AllergyWatch®

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

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Dendritic Cell FcεRI Expression: Two Results for the Price of One!

THE mast cell and basophil activation associated with immediate-type hypersensitivity are induced by high-affinity IgE receptor (FcεRI) and allergen-specific IgE. Although FcεRI is known to be expressed by type I dendritic cells (DC1), no previous studies have demonstrated its expression by type 2 dendritic cells (DC2). This study sought to clarify the expression of FcεRI by DCs and its relationship to allergic disease and serum IgE levels.

Flow cytometric studies were performed to measure expression of the FcεRI α chain by peripheral blood precursor DC1 and DC2 subsets from subjects with allergic asthma and healthy controls. Both precursor subsets expressed FcεRI, as did DCs isolated from tonsillar tissues. Levels of FcεRI expression were 12 times higher in basophils and 6.5 times higher in the precursor DC1 subset than in the precursor DC2 subset.

Expression of FcεRI by both the precursor DC1 and DC2 subsets was significantly higher in subjects with allergic asthma than in nonatopic controls. Levels of FcεRI expression by precursor DC1 and DC2 subsets and basophils were strongly correlated with serum IgE, across a wide range of IgE levels.

Both the precursor DC1 and DC2 subsets express FcεRI. Expression of FcεRI by precursor dendritic cells, and by basophils, is significantly elevated in patients with allergic asthma and is correlated with serum IgE level. Treatments aimed at downregulating FcεRI have the potential to influence both the sensitization and effector phases of the allergen-specific immune response.

THE high-affinity IgE receptor (FcεRI) is expressed by dendritic cells (DCs) and other antigen-presenting cells. Previous studies have shown significant downregulation of FcεRI by basophils during treatment with omalizumab, the monoclonal anti-IgE antibody. The effects of anti-IgE therapy on DC FcεRI expression were evaluated. ➤➤

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

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

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The analysis was based on a randomized, double-blind trial of omalizumab vs placebo in 24 patients with seasonal allergic rhinitis. Patients received their assigned treatment on days 0 and 28. Blood samples were obtained on days 0, 7, 14, 28, and 42, and flow cytometry was performed to measure expression of FcεRI α on precursor type 1 and 2 DCs (DC1 and DC2).

At all time points, patients taking omalizumab showed significant reduction in expression of FcεRI by precursor DC subsets, compared with no change in the placebo group. With anti-IgE therapy, peak reductions in FcεRI expression were 52% for precursor DC1 subset and 83% for the precursor DC2 subset. These reductions were similar in magnitude to the reduction in basophil FcεRI expression, and were significantly correlated with the reduction in serum free IgE level.

Allergic patients taking omalizumab show significant and rapid reductions in FcεRI expression by DCs. This finding suggests that anti-IgE therapy might significantly inhibit antigen presentation to T cells, and thus block both the sensitization and effector phases of the allergen-specific immune response.

COMMENT: *Dendritic cells play a role in the allergic response since some DCs express the FcεRI, which enhances the Th2 response. The initial report uses flow cytometry to measure the expression of FcεRI on DC1 and DC2 subsets. This FcεRI expression was highly correlated with serum IgE and basophil FcεRI expression in allergic asthmatic patients. The second study found that patients with allergic rhinitis treated with omalizumab (monoclonal anti-IgE) had reduced DC expression of FcεRI and, consequently, a reduction in free IgE. Not only did these researchers show that serum IgE concentration was a major determinant of FcεRI expression by DCs, but they also found that downregulation of FcεRI expression with anti-IgE affects both the sensitization and effector phases of the allergic response.*
S. M. F.

Foster B, Metcalfe D, Prussin C: Human dendritic cell 1 and dendritic cell 2 subsets express FcεRI: correlation with serum IgE and allergic asthma. ***J Allergy Clin Immunol.*** *2003;112:1132-1138.*
Prussin C, Griffith DT, Boesel KM, et al: Omalizumab treatment downregulates dendritic cell FcεRI expression.
J Allergy Clin Immunol. 2003;112;1147-1154. ♦♦

GST Genotypes Identify Genetically Susceptible Patients

DIESEL exhaust particles and other particulate pollutants contribute to the development and exacerbation of allergic airway disease, partially through production of reactive oxygen species. The glutathione-S-transferases (GSTs) play various roles in antioxidant defenses, including metabolism of reactive oxygen species and detoxification of the xenobiotics found in diesel exhaust particles. The effects of GST M1 and P1 genotypes on susceptibility to the adverse effects of diesel exhaust particles were studied in a group of allergic patients.

In random order, 19 ragweed-allergic volunteers underwent intranasal challenge with ragweed alone and ragweed plus diesel allergen particles. Responses were compared with the results of *GSTM1*, *GSTT1*, and *GSTP1* genotyping studies. The investigators hypothesized that the adjuvant effects of diesel exhaust particles on allergic responses would be influenced by the null genotypes for *GSTM1* and *GSTT1* and by the *GSTP1* codon 105 variants I105 and V105.

Nasal responses to allergen were significantly enhanced in the presence of diesel exhaust particles among subjects with the *GSTM1* null or the *GSTP1* I105 wild-type genotypes. The median increase in IgE was 102.5 U/mL in subjects with *GSTM1* null, compared to 45.5 U/mL in those ➤➤

with a functional *GSTM1* genotype. Increases in histamine were 14.0 vs 7.4 nmol/L, respectively. Subjects with the I105 *GSTP1* genotype also showed enhanced responses to allergen plus diesel exhaust particles, with a median increase of 120.3 vs 27.7 U/mL for IgE and 13.8 vs 5.2 nmol/L for histamine. Patients who had both the *GSTM1* null and the *GSTP1* I/I genotypes showed the greatest response to diesel exhaust particles.

In patients with allergic rhinitis, the impact of diesel exhaust particles on the response to allergen is affected by the *GSTM1* and *GSTP1* genotype. These polymorphisms may signal a large population that is genetically susceptible to increased adverse health effects of exposure to diesel exhaust particles.

COMMENT: *Cells in the lung are protected against oxidative stress by an extensive range of intracellular defenses. Members of the GST superfamily (ie,* GSTM1, GSTT1, *and* GSTP1*) are very important in this respect. Previous studies by these authors have shown that* GSTM1*-null children exposed to tobacco smoke in utero have an increased prevalence of early-onset asthma. In this study, individuals with* GSTM1*-null or the* GSTP *105 wild-type genotypes showed enhanced nasal allergic responses in the presence of diesel exhaust particles. These observations may allow us to identify individuals susceptible to air pollution, and possibly to develop ways of protecting them from adverse effects.*
E. J. B.
Gilliland FD, Li Y-F, Saxon A, Diaz-Sanchez D: Effect of glutathione-S-transferse M1 and P1 genotypes of xenobiotic enhancement of allergic responses: randomised, placebo-controlled crossover study.
Lancet 2004;363:119-125. ♦♦

A previous study of asthmatic children in Mexico City suggested that vitamin C and E supplementation lessened the adverse effects of exposure to ozone air pollution on lung function. The glutathione transferases play a key role in the defenses against ozone and other reactive oxygen species. The relationship between a *GSTM1* polymorphism and the lung function benefit of antioxidant supplementation was analyzed.

The study included 158 asthmatic children from the previous, placebo-controlled trial of antioxidant supplementation. All children were followed up with twice-weekly spirometry throughout the 12-week study. The treatment responses were compared with the results of *GSTM1* genotyping studies.

Thirty-nine percent of the children had the *GSTM1* null genotype. This genotype was more frequent among children with moderate and severe asthma, although baseline lung function and other characteristics did not vary by *GSTM1* status. For children receiving placebo who had the *GSTM1* null genotype, daily ozone levels were significantly and inversely related to FEF_{25-75}. In contrast, no such relationship was observed for *GSTM1* positive children in the placebo group. Most of the benefit of antioxidant supplementation was concentrated in children with the *GSTM1* null genotype. The FEF_{25-75} difference between the antioxidant and placebo groups was 2.7% in *GSTM1* null children, compared with 0.9% for *GSTM1* positive children.

For children with asthma, a genetic deficiency of *GSTM1* may be associated with increased susceptibility to the damaging effects of ozone exposure. The same group of patients may also derive the greatest protective effect for supplementation with antioxidant vitamins.

COMMENT: *Previous studies have shown that certain dietary components--including higher levels of antioxidants--have a protective influence on the risk of asthma. These authors make use of deletion of glutathione S-transferase M1 (GSTM 1 null genotype), a gene involved in response to oxidative stress, to study ozone-related decline in* FEF_{25-75} *and benefit of antioxidant supplementation. The sample size was too small to allow formal tests of interaction between dietary supplementation, genotype, and outcome. However, the study showed that asthmatic children with the GSTM1 null genotype may derive greater benefit from antioxidant supplementation.*
E. J. B.
Romieu I, Sienra-Monge M, Ramírez-Aguilar M, et al: Genetic polymorphism of GSTM1 *and antioxidant supplementation influence lung function in relation to ozone exposure in asthmatic children in Mexico City.*
Thorax. 2004;59:8-10. ♦♦

Survey Finds One Percent Prevalence of Peanut/Tree Nut Allergy

THE prevalence of allergy to peanut and tree nuts appears to be increasing. A survey study was performed to assess the prevalence of peanut and tree nut allergy in the United States, including comparison with a previous survey.

The random telephone survey included 4,855 U.S. households, comprising a total of 13,493 children and adults. The survey response rate was 53%. Peanut and/or tree nut allergy was reported by 1.2% of individuals and 3.2% of households. This was similar to the prevalence rate reported in a similar survey conducted in 1997. Of affected respondents, 79% reported reactions affecting the respiratory system or multiple organ systems, while 66% reported more than five past reactions. Nevertheless, medical care had been sought for only 74% of children and 44% of adults with a history of allergic reactions to peanut or tree nuts.

With adjustment for unconvincing reactions and false positive reports, the prevalence of allergy to peanut or tree nuts was estimated at 1.04% (95% confidence interval 0.9% to 1.24%). For children under age 18, the prevalence was 1.7% for males vs 0.7% for females. For adults, the predominance pattern was reversed: 0.9% for males vs 1.7% for females. The reported rate of peanut and/or tree nut allergy increased from 0.6% to 1.2% from the 1997 to 2002 surveys, although the difference was not significant.

These survey results suggest that the prevalence of allergy to peanut and tree nuts among U.S. children has doubled in recent years. Although the overall prevalence has not changed significantly, the findings suggest that over 3 million Americans report peanut and/or ➤➤

tree nut allergy. These allergies appear to be undertreated, despite their high frequency and severity.

COMMENT: *The true prevalence of peanut and tree nut allergy is difficult to determine. Many people have the impression that this type of allergy, like many others, has been increasing. This is the second study of that prevalence, conducted by telephone survey on two occasions 5 years apart, in the United States. Although surveys of self-reported allergy can be faulted, these excellent researchers concluded that peanut allergy in children doubled from 1997 to 2002. This result is similar to that of a previous British study. The total prevalence of peanut allergy in children approaches 1%, and most reactions are anaphylactic. Strategies to prevent sensitization to peanut and tree nuts are needed.*
R. J. M.
Sicherer SH, Muñoz-Furlong A, Sampson HA: Prevalence of peanut and tree nut allergy in the United States determined by means of a random digit dial telephone survey: a 5-year follow-up study.
J Allergy Clin Immunol. 2003;112:1203-1207. ♦♦

Nasal Polyps Linked to Mammaglobulin Gene

NASAL polyps are a common and frequently recurrent problem. The pathogenesis of nasal polyps remains unknown, but may involve genetic factors. Gene-chip microarray studies and quantitative polymerase chain reaction assays were used to evaluate specific genes associated with nasal polyposis.

Total RNA was isolated from nasal mucosa specimens from 20 adult patients with allergic rhinitis, 10 with and 10 without nasal polyps. The biopsies were obtained after a 2-week period without topical or systemic steroid treatment. Of a total of 12,000 transcribed genes, 34 showed differential expression between the patients with and without nasal polyposis. The differences included genes for inflammatory molecules and growth factors. However, the single largest difference was noted for the neoplasia-related gene mammaglobulin, with expression 12 times higher in the polyposis group. Lipophilin B, a gene associated with mammglobulin in breast cancer cases, also showed increased expression in patients with nasal polyps.

Reverse-transcription PCR assays were performed in 10 additional patients with allergic rhinitis. Those with nasal polyps had an average 64-fold increase in mammaglobulin mRNA expression, compared to patients without polyposis. Neither group showed increased mammaglobulin mRNA in plasma samples.

The nasal mucosa of patients with polyposis overexpresses the mammaglobulin gene, which has previously been linked to breast cancer. Genes associated with inflammatory mediators are also differentially expressed in allergic patients with nasal polyps. The pathogenesis of nasal polyposis may involve deregulation of cell growth, with gene activation patterns similar to those of neoplasia.

COMMENT: *What do breasts and noses have in common? If the breasts have cancer and the noses have polyps, they both have excessive amounts of an obscure protein called mammaglobulin. There is a 64-fold higher amount of mammaglobulin RNA in nasal polyp tissue compared to plain allergic rhinitis. Little is known about the role of mammaglobulin in promoting neoplasia, but this finding may be a long-sought clue to the genetics and pathogenesis of nasal polyps.*
R. J. M.
Fritz SB, Terrell JR, Conner ER, et al: Nasal mucosal gene expression in patients with allergic rhinitis with and without nasal polyps.
J Allergy Clin Immunol. 2004;112:1057-1063. ♦♦

Asthma Severity Classification Varies Over Time

UNDER current guidelines, patients with asthma are characterized as having intermittent, mild, moderate, or severe disease. However, it is unclear whether patients remain in any single severity classification over time. This follow-up study examined variations in asthma severity among patients not yet placed on maintenance therapy.

The analysis included 85 asthmatic patients treated with β_2-agonist medications only, drawn from the placebo groups of two randomized, controlled trials. All were initially classified as having moderate or severe persistent asthma, based on a mean FEV_1 of 64% predicted, or on frequent asthma symptoms or albuterol use. Throughout the 12-week study period, the findings of regular clinic visits were used to classify the patients' asthma severity, based on symptoms, albuterol use, and morning peak expiratory flow.

Twelve percent of patients met criteria for intermittent asthma during at least 1 of the 12 study weeks, while 38% met criteria for mild asthma during at least 1 week. Overall, the patients met all criteria for intermittent or mild asthma for an average of 23% of study weeks. Variation was particularly wide when severity was assessed on the basis of albuterol use, with less than half of patients meeting criteria for moderate to severe disease during any given week. Based on symptoms, the patients spent 18% of weeks with intermittent asthma, 27% with mild asthma, and 55% with moderate to severe asthma.

This study documents frequent variations in asthma severity, even in a group of patients meeting criteria for moderate to severe asthma at baseline. Current guidelines, based on cross-sectional evaluation, may tend to underestimate disease severity. The authors call for more refined techniques of assessing asthma control over time for individual patients.

COMMENT: *National Asthma Education and Prevention Program guidelines characterize four degrees of asthma severity, based on symptoms, rescue medication use, and spirometry. However, this very sensible paper proves that asthma patients move frequently among the categories when analyzed longitudinally, because asthma is a dynamic condition. The observations may help explain why so-called "mild"* ➤➤

patients are as likely to die from asthma as those called "moderate" or "severe." Therapeutic dogma may have to be revised, in favor of upgrading treatment.
R. J. M.
Calhoun WJ, Sutton LB, Emmett A, Dorinsky P: Asthma variability in patients previously treated with β_2-agonists alone.
J Allergy Clin Immunol. 2003;112:1088-1094. ♦♦

Long-term Topical Steroids Don't Increase Fracture Risk

THERE is concern about bone loss as a side effect of long-term topical corticosteroid use, particularly in terms of osteoporosis and fracture risk. Previous studies of the relationship between fracture and inhaled corticosteroids have yielded mixed results. This population-based cohort study analyzed the association between inhaled and nasal corticosteroid use and fracture risk in older adults.

Canadian health insurance data were used to identify a cohort of over 200,000 older adults with at least three prescriptions for respiratory drugs in any 1-year period between 1988 and 2001. A nested case-control study included 9,624 patients with new fractures of the hip or upper limb and 191,622 age-matched controls. Mean age was 81 years in both groups; all subjects were followed up for at least 4 years. Topical corticosteroid use and other factors were evaluated for relationship to fracture risk.

About 35% of the fractures involved the hip. Crude and adjusted relative risks of fracture were not increased for patients using inhaled or nasal corticosteroids. Mean daily inhaled corticosteroid dose was slightly higher in cases than controls--with adjustment for covariates, fracture risk increased by 6% for each 1,000 µg increase in the daily inhaled corticosteroid dose. Relative risk of upper extremity fracture was slightly higher: 12% per 1,000 µg/d increase. At 8 years' follow-up, there was a significant increase in hip fracture risk for patients taking an inhaled corticosteroid dose of over 2,000 µg/d.

At usual doses, long-term inhaled and nasal corticosteroid use does not appear to increase fracture risk in older adults. Increased fracture risk is apparent only at very high doses of inhaled corticosteroids; no increase is seen at any dose of nasal corticosteroids.

COMMENT: *This paper is an excellent evaluation of the risk of fracture in older patients taking inhaled or intranasal corticosteroids for at least 4 years. There was no increased risk of fracture noted in patients taking recommended doses of topical corticosteroids for as long as 8 years. There was increased risk (relative risk 1.61) only in the group of patients taking more than 2,000 µg/d. These data in a very large cohort of patients observed over a prolonged time are reassuring of the safety in terms of orthopedic-risk elderly patients.*
G. D. M.
Suissa S, Baltzan M, Kremer R, Ernst P: Inhaled and nasal corticosteroid use and the risk of fracture.
Am J Respir Crit Care Med. 2004;169:83-88. ♦♦

Trial Shows Safety and Efficacy of Oral Immunotherapy with Grass Pollen

UNLIKE symptomatic treatments, conventional allergen immunotherapy can induce long-term remission of allergic diseases. However, subcutaneous immunotherapy carries disadvantages, including discomfort, the need for prolonged treatment, and potentially serious adverse effects. An oral immunotherapy technique, using microencapsulated antigen in enteric-coated beads, has recently been developed. This controlled trial evaluated the safety and efficacy of oral immunotherapy with timothy grass pollen extract.

Twenty-four adult patients with allergy to grass pollen were randomized to receive microencapsulated timothy grass pollen extract or placebo, once daily for 10 weeks. The dose of pollen extract was doubled weekly, starting at 12.5 bioequivalent allergy units (BAU) and increasing to 6,400 BAU. Assessment included safety and efficacy outcomes, as well as immunologic indicators.

A combined medication/symptom score decreased for 91.7% of patients receiving active oral immunotherapy, compared with 40.0% of those receiving placebo. In vitro lymphocyte studies showed at least a 30% reduction in the proliferative response to timothy grass in 75.0% of the active treatment group vs 27.2% of the placebo group. Active oral immunotherapy was also associated with reduction in allergen-induced interleukin-5 mRNA. No changes in IgG, IgE, or skin reactivity were observed. Oral immunotherapy was well tolerated, with no significant adverse events.

The results support the safety and efficacy of oral immunotherapy using microencapsulated timothy grass pollen extract. Allergy symptoms and medication use are significantly reduced, and these benefits persist several months after the end of therapy. The observed reduction in proliferative response suggests that oral immunotherapy induces a form of T-cell tolerance.

COMMENT: *The clinical database continues to expand on the efficacy of oral immunotherapy. Many questions remain to be answered prior to its introduction. Clinical and economic comparison studies must be undertaken with traditional subcutaneous immunotherapy with multiple antigens before we can determine the true impact of this therapy.*
A. M.
TePas EC, Hoyte EG, McIntire JJ, Umetsu DT: Clinical efficacy of microencapsulated timothy grass pollen extract in grass-allergic individuals.
Ann Allergy Asthma Immunol. 2004;92:25-31. ♦♦

Human Metapneumovirus as a Cause of Lower Respiratory Illness in Children

VIRAL cultures are negative in many children with lower respiratory tract disease. Recent reports have described acute respiratory infections with the newly described human metapneumovirus, a close relative of avian pneumovirus. A large research center ➤➤

database was analyzed to assess human metapneumovirus as a cause of lower respiratory tract infections in children.

The analysis included 2,009 previously healthy children with acute respiratory illnesses seen between 1976 and 2001. In 5,061 child-years of follow-up, there were 1,127 visits resulting in a diagnosis of lower respiratory tract infection. In 687 visits, nasal wash specimens were obtained; of these specimens, 321 were negative on viral cultures. For the current study, 248 previously negative samples were retested for the presence of human metapneumovirus.

On reverse-transcription polymerase chain reaction, 49 specimens were positive for human metapneumovirus, a rate of 20%. In 22 of these isolates, the virus was recovered in culture and its presence confirmed by further observations. Human metapneumovirus accounted for an estimated 12% of lower respiratory tract illness in the overall study cohort.

The clinical findings most frequently associated with human metapneumovirus were cough, coryza, rhinitis, and fever, with wheezing in many cases. Boys were affected nearly twice as often as girls; nearly 80% of illness occurred from December to April. Two percent of patients were hospitalized. Human metapneumovirus was also found in 15% of specimens from patients with upper respiratory tract infections.

Human metapneumovirus appears to be a major cause of respiratory illness in children, including bronchiolitis and croup. The clinical features of human metapneumovirus infection appear similar to those of paramyxovirus.

COMMENT: *There is a "new" respiratory pathogen on the scene: human metapneumovirus. Folks at Vanderbilt University have been saving snot from children with respiratory infections for 25 years, and now it has paid off. They found evidence of human metapneumovirus in 20% of all previously virus-negative lower tract illnesses (and 15% of upper tract infections). The clinical patterns were bronchiolitis, croup, and pneumonia. Over half wheezed. Respiratory syncytial virus has competition!*
R. J. M.

Williams JV, Harris PA, Tollefson SJ, et al: Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children.
N Engl J Med. 2004; 350:443-450. ♦♦

Gender Differences in Asthma Shift with Age

PREVIOUS studies have suggested significant gender differences in the burden of asthma. However, the impact of these differences on the prevalence and outpatient management of asthma are unclear. These questions were addressed using a large health system database.

From the Southern California Kaiser-Permanente database, the researchers identified 60,694 patients with asthma. All were aged 2 to 64 years and continuously enrolled during 1999-2000. At ages between 2 and 13 years, boys accounted for approximately 65% of cases of asthma. Gender prevalences were similar between 14 and 22. However, the pattern reversed at age 23 and older, with females accounting for 65% of cases.

Among children aged 2 to 13, measures of health care utilization and asthma medication use were greater in boys than girls. From age 14 to 22, females made more outpatient and emergency visits and received more oral steroids than males. From age 23 to 64, nearly all utilization measures were higher in women, except for β-agonist use and dispensing of inhaled steroids.

Asthma prevalence appears higher in boys than girls through puberty, similar in adolescence and young adulthood, and higher in women after the early twenties. Asthma severity and associated health care utilization are higher in males up to age 13 and higher in females thereafter, especially after age 23. More study is needed to identify the mechanisms of these sex-related differences.

COMMENT: *The authors use an extremely large and important database to reconfirm the early male predominance of asthma. Their data further address the female predominance of severe asthma after age 23. Since the study used a single health care system, the researchers were able to analyze utilization patterns. The striking differences suggest that there may be perceptual differences in the disease process, biases among providers, and differences in compliance. This striking gender gap will require further study to understand the implications for treatment!*
A. M.

Schatz M, Camargo CA Jr: The relationship of sex to asthma prevalence, health care utilization, and medications in a large managed care organization.
Ann Allergy Asthma Immunol. 2003;91:553-558. ♦♦

Childhood Factors Predict Adult Asthma Symptoms

IDENTIFYING childhood predictors of adult asthma has important implications for prognosis and, possibly, prevention. Using likelihood ratios (LRs), the authors developed an algorithm for predicting which children with asthma will have asthma symptoms in adulthood.

The analysis used data from 575 Australian subjects, recruited at age 8 to 10 years then re-evaluated at age 23 to 27 years. Potential childhood predictors included respiratory symptoms, lung function, airway responsiveness, and atopic status. Adult asthma outcomes included "asthma symptoms" and "troublesome asthma."

As adults, 200 subjects had asthma symptoms and 82 had troublesome asthma. A number of childhood factors were independently associated with asthma symptoms in adulthood. These factors, and their adjusted LRs, were: obstructive spirometry, LR 2.9; airway hyperresponsiveness, LR 2.6; atopy, LR 2.0; recent wheezing, LR 1.9; and female sex, LR 1.29. Subjects with all five risk factors in childhood had an LR of 36.9 for asthma symptoms in adulthood.

Several childhood characteristics are indepen- ➤➤

dently associated with the presence of asthma symptoms in adulthood. Children with an obstructive pattern on spirometry, airway hyperresponsiveness, and atopy are at high risk of having asthma as adults and thus likely to benefit from preventive measures. The authors' algorithm may be a useful prognostic tool for use with asthmatic children.

COMMENT: *This is an interesting study looking at risk factors in children that predict the development of asthma as adults. The authors use the technique of likelihood ratios, instead of simple risk factors, to identify those children who were most likely to develop asthma as adults. The population (575) was studied at age 8 to 10 and reassessed 15 to 17 years later. Decrease in FEV_1, airway hyperresponsiveness, atopy, recent wheeze, (ie, after an upper respiratory infection), and female gender all had increased LRs for asthma. In females who had evidence of the other four parameters, the LR was 36.9 for adult asthma symptoms. This study provides another, possibly more sensitive way of identifying at-risk patients for future intervention protocols to prevent development of adult asthma.*
G. D. M.

Toelle BG, Xuan W, Peat JK, Marks GB: Childhood factors that predict asthma in young adulthood.
Eur Respir J. 2004;23:66-70. ♦♦

Smoking Reduces Response to Oral Steroids in Asthma Patients

MORE than one-fifth of adult patients with asthma smoke cigarettes. Smoking by asthmatic patients has been linked to more severe symptoms, more rapid decline in lung function, and increased hospitalization and mortality rates. This study examined the influence of smoking on the effectiveness of systemic corticosteroid therapy for chronic stable asthma.

The trial included 50 patients with chronic, stable asthma. By smoking history, 14 were current smokers, 10 former smokers, and 26 never-smokers. The three groups had comparable baseline characteristics, including an FEV_1 predicted of about 70% before and 85% after albuterol. In randomized, crossover fashion, the patients were studied after 2 weeks of treatment with oral prednisolone, 40 mg/d; and 2 weeks of treatment with placebo. Outcome measures included pulmonary function values and asthma control score.

Oral prednisolone led to a significant mean 237 mL improvement in FEV_1 for patients in the never-smoking group. In contrast, for the current and former smokers, the mean change in FEV_1 was not significant: 47 and 143 mL, respectively. For never-smokers, the improvement in FEV_1 was similar whether they received prednisolone or placebo first. Prednisolone was associated with improved morning and nighttime peak expiratory flow for never-smokers and former smokers, but not for current smokers. Asthma control score and symptom scores improved for never-smokers only.

For patients with chronic stable asthma, cigarette smoking is associated with reduced responsiveness to high-dose oral corticosteroid therapy. In current smokers, a 2-week course of oral prednisolone yields no significant improvement in pulmonary function or asthma symptoms. Responses may also be reduced in former smokers as well. The mechanism of smoking-related corticosteroid insensitivity in asthma is unclear.

COMMENT: *The instructions for asthma patients to stop smoking are generally based on overall health concerns and the potential for increased disease activity. This study shows a decrease in the effectiveness of systemic steroids on FEV_1, peak expiratory flow, and symptom scores in asthma patients who are current smokers, compared with those who never smoked. Former smokers have a better response to prednisolone than current smokers, but less so than those who have never smoked. Given risk factors for starting to smoke in our society, these data reinforce the need for smoking prevention efforts in asthma patients.*
G. D. M.

Chaudhuri R, Livingston E, McMahon AD, et al: Cigarette smoking impairs the therapeutic response to oral corticosteroids in asthma.
Am J Respir Crit Care Med. 2003;168:1308-1311.

Childhood Infections Don't Explain Protective Effect of Siblings on Atopy Risk

STUDIES from several countries have suggested lower rates of atopy and hay fever in children from larger families. One proposed explanation is that children with siblings have early exposure to infection, promoting development of Th1-type lymphocytes. The relationship between childhood infections and adult atopy was evaluated in a British cohort study.

The analysis included 583 women, recruited during antenatal care for a prospective study of childhood asthma; and 480 of their partners. Median age was 28 years. Atopy was assessed by skin-prick testing with common aeroallergens, while data on childhood infections, antibiotic prescriptions, and other factors were gathered by questionnaire and review of medical records.

Atopy was detected in 37% of subjects, with a higher rate in men and subjects with a family history of allergy. Atopy was inversely related to number of siblings during early life: odds ratio (OR) 0.85 per additional sibling (95% confidence interval 0.77 to 0.94). This association reflected only brothers, OR 0.76 (0.60 to 0.87), with no protective effect of sisters.

The relationship between siblings and atopy could not be explained by serologic evidence of hepatitis A or *Helicobacter pylori* infection. Atopy risk was unaffected by number of childhood infections or antibiotic prescriptions, although number of GI infections before age 5 was inversely related to atopy. Other possible protective factors included owning a dog and moving homes before age 5.

The study confirms the protective effect of family size on atopy risk. However, this association does not appear to be influenced by childhood history of infections. The protective effect of siblings appears to be largely ➤➤

explained by the number of brothers, not sisters.

COMMENT: *The hygiene hypothesis indicates the protective effects of having siblings in risk for allergic disease. The mechanism most often advanced focuses on increased infections in the younger sibling, which can protect against the development of allergy and asthma later in life. This study examined the infection history of siblings, correlated with family size and prevalence of atopy. Family size inversely correlated with atopy. Other factors, such as the presence of a dog and frequency of moving in childhood, appear protective. However, history of infections or antibiotic prescriptions did not correlate with incidence of atopy. This study implies that the sibling effect for protection against atopy cannot be explained solely by infectious etiologies.*

G. D. M.

Cullinan P, Harris JM, Newman Taylor AJ, et al: Can early infection explain the sibling effect in adult atopy?
Eur Respir J. 2003 22:956-961. ♦♦

Does Weight Matter in Asthma?

RECENT decades have seen concomitant increases in childhood obesity and asthma. Studies have linked increased body mass index (BMI) with increased incidence and prevalence of asthma, although the mechanisms of this relationship are unclear. Randomized trial data were used to assess the relationship between BMI and lung function indices in children with asthma.

The analysis included baseline data on 1,041 asthmatic children from the Childhood Asthma Management Program study. On multivariate analysis, the only asthma symptom significantly related to BMI was cough and wheezing with exercise: odds ratio (OR) 1.05 (95% confidence interval 1.01 to 1.10). Analysis of intermediate phenotypes of asthma and atopy found a negative association between BMI and airway response to methacholine, but this association disappeared after adjustment for FEV_1.

On analysis of pulmonary function measures, BMI was significantly and positively associated with FEV_1, forced vital capacity, and peak flow. In addition, as BMI increased, the FEV_1/FVC ratio decreased: for each 5-unit increase in BMI, the FEV_1/FVC ratio decreased by more than 1%. These relationships differed by sex, with girls showing stronger associations of BMI with FEV_1 and FVC. However, boys showed a greater reduction in FEV_1/FVC ratio at increased BMI.

Body mass index does not seem to be related to measures of atopy and asthma severity in children. However, there is some evidence of a relationship between BMI and pulmonary function variables in childhood asthma. The observed link between increased BMI and a decrement in the FEV_1/FVC ratio suggests that a relationship between body weight and asthma severity may yet be found.

COMMENT: *The authors hypothesized that BMI would be independently associated with measures of asthma severity in children with mild to moderate asthma. They found that BMI at baseline was not related to respiratory symptomatology or to any of four prominent intermediate phenotypes of asthma and atopy. They did observe a decrement in FEV_1/FVC ratio in association with increasing BMI. They advocate further studies to evaluate specific aspects of BMI/asthma relationships to provide further insights into the pathogenesis and treatment of childhood asthma.*

E. J. B.

Tantisira KG, Litonjua AA, Weiss ST, Fuhlbrigge AL: Association of body mass with pulmonary function in the Childhood Asthma Management Program.
Thorax. 2003;58:1036-1041. ♦♦

BECAUSE of the inflammatory and mechanical effects of obesity, high birthweight might be a contributor to the rising rates of childhood asthma. The relationship between birthweight and childhood asthma was evaluated in a prospective, population-based study.

The analysis included all 83,595 term infants born in Alberta from 1985 to 1988. The infants were classified as low, normal (2.5 to 4.5 kg), or high birthweight. The three groups were compared for their rates of emergency department visits for asthma through 10 years' follow-up.

The crude rate of emergency department visits for asthma was 136.2/10,000 person-years for girls and 235.5/10,000 for boys. Infants with birthweights over 4.5 kg had a significantly higher rate: adjusted relative risk 1.16 (95% confidence interval 1.04 to 1.29) compared with normal-birthweight infants. Each 0.10 kg increase over 4.5 kg carried a 10% increase in the 10-year risk of emergency visits. Low-birthweight children were not at increased risk. Other significant risk factors were male sex, aboriginal race, and low income level.

Above-normal birthweight is associated with an increased risk of emergency department visits for asthma during childhood. The mechanism of this association is unclear, though it may reflect the increased rates of obesity in high-birthweight children. In contrast to some previous reports, this study finds no increase in asthma risk for low-birthweight children.

COMMENT: *Another serious issue related to obesity: asthma! And, it may start at birth (or before)! To my knowledge, this is the first study that gives convincing evidence relating* high *birth weight to an increased risk of developing acute asthma. It also gives additional support to the belief that low birth weight (in full-term infants) is* not *related to increased asthma risk. The power of this prospective study is impressive: all infants born in Alberta, Canada, at term from 1985 to 1988--N = 83,585--followed up for 10 years. In future studies, it would be interesting to know whether the mothers of these overweight babies were obese and their relative weight gain during pregnancy. Given the importance of family history of asthma, it is too bad that this was not assessed and compared with other parameters in the study. Also, it is not known if the children who were large at birth were still "overweight" at the time of asthma diagnosis.*

J. A. A.

Sin DD, Spier S, Sheldon LW, et al: The relationship between birth weight and childhood asthma: a population-based cohort study.
Arch Pediatr Adolesc Med. 2004;158:60-64. ♦♦

Frequency of Latex Sensitization vs Allergy

LATEX glove allergy is reportedly a widespread problem among health care workers, with prevalence estimates ranging from 3% to 15%. Rates, risk factors, and characteristics of latex hypersensitivity were assessed among workers at Veterans Affairs (VA) medical centers.

The study included a total of 1,959 workers at 3 Midwest VA centers. In addition to an interview and questionnaire, the workers underwent measurement of serum antilatex IgE antibody and skin testing with common aeroallergens. The type and extent of latex glove use were assessed, along with rates of latex hypersensitivity.

The overall rate of symptomatic latex glove allergy and/or a positive CAP test for latex allergy was 8.1%. Of those workers reporting any latex glove use, 22.2% used powdered gloves. The mean number of pairs of powdered gloves used was 2.31 per day. Just 11 of 133 workers reporting allergic symptoms related to latex gloves had a positive CAP test--thus the prevalence of confirmed latex glove allergy was only 0.6%. Subjects with positive CAP results were more likely to be atopic than those with negative results. Risk factors for latex allergy symptoms and/or sensitization included high exposure to latex gloves, nonwhite race, and atopy.

Although 8% of health care workers in this study report symptoms related to latex allergy, under 1% of symptomatic workers are sensitized to latex. This low rate of confirmed sensitization may reflect the low use of nonpowdered gloves and underscores the need for objective IgE testing.

COMMENT: *These important observations on latex allergy in health care workers are an important reminder to clinicians. Latex allergy remains a significant problem in health care workers, but the extent of the problem may be less that previously reported. Whether this apparent decrease is due to differences in study design or better avoidance measures, the results are very encouraging!*
A. M.

Zeiss CR, Gomaa A, Murphy FM, et al: Latex hypersensitivity in Department of Veterans Affairs health care workers: glove use, symptoms, and sensitization.
Ann Allergy Asthma Immunol. 2004;91:539-545. ♦♦

Chronic Cough Linked to Elevated Sputum Inflammatory Mediators

EVEN after extensive workup, no cause of chronic cough is identified in as many as one-fifth of cases. Some reports have described airway inflammation in patients with chronic cough, suggesting a role of tussive mediators with activation of sensory nerve endings. Inflammatory and tussive mediators were measured in induced sputum samples from patients with chronic cough.

The investigators obtained induced sputum supernatants from a representative sample of 20 patients with cough variant asthma or eosinophilic bronchitis, 20 with nonasthmatic chronic cough, and 22 with idiopathic chronic cough, along with 18 healthy controls. Median sputum histamine level was 8.0 ng/mL in patients with idiopathic chronic cough and 10.2 ng/mL in those with cough variant asthma/eosinophilic bronchitis. These were significantly higher than the values in controls and patients with nonasthmatic chronic cough: 2.6 and 3.3 ng/mL, respectively. All three chronic cough groups had elevated levels of sputum proinflammatory mediators, including prostaglandin D_2 and prostaglandin E_2.

The study is the first to show elevated sputum levels of protussive mediators in patients with chronic cough. Sputum histamine is increased in patients with idiopathic chronic cough and cough variant asthma/eosinophilic bronchitis. More study will be needed to clarify the role of protussive mediators in the mechanism of chronic cough.

COMMENT: *Patients with chronic cough are often referred for evaluation of possible cough variant asthma vs bronchitis vs other causes (endobronchial lesions, etc.). Therapies often involve chronic cough suppressants, which may be minimally effective. This study looked for the presence of inflammatory mediators, including histamine, leukotrienes, prostaglandins, and interleukin-8. Results indicated the presence of various inflammatory mediators in sputum samples compared to normals. This suggests potential therapeutic value of anti-inflammatory agents for at least some patients with chronic cough for whom asthma is not a proper diagnosis.*
G. D. M.

Birring S, Parker D, Brightling CE, et al: Induced sputum inflammatory mediator concentrations in chronic cough.
Am J Respir Crit Care Med. 2004;169:15-19. ♦♦

Age at Onset and Lung Eosinophils Define Phenotypes of Severe Asthma

ALTHOUGH asthma is recognized as a heterogeneous condition, there are few data on the various asthma phenotypes and their immunologic, physiologic, and pathologic characteristics. This study compared the phenotypes of early-onset, severe asthma vs late-onset asthma, including the impact of eosinophilia.

The cross-sectional study included 80 patients referred for evaluation of severe, refractory asthma. Fifty had early-onset disease (before age 12): 56% females, mean age 29 years. The remaining 30 patients had late-onset asthma: 59% females, mean age 42 years. Integrated clinical, physiologic, and pathologic data were analyzed, including the presence vs absence of pulmonary eosinophils.

Skin tests were positive in 98% of patients with early-onset asthma compared with 76% in the late-onset group. Early-onset asthma was also associated with increased allergic symptoms. However, despite ➤➤

their shorter duration of disease, patients with late-onset asthma had lower pulmonary function values: mean FEV_1 48% predicted, compared with 56% predicted in the early-onset group.

Regardless of age at onset, general asthma symptoms were severe. In both groups, patients with persistent eosinophilia had more severe symptoms and poorer lung function. Lung eosinophil numbers were highest in the late-onset asthma group, but a lymphocytic/mast cell inflammatory process appeared only in the early-onset group. Subepithelial basement membrane thickening was not observed in patients with late-onset asthma who did not have eosinophilia.

For patients with severe asthma, information on early vs late onset and presence vs absence of eosinophils may help in distinguishing disease phenotypes. The four phenotypes identified in this study may have implications for asthma genetics and treatment.

COMMENT: *These Denver researchers examined differentiating features in 80 patients with severe steroid-dependent asthma. They were able to separate the group into four different phenotypes. In general, those with childhood-onset asthma had a nonallergic eosinophilic inflammatory response. Should we return to the old extrinsic vs intrinsic asthma categories? It's taken a long time to challenge this older paradigm in favor of considering asthma triggers and severity in our classification. Further research in differentiation of asthma phenotypes is particularly helpful, since it could improve our understanding of disease progression and eventually target therapy to specific groups.*
S. M. F.

Miranda C, Busacker A, Balzar S, et al: Distinguishing severe asthma phenotypes: role of age at onset and eosinophilic inflammation.
J Allergy Clin Immunol. 2004 113:101-108. ♦♦

Oral Prednisolone Reduces Symptoms in Toddlers with Viral Respiratory Distress

THERE is ongoing debate over the use of systemic corticosteroids for preschool-aged children with acute wheezing. Oral prednisolone was compared with placebo for management of acute respiratory distress in infants and young children.

The trial included 230 children, aged 6 to 35 months, seen in the emergency department for lower airway disease related to viral respiratory infection. Patients with diagnosed asthma or two or more previous episodes of wheezing were excluded. The children were randomized to receive 3 days of treatment with oral prednisolone, 2 mg/kg/d, or placebo.

Children receiving prednisolone had a somewhat lower rate of hospitalization lasting 3 days or longer, 47.5% vs 67.7%. Oral prednisolone therapy was associated with a reduced need for additional asthma medication, 18.0% vs 37.1%. In addition, symptoms of respiratory distress cleared more rapidly in the prednisolone group: median 1 vs 2 days for both hospitalized and nonhospitalized children.

A short course of oral prednisolone therapy appears beneficial for toddlers with viral-induced respiratory distress. Although hospitalization rate is unaffected, symptom duration and disease severity are significantly reduced in children receiving prednisolone vs placebo.

COMMENT: *I'm confused! There seems to be no end to the controversy regarding the value of systemic corticosteroids in treating clinical symptoms of viral-induced wheezing in young children (bronchiolitis?). Just when I was convinced that oral steroids don't work in bronchiolitis, along comes this randomized, double-blind, placebo-controlled trial involving 230 children aged 6 to 35 months, who are first- or second-time "wheezers" with a viral infection. Asthmatics were not included. No frank diagnosis of bronchiolitis was made and the viral cause was not determined. All children were treated with inhaled salbutamol. These Finnish researchers determined that prednisolone 2 mg/kg/d for 3 days, begun in the emergency department, did not prevent hospitalization. However, it did decrease the number of days until the children were asymptomatic, regardless of history of previous wheezing. In an editorial, Miles Weinberger places this study in perspective with other studies involving the management of bronchiolitis.*
J. A. A.

Csonka P, Kaila M, Laippala P, et al: Oral prednisolone in the acute management of children age 6 to 35 months with viral respiratory infection-induced lower airway disease: a randomized, placebo-controlled trial. **J Pediatr.** 2003;143:725-730. ♦♦

Pertussis Vaccine Doesn't Increase Allergic Disease Risk

SOME studies have suggested that pertussis vaccination in infancy leads to an increased risk of allergy and asthma. However, previous prospective trials have found no difference in the rates of these diseases among immunized and nonimmunized children. Allergic disease outcomes were analyzed in a large cohort of immunized children.

In 1992, 2-month-old infants in 14 Swedish centers were randomized to receive one of three pertussis vaccines--a 2-component, 5-component, or whole-cell vaccine, given together with diphtheria or tetanus toxoid--or a diphtheria-tetanus vaccine alone. Allergic disease outcomes were assessed at age 7 in 667 children, including skin-prick testing in 538.

The overall cumulative rate of allergic disease was 34.9%. By vaccine group, the range was 33.3% to 37.3%. The differences between groups were not significant, even with adjustment for family history, sex, and exposure to pets and environmental tobacco smoke. Children with a family history of allergy had higher rates of bronchial asthma, allergic rhinoconjunctivitis, and positive skin-prick tests. An experimental 2-component pertussis vaccine, no longer in use, was associated with a higher rate of skin-prick test results.

This follow-up study finds no increase in allergic ➤➤

disease among children receiving pertussis vaccines in infancy. In the lack of evidence showing a causal relationship with asthma and other allergic diseases, the results support continued pertussis vaccination during early infancy.

COMMENT: *Three prior observational studies (1994 to 1998) have suggested an increased risk of both allergy and asthma after routine pertussis infant immunization. This prospective, double-blind study Swedish study of 2-month-old infants begun in 1992 examined the effect of either pertussis plus diphtheria-tetanus (DPT) or diphtheria-tetanus (DT) on the development of clinical allergy asthma and the results of allergy prick test at 7 years. Fortunately, there was no statistical difference in the rate of allergies, asthma, or positive skin tests! Four hundred ninety children received one of three DPT vaccine types, while 177 received DT injections. This study reinforces the safety of DPT shots, particularly in families where the potential for asthma and allergy is higher.*
J. A. A.
Nilsson L, Kjellman N-IM, Björkstén B: Allergic disease at the age of 7 years after pertussis vaccination in infancy. results from the follow-up of a randomized controlled trial of 3 vaccines.
Arch Pediatr Adolesc Med. 2003;157:1184-1189.

Interferon-alpha Shows Benefits in Steroid-Resistant Asthma

THE cytokine interferon-α (IFN-α), with its multiple immunologic effects, has been used to treat benign neoplasia and viral diseases, as well as corticosteroid-resistant hypereosinophilic syndrome. This study evaluated the clinical and immunologic effects of IFN-α in patients with severe corticosteroid-resistant asthma.

Ten patients with severe corticosteroid-resistant asthma were treated, three of whom met criteria for Churg-Strauss syndrome. All received IFN-α, 3 x 10^6 IU/d, in addition to their previous dose of prednisone. The prednisone dose was lowered according to the patients' clinical response, but was held stable for at least 2 weeks in 7 of the 10 patients. Clinical and immunologic responses were evaluated at 2 to 4 weeks and at 5 to 10 months.

After starting treatment with IFN-α, the patients showed rapid improvement in lung function parameters and in required prednisone dose. Immunologic effects included a reduction in leukocyte numbers, increased differentiation of Th1 cells, and increased expression of interleukin-10 in peripheral blood mononuclear cells.

Interferon-α therapy yields dramatic benefits in patients with corticosteroid-resistant asthma, including those with Churg-Strauss syndrome. Although further study is needed, the mechanism of this benefit may involve correction of the Th1/Th2 balance and stimulation of the anti-inflammatory interleukin-10 gene.

COMMENT: *This preliminary study of 10 patients with steroid-resistant asthma evaluated the efficacy of IFN-α treatment and the changes in immune cells in blood. Interestingly, the IFN-α has a rapid beneficial effect on this group of patients, 3 of whom had fulfilled the diagnostic criteria of Churg-Strauss syndrome. When IFN-α was withdrawn, all clinical and immunologic effects were reversible. Suggested mechanisms of action included rebalancing of Th1/Th2 status and induction of the anti-inflammatory IL-10 gene.*
E. J. B.
Simon H-U, Seelbach H, Ehmann R, Schmitz M: Clinical and immunologic effects of low-dose IFN-α treatment in patients with corticosteroid-resistant asthma. **Allergy.** 2003;1250-1255. ♦♦

REVIEWS OF NOTE

COMMENT: *This exceptionally insightful review queries a number of important unanswered questions regarding airway remodeling (AR) in asthma. These include whether AR affects all asthma patients, the physiologic relevance of AR, factors predisposing to AR, biomarkers predicting AR, and--most importantly--the effect of current asthma therapies on AR and disease progression.*
E. J. B.
Lazaar AL, Panettieri RA Jr: Is airway remodeling clinically relevant in asthma?
Am J Med. 2003;115:652-659.

COMMENT: *This panel of asthma experts reviews several important questions surrounding inhaled corticosteroids (ICS) and their potential side effects. An extensive literature review supports the use of low and medium ICS doses in asthmatic children. There is strong evidence that these doses of ICS do not lead to significant changes in adult height or decreased bone density. In adults, bone mineral density may be decreased, especially in individuals requiring higher doses of ICS. As a general rule, it is a prudent move to decrease ICS doses as tolerated and use add-on asthma therapy in order to minimize ICS side effects. The authors suggest that the information here provides a knowledge base to build in the future.*
A. L. L.
Leone FT, Fish JE, Szefler SJ, et al: Systematic review of the evidence regarding potential complications of inhaled corticosteroid use in asthma: collaboration of American College of Chest Physicians, American Academy of Allergy, Asthma, and Immunology, and American College of Allergy, Asthma, and Immunology.
Chest. 2003;124:2329-2340.

COMMENT: *Allergists are distinguished in part from other physicians by knowledge of the environment as a source of allergens. This paper suffers from limited information on specific regional concerns, most* ➤➤

likely due to space limitations. However, it does provide an excellent overview of the major allergenic pollens.
D. K. L.
White JF, Bernstein DI: Key pollen allergens in North America.
Ann Allergy Asthma Immunol. 2003;91:425-435. ♦♦

COMMENT: *The TENOR study is remarkable for many reasons. This database contains information on almost 5,000 "difficult-to-treat" asthmatics from over 400 centers. The prospective nature of the study has yielded important baseline observations, but more importantly will provide the framework for future observations on the natural history of this challenging group of patients.*
A. M.
Dolan CM, Fraher KE, Bleecker ER, et al: Design and baseline characteristics of The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study: a large cohort of patients with severe or difficult-to-treat asthma.
Ann Allergy Asthma Immunol. 2004;92:32-39. ♦♦

COMMENT: *This review provides an excellent source of information about the safety of vaccines in regard to preservatives and other additives/residuals. The issues concerning the risk of residual egg protein in influenza vaccine and the lack of risk in measles or mumps vaccine are clear-cut. The potential of hypersensitivity reactions to gelatin is highlighted, along with a table in 14 different U.S. vaccines (in 2003) containing gelatin. In addition, a great deal of the article is devoted to other issues such as mercury exposure in vaccines containing thimerosal, the safety of aluminum as an adjuvant, human serum albumin as a stabilizer, and the only-theoretical risk of "mad-cow disease" from bovine-derived agents.*
J. A. A.
Offit PA, Jew RK: Addressing parents' concerns: do vaccines contain harmful preservatives, adjuvants, additives, or residuals?
Pediatrics. 2004;112:1394-1401. ♦♦

COMMENT: *Patients with chronic obstructive pulmonary disease (COPD) are usually treated by a pulmonologist rather than an allergist/immunologist. However, many if not most patients have features of both asthma and COPD. For example, more than 70% of COPD sufferers have airway hyperreactivity and/or chronic mucus production. Thus allergists/immunologists are often involved in the care of patients with possible COPD. These two papers provide a thorough review of the literature and current treatment options.*
D. K. L.
Sin DD, McAlister FA, Man SFP, Anthonisen NR: Contemporary management of chronic obstructive pulmonary disease: scientific review. JAMA. 2003;290:2301-2312; Man SFP, McAlister FA, Anthonisen NR, Sin DD: Contemporary management of chronic obstructive pulmonary disease: clinical applications. **JAMA.** 2003;290:2313-2319. ♦♦

COMMENT: *The first section of the respiratory tract, the nose, is frequently overlooked in pulmonary diseases, especially sleep-disordered breathing (SDB). This review discusses several nasal disorders that may have a significant impact on SDB. It is as plain as the nose on your face to consider nasal disorders in SDB!*
A. L. L.
Rappai M, Collop N, Kemp S, deShazo R: The nose and sleep-disordered breathing: what we know and what we do not know. Chest. 2003;124:2309-2323. ♦♦

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