilia before randomization, suggesting that the decrease in eosinophils may have resulted partly from improved compliance with background inhaled corticosteroid medication.*

J. R. B.

Li X, Ward C, Thien F, et al: An antiinflammatory effect of salmeterol, a long-acting β_2 agonist, assessed in airway biopsies and bronchoalveolar lavage in asthma. *Am J Respir Crit Care Med* 160:1493-1499, 1999. ◆◆

Low Humidity Helps to Control Dust Mites

KEEPING the indoor relative humidity (RH) below 50% helps to control house dust mites. However, RH may fluctuate during the day. *Dermatophagoides farinae* can exploit even brief periods of increased RH to complete their life cycle. This study evaluated the effects of various intervals of low vs high RH on the population survival and growth of *D. farinae*.

Female mites were placed in culture chambers maintained at varying RH conditions during the day, including brief, daily periods of moist air (75% or 85% RH) alternating with long spells of low RH (0% or 35%). Mite populations decreased when the mites received only 2 h/d of high humidity, alternating with 22 h/d of low humidity. Small population growths occurred when the duration of high humidity was increased to 4, 6, or 8 h/d. Mite populations declined or did not develop when RH was maintained at 85% continuously. Population growth occurred in inverse proportion to the number of hours spent at 85% RH. The greatest population growth occurred at 4 h/d of 85% RH, alternating with 20 h/d at 35% RH.

Keeping indoor RH at less than 50% will help to control the growth of house dust mite populations, and thus the production of allergen. This is so even if the RH increases to higher than 50% for 2 to 8 h/d. The dust mite population can be contained by keeping RH below 35% for at least 22 h/d, when the RH is 75% to 85% for the rest of the day.

COMMENT: *Most allergic patients assume their dust mite allergy is worse in the winter, "when the heat >>>*

goes on.” The life cycle of the house dust mite, however, suggests the opposite. Dust mites require humidity to propagate, but how much, and for how long, is the subject of this investigation. The esoteric answers to your nagging questions about humidity can be found here. (Hint: The patients will need lots of skin lotion.)

R. J. M.

Arlian LG, Neal JS, Vyszynski-Moher DL: Reducing relative humidity to control the house dust mite *Dermatophagoides farinae*. *J Allergy Clin Immunol* 104:852-856, 1999. ◆◆

Premenstrual Asthma Attacks Linked to Increased Leukotriene Levels

MANY asthmatic women have asthma attacks around the time of their menstrual period. It has been suggested that these premenstrual exacerbations of asthma (PMA) may arise from systemic activation of mast cells, which contain inflammatory mediators such as histamine, leukotrienes (LTs), and cytokines. The role of these cellular mediators in the development of PMA was investigated.

Women attending an asthma clinic were asked about variation in asthma symptoms around the time of their menstrual cycle: 5 women with PMA and 5 age-matched women without PMA were identified. In the PMA group, blood samples were obtained just before or during the menstrual period—when peak expiratory flow rate (PEFR) began to decrease—and during the midcycle week—when PEFR returned to baseline. Samples were obtained at the same times from the patients without PMA. Serum levels of LTB₄, LTC₄, platelet-activating factor, histamine, interleukin (IL)-1, IL-4, IL-5, IL-6, and granulocyte-macrophage colony-stimulating factor were measured in each sample.

Women with PMA had higher serum LTC₄ levels during asthma exacerbations than during the recovery period, 69 vs 24 pg/mL. The other inflammatory mediators were no different between these two periods. The non-PMA group showed no change in cellular mediators between the two sampling periods. In patients with PMA, oral treatment with the LT receptor antagonist pranlukast, 225 mg twice daily, improved asthma symptom scores.

This study documents increased serum levels of LTC₄ during asthma exacerbations in women with PMA. The source of these cysteinyl LTs is unclear, but may include T lymphocytes, basophils, or mast cells. Treatment with LT receptor antagonists may help to prevent PMA.

COMMENT: It is estimated that 30% to 40% of women with asthma have increased symptoms just before and during menstruation. These authors examined the role of leukotrienes in the pathogenesis of premenstrual asthma, and found increased LTC₄ in the serum associated with symptoms. There was objective and subjective improvement in premenstrual asthma with leukotriene receptor antagonists. This study adds premenstrual asthma to the list of “types” of asthma that may benefit from leukotriene receptor antagonists.

M. S. B.

Nakasato H, Ohrui T, Sekizawa K, et al: Prevention of severe premenstrual asthma attacks by leukotriene receptor antagonist. *J Allergy Clin Immunol* 104:585-588, 1999. ◆◆

Methacholine Dose, Not Concentration, Determines Bronchial Response

THIS study sought to determine whether the methacholine dose or concentration was the most important determinant of the response to methacholine challenge testing. The participants were 10 patients with mild asthma, FEV₁ greater than 70% predicted and methacholine PC₂₀ less than 4 mg/mL. The patients were permitted to continue inhaled corticosteroid use if they had been on a stable dose before the study. In random order on two different days, they performed one methacholine challenge test with 30-second inhalations of methacholine and another with 2-minute inhalations.

The patients had a geometric mean 2-minute PC₂₀ of 1.1 mg/mL compared with a 30-second PC₂₀ of 5.7 mg/mL. Thus the 30-second PC₂₀ was more than 5 times greater than the 2-minute PC₂₀. On paired t-test, the 2-minute PC₂₀ multiplied by 4 was not significantly different from the 30-second PC₂₀.

In methacholine challenge testing, the methacholine dose is the main factor responsible for the bronchial response, not the methacholine concentration. When a 30-second inhalation is used, the methacholine concentration must be 4 times higher than with a 2-minute inhalation to produce the same response.

COMMENT: Many allergists perform in-office methacholine tests using multiple dosing and interval schedules. This article confirms previous observations that total dose is more important than concentration in triggering bronchospasm in patients with bronchial hyperresponsiveness. This should be relevant information for those clinicians who perform or interpret “abbreviated” methacholine challenges.

A. M.

Drotar DE, Davis BE, Cockcroft DW: Dose versus concentration of methacholine. *Ann Allergy Asthma Immunol* 83:229-230, 1999. ◆◆

Subclinical Allergen Doses Produce Eosinophil and Bronchial Responses

THE effects of repeated exposure to low doses of cat allergen were examined in 12 asymptomatic asthma patients with clinical sensitization to cat allergen but not exposed to cat allergen at home. The patients received an 8-day series of inhalations of cat allergen at doses too small to produce asthma symptoms. Evaluation included pre- and postexposure methacholine challenge testing and measurement of eosinophil cationic protein (ECP) levels in bronchoalveolar lavage (BAL) fluid and blood.

None of the patients developed asthma symptoms in response to allergen exposure. However, there was a significant reduction in geometric mean PD₂₀ for methacholine, from 263 to 126 µg. The median >>

ECP level increased from 0.8 to 3.1 $\mu\text{g/L}$ in BAL and from 15.9 to 31.4 $\mu\text{g/L}$ in serum. No changes occurred in response to saline inhalation.

Subclinical doses of allergen can increase bronchial responsiveness to methacholine and increased levels of ECP in both BAL and serum in patients with mild asthma. The findings lend insight into natural exposure to cat allergen, as well as the subclinical changes occurring in the airway before an asthma attack. Eosinophil activation causes a rise in serum ECP levels, which could be a useful marker of allergen exposure in patients with allergic asthma.

COMMENT: *In this study, inhaling subclinical amounts of cat allergen resulted in impressive increases in nonspecific bronchial hyperresponsiveness and in both serum and BAL fluid eosinophilic cationic protein levels. Although we do not know how closely these results apply to real-life subclinical allergen exposures, measuring symptoms and spirometry may not be particularly sensitive in detecting the initiation of an allergic response.*

S. A. T.

de Blay F, Krieger P, Spirlet F, et al: Repeated inhalation of low doses of cat allergen that do not induce clinical symptoms increases bronchial hyperresponsiveness and eosinophil cationic protein levels. Int Arch Allergy Immunol 120:158-165, 1999. ◆◆

Monosensitized Children Are at Risk of Polysensitization Over Time

THE factors affecting allergic sensitization in children, including those affecting sensitization to one allergen rather than others, remain unclear. There have been no studies of how monosensitization varies over time. This study reviewed changes in allergic sensitization over time in 165 Italian children with asthma who were originally monosensitized. At initial evaluation, 98 children were preschool aged and 67 were school aged. Follow-up examinations included skin prick testing to common aeroallergens, case history, and physical examination.

Forty-four percent of the children became polysensitized by their follow-up visit. The rate was similar by age: 48% among preschool-aged and 37% among school-aged children. Polysensitization rate also varied by the allergen to which the children were originally monosensitized: 45% for children originally monosensitized to dust mite vs 32% among those originally monosensitized to pollen.

Many asthmatic children who are originally sensitized to only one class of allergens will go on to develop polysensitization during follow-up. The proportion of polysensitized children increases over time. The rate of polysensitization is particularly high among children originally monosensitized to dust mite. An airway response to one allergen may enhance the early and late airway responses to subsequent challenges with other allergens.

COMMENT: *In this important longitudinal study of Italian children, the authors make several important*

observations. While the risk of allergic sensitization in genetically predisposed individuals is likely to be multifactorial, these authors have noted that children who were originally monosensitized to dust mite frequently become polysensitized. These observations should highlight the importance of aggressively recommending environmental control measures to children who are at risk for or who have developed dust mite sensitivity, as this may be a triggering event in the development of further allergic disease.

A. M.

Silvestri M, Rossi GA, Cozzani S, et al: Age-dependent tendency to become sensitized to other classes of aeroallergens in atopic asthmatic children. Ann Allergy Asthma Immunol 83:335-340, 1999. ◆◆

“Skeeter Syndrome” Describes Local Allergic Reactions to Mosquito Bites

CHILDREN and other patients may develop severe reactions to mosquito bites, consisting of a large local inflammatory reaction with fever. Although often presumed to be infectious in nature, these reactions actually result from allergenic polypeptides in the saliva of mosquitoes. The authors describe five cases of such reactions, which they term “skeeter syndrome,” in 2- to 4-year-old children.

All patients developed a large local inflammatory reaction at the site of a witnessed mosquito bite. The reactions developed within hours after the bite, and were diagnosed by primary care physicians as cellulitis. After a period of months, the children were referred to the allergy clinic of a children’s hospital. There the diagnosis of skeeter syndrome was confirmed using an indirect enzyme-linked immunosorbent assay to measure specific IgE and IgG to salivary gland antigens of the mosquito species predominant in the area. Serum concentrations of these specific immunoglobulins were significantly elevated in the children with skeeter syndrome, compared to control children with typical local reactions to mosquito bites.

Clinical examination alone cannot differentiate between inflammation caused by an allergic response to a mosquito bite versus that caused by infection. Specific IgE and IgG play a key role in mosquito allergy. Local inflammatory reactions caused by allergy to mosquitoes appear to have a good prognosis, although long-term prospective studies are needed. Exposure to mosquitoes must be minimized for patients with such severe reactions.

COMMENT: *A common manifestation of mosquito bites in young children is a large local reaction at the site of the bite. Many of these reactions are extensive and thought to be “cellulitis.” Simons and Peng describe this condition as “skeeter syndrome” and document increased levels of IgE and the different IgG subclasses to Aedes species compared to controls. Recognition of this condition should prevent unnecessary evaluations and use of antibiotics.*

M. S. B.

Simons FER, Peng Z: Skeeter syndrome.

J Allergy Clin Immunol 104:705-707, 1999. ◆◆

Allergen Levels Vary by Season and Housing Type

SEASONAL variations in allergen levels were measured in 20 Boston-area homes, with consideration of other potential sources of variation. Dust samples were obtained monthly for measurement of the dust mite allergens Der f 1 and Der p 1; the cat allergen Fel d 1; and the cockroach allergen Bla g 1. Relative and absolute humidity were measured, and the characteristics of each home were assessed.

Levels of Der f 1 and Der p 1 peaked in autumn, whereas Fel d 1 levels were highest in winter and spring and Bla g 1 levels highest in summer. Dust mite allergen levels were twice as high in autumn as in spring, and cat allergen levels were twice as high in spring as summer. However, the characteristics of the home had a far greater impact on allergy levels. Dust mite allergen levels were 19 to 31 times higher in houses than in apartments, while cat allergen levels were 224 times higher in homes with vs without cats. Cockroach allergen levels were twice as high in summer as in winter, and five times higher in apartments than in homes.

Indoor allergen levels vary significantly by season in the northeastern United States. However, the type of housing and the presence of a cat are far more important contributors to allergen levels than the seasonal variation. Information on seasonal variation should improve estimates of exposure to dust mite, cat, and cockroach allergen.

COMMENT: *This study examined seasonal variation of dust mite, cat, and cockroach indoor allergen concentrations in Boston. Dust mite allergen levels were highest in autumn and decreased through spring. Cat allergen peaked in winter and spring and cockroach allergen was highest in summer. The influence of housing type and the presence of a cat far outweighed seasonal variations—ie, apartments had levels five times higher than houses.*

E. J. B.

Chew GL, Higgins KM, Gold DR, et al: *Monthly measurements of indoor allergens and the influence of housing type in a northeastern US city. Allergy* 54:1058-1066, 1999. ◆◆

Role of *Chlamydia pneumoniae* in Asthma and COPD Reviewed

PREVIOUS reports have suggested that infection with *Chlamydia pneumoniae* (*Cpn*) may play a role in asthma and chronic obstructive pulmonary disease (COPD). Asthma was once believed to be a noninfectious condition caused by inflammation. More recently, a contribution of viral infections has been suggested, especially occurring during key times in immune development. It is now thought that infection may play a role in causing chronic asthma symptoms. *Chlamydia pneumoniae*, one of four recognized *Chlamydia* species, is an obligate intracellular procaryon with a unique reproductive life cycle. Respiratory infection with *Cpn* is more like *Mycobacterium tuberculosis* infection—an

opportunistic infection associated with intracellular persistence, dissemination, and reactivation—than a typical pyogenic respiratory infection. The *Cpn* organisms may persist for long periods after acute respiratory illness. The pathogenesis of chlamydial disease appears to involve chlamydial heat shock protein 60, which has recently been linked to asthma.

The lack of diagnostic facilities and the controversy regarding diagnostic criteria make it difficult to diagnose *Cpn* infection. The standard criteria for acute *Cpn* infection include a 4-fold or greater increase in IgM and/or IgG microimmunofluorescence antibody titer observed in paired sera obtained at least 4 weeks apart. Chronic infection is associated with the persistent presence of serum IgA and/or chlamydial immune complexes.

Several studies have linked *Cpn* infection to asthma and COPD. Of 18 controlled studies, 15 showed significant associations between *Cpn* infection and asthma. One study found increased levels of chlamydial immune complexes among smokers, while another found that acute or chronic *Cpn* infection is common among COPD patients. Several case reports and uncontrolled case series have documented the complete resolution of asthma symptoms after prolonged antibiotic therapy against *Cpn*.

There is now considerable evidence that acute *Cpn* infection can trigger attacks of asthma and wheezing, and may sometimes initiate asthma in previously asymptomatic patients. The clinical implications of the link between *Cpn*, asthma, and COPD remain to be determined. However, testing for *Cpn* infection—or even empiric antibiotic therapy—may be considered for selected patients with severe persistent asthma. Without treatment, the infection may lead to an accelerated decline in lung function.

COMMENT: *In this analysis of the literature, Dr. Hahn reviews the evidence regarding *Cpn* infections in asthma and COPD. While the majority of studies addressing this issue have indicated therapeutic responses to treatment, many of the studies have had methodologic problems. Reliance on serologic testing is problematic. The cost and morbidity of long-term antibiotics should prevent widespread use of *Cpn* treatment until more prospective controlled data are available.*

A. M.

Hahn DL: *Chlamydia pneumoniae, asthma, and COPD: what is the evidence? Ann Allergy Asthma Immunol* 83:271-292, 1999. ◆◆

Asthma Self-Management Program Does Not Improve Outcomes Over Usual Care

MANY different self-management programs have been introduced to improve asthma self-management by children and adults. Previous studies have suggested that these programs can improve functional status and reduce inappropriate use of health care services. The authors sought to replicate the positive

results reported for their asthma self-management program, including comparison with a usual-care control program.

Two hundred thirty-two patients with moderate to severe asthma were randomized to receive a proven-efficacious asthma self-management program, a condensed program consisting of the core element of the full program, or usual care. The self-management programs included a workbook, patient counseling, training in asthma self-monitoring, and telephone follow-up. Over a 2-year period, the groups were compared on outcome measures including adherence to prescribed medication and inhaler use, asthma symptoms, respiratory illness, functional status, and use of health care services.

All three treatment groups improved significantly in the major outcome measures. The two asthma self-management groups had no better outcomes than the usual-care group.

The findings do not replicate the positive results achieved with the authors' and other asthma self-management programs. The discrepancy may reflect patient selection, as well as the increased emphasis on patient education in asthma care. The results suggest that asthma patients receiving specialist care that meets accepted guidelines do not necessarily need an extra patient education component.

COMMENT: *In this study "usual care" produced outcomes just as good as those achieved with more structured self-management programs for patients with moderate to severe asthma. The structured programs included a workbook, individual counseling, support groups, and telephone follow-up. The authors attribute this finding to the adequacy of "usual care" provided by pulmonary specialists who follow established guidelines, educate their patients, and prescribe state-of-the-art therapy including inhaled corticosteroids.*

J. R. B.

Bailey WC, Kohler CL, Richards JM Jr, et al: *Asthma self-management: do patient education programs always have an impact?* *Arch Intern Med* 159:2422-2428, 1999. ◆◆

Asthma Deaths Associated with Frequent Symptoms, Chances for Intervention

IN Canada as in other countries, mortality from asthma has been increasing. This study analyzed risk factors for asthma deaths in the Canadian prairie provinces, which have the highest asthma mortality rates. The study included 35 patients, aged 5 to 50 years, who died from asthma between 1992 and 1995. Death from asthma was confirmed pathologically, when possible, or by rigorous clinical review. Other information was gathered by mail questionnaire and telephone interviews with next of kin. The findings were compared with those of 209 matched controls.

Both groups had regular, frequent asthma symptoms. Cases were more likely to have severe disease, to have a previous hospitalization for asthma, or to have a history of cardiopulmonary resuscitation or intubation. The two groups were similar in terms of medication use, except that the patients who died were more

likely to use β -agonist bronchodilators, and to use them in higher than prescribed doses. Controls were more likely to report a cold or flu before the index event, but cases were more likely to be reported sad or depressed. The cases had a significantly shorter time between symptom onset and the event—less than 2 hours for most.

This study identifies risk factors for asthma mortality among patients with frequent, regular symptoms, suggesting poor asthma management. There are few important differences between groups in events occurring immediately before the index attack. In both groups, there appear to be opportunities for intervention before the attack. The time between symptom recognition and death can be very short, so high-risk patients should know how to monitor their condition and to respond according to predetermined criteria.

COMMENT: *In this important study of risk factors for asthma fatalities, the Canadian authors report a retrospective, case-controlled analysis of 35 deaths occurring from 1992 to 1995. The results confirm previous observations that patients who die from asthma are more likely to have been hospitalized or intubated because of their asthma. Psychologic factors appeared more prevalent in fatal cases of asthma. Importantly, the authors documented that almost 60% of patients who died had felt unwell for less than 2 hours before their death. Although asthma deaths are unusual, the findings highlight risk factors that clinicians should be aware of and potentially address in at-risk patients.*

S. R. W.

Hessel PA, Mitchel I, Tough S, et al: *Risk factors for death from asthma.* *Ann Allergy Asthma Immunol* 83:362-368, 1999. ◆◆

Mometasone and Budesonide Have No Short-Term Growth Effects

THE synthetic heterocyclic corticosteroid mometasone furoate (MF) has high topical potency with minimal side effects. It is hoped that intranasal MF will avoid adverse systemic side effects, including growth retardation in children. Knemometry is a technique of evaluating the effects of topical steroids in children, measuring changes in lower leg length with an accuracy of 0.1 mm. This technique was used to compare the short-term growth effects in children receiving MF and budesonide.

The study included 22 preadolescent children, aged 7 to 12 years, with seasonal or perennial allergic rhinitis. They were randomized to receive intranasal MF aqueous nasal spray, 100 or 200 μ g; budesonide, 400 μ g; or placebo. After each 2-week treatment period and a 2-week washout interval, the patients were crossed over to one of the other treatments. Knemometry to measure lower leg growth was performed before and after each treatment period.

Knemometry was associated with a technical error of 0.07 mm. Mean lower leg growth rates were 0.35 mm/wk with placebo, 0.58 mm/wk with MF >>>

100 µg, 0.48 mm/wk with MF 200 µg, and 0.37 mm/wk with budesonide 400 µg. The order of treatments had no effect on growth rate.

Children with rhinitis show no short-term adverse effects on growth while taking therapeutic doses of intranasal MF or budesonide. There is even a trend toward increased growth at the lower dose of MF studied; the reason for this finding is unknown. Knemometry is a sensitive technique for identifying inhaled corticosteroid doses that are unlikely to cause adverse growth effects.

COMMENT: *A recent study of intranasal aqueous beclomethasone given daily for 12 months demonstrated partial whole-body growth suppression in prepubertal children. In response, the FDA issued warnings applicable (for now) to all intranasal corticosteroids. Some corticosteroids may be less bioavailable than others. These authors are known for a technique called knemometry, which can measure small changes in short-term lower leg growth. They found no suppression of 2-week lower leg growth with either mometasone or budesonide nasal sprays, but did not include a beclomethasone group. The hope that the two newer steroids will have no growth effect awaits long-term whole-body growth studies.*

R. J. M.

Agertoft L, Pedersen S: *Short-term lower leg growth rate in children with rhinitis treated with intranasal mometasone furoate and budesonide.* *J Allergy Clin Immunol* 104:958-952, 1999. ◆◆

Acute Asthma Associated With Increased Eotaxin Levels

THE chemotactic cytokine eotaxin is involved in eosinophil recruitment via activation of the CCR3 chemokine receptor, and may be an important mediator of acute asthma. This study sought to determine whether plasma levels of eotaxin are elevated during acute asthma attacks. The case-control study included 46 patients receiving emergency treatment for acute asthma attacks, as well as 133 controls with stable asthma. In addition to comparing plasma eotaxin levels between groups, the investigators assessed correlations between eotaxin levels and disease activity and response to treatment.

Mean plasma eotaxin level was 520 pg/mL in patients having acute asthma attacks vs 350 pg/mL for those with stable asthma. Eotaxin level was lower in patients whose peak expiratory flow rate increased by at least 20% of their predicted normal value in response to emergency treatment than in nonresponders: 410 vs 660 pg/mL. Eotaxin levels tended to be higher in patients who were hospitalized than in those discharged home.

Plasma eotaxin levels are elevated in patients having acute asthma attacks, particularly in those who do not respond to emergency treatment. The findings suggest that eotaxin is mechanistically involved in asthma exacerbations or acts as a biomarker for activity of the CCR3 receptor ligand system, which plays a functional role in asthma.

COMMENT: *Airway epithelial cells produce eotaxin, a chemotactic cytokine that recruits eosinophils by activating a receptor called CCR3. Eotaxin is expressed after allergen challenge, and levels of eotaxin are inversely proportional to FEV₁. This study compared plasma levels of eotaxin in asthmatic subjects having an acute exacerbation in hospital emergency rooms with those of stable asthmatics. A direct association was found between eotaxin levels and several measures of severity of asthma. Wouldn't it be interesting to see what a CCR3 receptor antagonist would do?*

R. J. M.

Lily CM, Woodruff PG, Camargo CA Jr, et al: *Elevated plasma eotaxin levels in patients with acute asthma.*

J Allergy Clin Immunol 104:786-790, 1999. ◆◆

Childhood Cat Exposure Reduces the Adult Sensitization Rate

PREVIOUS studies implicate furred pets—especially cats—as a key risk factor for allergic respiratory disease. As part of the European Community Respiratory Health Survey (ECRHS), this study examined childhood and present factors associated with allergic sensitization to cats. The multicenter ECRHS included more than 18,000 subjects, with blood samples available from 13,500 of these. Specific IgE levels were measured in blood, and information on cat exposure and other variables was assessed by interview.

Nine percent of subjects were sensitized to cats, with a serum specific IgE level of greater than 0.35 kU/L. The prevalence of sensitization was significantly higher among subjects who owned cats, particularly when the cat was kept indoors. Subjects who had been exposed to cats in childhood were less likely to be sensitized to cats as adults, particularly among those with a family history of atopy. Subjects sensitized to cats in adulthood were less likely to have been exposed to cats and other animals during childhood.

Living with a cat, particularly if the cat is allowed indoors, is associated with an increased likelihood of cat sensitization. In contrast, childhood exposure to cats appears to lower the risk of sensitization, including a lower prevalence of specific IgE in adulthood and a lower rate of allergic rhinitis and asthma in schoolchildren. Keeping a cat outdoors may significantly reduce allergen exposure. The clinical implications of these findings require long-term prospective studies.

COMMENT: *Epidemiologic studies linking exposure to cats with allergic diseases fit a simple notion of cause and effect. But immunology is much more complicated than that, as this study shows. In fact, the authors found that early childhood exposure to cats was negatively associated with specific sensitization in adulthood, and they postulate a childhood deviation toward the nonallergic TH1 phenotype. They stop short of recommending this as a clinical strategy, however.*

R. J. M.

Roost H-P, Künzli N, Schindler C, et al: *Role of current and childhood exposure to cat and atopic sensitization.*

J Allergy Clin Immunol 104:941-947, 1999. ◆◆

Oral Contraceptives Block Perimenstrual Changes in Cytokine Balance

ASTHMA and other immune-based conditions may vary with the menstrual cycle, often worsening during the perimenstrual interval—the days before and after the onset of menses. These changes may involve alterations in the balance of type-1/type-2 cytokine balance. This study examined changes in the type-1/type-2 cytokine balance in healthy women during the menstrual cycle, including the effects of oral contraceptive pills (OCPs). Fourteen healthy women provided peripheral blood mononuclear cells during the perimenstrual interval and during the midcycle interval. Seven of the women were taking monophasic OCPs. After the cells were stimulated with PHA, the culture supernatants were evaluated for production of the type-1 cytokine interferon (IFN)- γ and the type-2 cytokine interleukin (IL)-10.

Production of IFN- γ decreased and production of IL-10 increased during the perimenstrual interval. The result was a decreased IFN- γ :IL-10 ratio compared with the midcycle interval. This change did not occur in women taking OCPs, who had a lower midcycle IFN- γ :IL-10 ratio than the control group.

In healthy women, the type-1/type-2 cytokine balance shifts toward a type-2 response during the perimenstrual period. This response is lessened in women taking oral contraceptives. The findings may help in explaining the exacerbations of asthma and other immune diseases during the perimenstrual period, and may pave the way for new treatments to prevent these exacerbations.

COMMENT: Allergists have noted for decades the apparent perimenstrual increase in allergic diseases such as urticaria and angioedema. These new observations lend further insight into the pathogenesis of these changes. The apparent blunting of increased TH2 expression by OCPs may provide the basis for further therapies for perimenstrual increase in allergic disease. A. M.

Agarwal SK, Marshall GD Jr: Perimenstrual alterations in type-1/type-2 cytokine balance of normal women. *Ann Allergy Asthma Immunol* 83:222-228, 1999. ◆◆

Fluconazole Is Effective in Trichophyton-Sensitized Asthma Patients

A possible link between late-onset asthma and sensitization to proteins derived from dermatophyte fungi of the genus *Trichophyton* has long been proposed. In a previous report, the authors defined the immune response to various *Trichophyton* proteins. They report the results of treatment with oral fluconazole in patients with onychomycosis-related asthma. The study included 11 patients with moderate to severe persistent asthma and a positive skin test response to *Trichophyton* proteins. The patients were randomized to receive 5 months of treatment with fluconazole, 100 mg/d; or placebo.

During the subsequent 5 months, all patients received fluconazole.

Treatment with fluconazole was associated with significant reductions in bronchial sensitivity to *Trichophyton* challenge, steroid requirements, and symptom scores. By the end of the open treatment phase, 9 patients had increased peak expiratory flow. The clinical improvements persisted throughout 36 months of continued treatment.

Oral fluconazole appears to be a safe and effective treatment for patients with late-onset asthma associated with sensitivity to the dermatophyte *Trichophyton*. The results support the theory that allergic disease can result from sensitivity to fungi infecting the skin and nails. *Trichophyton* sensitization may occur in patients without any other sensitivity, or in those with immediate hypersensitivity to other allergens.

COMMENT: Controlling patients with severe persistent asthma can be difficult because of poor response to conventional treatment regimens. The group from the University of Virginia reports a subset of asthmatics with the development of asthma in adulthood and dermatophyte infection whose asthma responded to systemic antifungal medication. The authors document IgE hypersensitivity to *Trichophyton* protein as a possible mechanism in these patients. Physicians should check for tinea pedis and onychomycosis in adult asthmatics, as antifungal treatment may lead to improved asthma control.

M. S. B.

Ward GW Jr, Woodfolk JA, Hayden ML, et al: Treatment of late-onset asthma with fluconazole.

J Allergy Clin Immunol 104:541-546, 1999. ◆◆

Role of Neutrophilic Inflammation in Severe, Persistent Asthma Studied

ALTHOUGH little is known about the nature of airway inflammation in severe asthma, there is evidence that neutrophils may be involved. Sputum was induced from 23 patients with mild, 16 with moderate, and 16 with severe, persistent asthma. The mild group had an FEV₁ of 91% with peak expiratory flow (PEF) variability of 10.5%, requiring only inhaled β_2 -agonists; the medium group had an FEV₁ of 88% with PEF variability of 9.1%, requiring medium-dose inhaled steroids; and the severe group had an FEV₁ of 61% and PEF variability of 36.2%, despite inhaled and oral steroid therapy. Sputum profiles were compared between groups. Exhaled NO was measured as a marker of inflammation.

Percentage neutrophils in sputum was 28% in normal controls and 35% in patients with mild asthma vs 49% in those with moderate asthma and 53% in those with severe asthma. Asthma was associated with increased sputum levels of interleukin (IL)-8 and neutrophil myeloperoxidase, highest in the patients with severe asthma. Both the mild and severe asthma groups had elevated eosinophils. Patients with mild asthma had the highest IL-5 levels, while those with severe asthma had the highest eosinophil cationic protein levels. ➤➤

Asthma patients who were not receiving corticosteroids had the highest exhaled NO levels. There was no difference in exhaled NO among patients with moderate and severe asthma, both of whom were taking corticosteroids.

Airway inflammation in patients with severe asthma appears to involve both eosinophils and neutrophils, perhaps regulated in part by IL-8. High-dose corticosteroid therapy may contribute to the neutrophilic inflammation in severe asthma. The effects of persistent neutrophil activation are unknown, but may include airway remodeling.

COMMENT: *The investigators used sampling by sputum induction to avoid the risks of bronchoscopy in patients with severe asthma. The prominence of neutrophilic inflammation may explain the failure of some severe asthmatics to respond to conventional therapy. In comparison with eosinophilic inflammation, neutrophilic inflammation may be less responsive to therapy with glucocorticoids.*

J. R. B.

Jatakanon A, Uasuf C, Maziak W, et al: *Neutrophilic inflammation in severe persistent asthma.* *Am J Respir Crit Care Med* 160:1532-1539, 1999. ◆◆

Pregnant Women Receive Suboptimal Asthma Treatment

AS many as 4% of pregnancies are complicated by asthma. Two prospective cohort studies were performed to compare the characteristics, treatment, and outcomes of pregnant and nonpregnant women seen in the emergency department for acute asthma. Fifty-one pregnant and 500 nonpregnant women, aged 18 to 39 years, were compared. The 2 groups were similar in

their demographic and clinical characteristics. Median duration of symptoms was 0.75 day in both groups; initial peak expiratory flow rate was 51% in the pregnant group and 53% in the nonpregnant group.

However, only 44% of pregnant women received corticosteroids in the ED, compared with 66% of nonpregnant women. Admission rates were similar, but pregnant women who were discharged home were less likely to receive corticosteroids. At 2-week follow-up, the relapse rate was similar between groups: 11% in pregnant and 15% in nonpregnant women. However, the rate of ongoing asthma exacerbation was 35% vs 23%. On multivariate analysis, the pregnant women were at 3-fold higher risk of ongoing exacerbation.

Even given similar clinical characteristics, treatment differs for pregnant vs nonpregnant women seen in the ED for acute asthma. Pregnant women are less likely to receive corticosteroids, both in the ED and after discharge home. They are also at higher risk of ongoing asthma exacerbation at follow-up. Because of the impact on neonatal outcomes, pregnant women should receive maximal therapy for asthma exacerbations.

COMMENT: *This study combines data from two prospective cohort studies that compared the clinical presentation, treatment, and 2-week outcome of acute asthma among pregnant vs nonpregnant women. Although the two groups had the same clinical presentation, pregnant women were undertreated with systemic corticosteroids compared with their nonpregnant peers. As well, pregnant women were three times more likely to report an ongoing asthma exacerbation at a 2-week follow-up.*

J. B.-M.

Cydulka RK, Emerman CL, Schreiber D, et al: *Acute asthma among pregnant women presenting to the emergency department.* *Am J Respir Crit Care Med* 160:887-892, 1999. ◆◆

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