AllergyWatch®

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

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ACRN Reports New Technique of Comparing Systemic Effects of Inhaled Corticosteroids

THE choice of inhaled corticosteroids for asthma treatment should consider not only their efficacy but also their potential for adverse systemic effects. This article reports on a new method of assessing the systemic bioavailability of inhaled corticosteroids, as well as determining their equisystemic effects in asthma patients.

The Asthma Clinical Research Network (ACRN) multicenter trial included 156 asthmatic patients with no previous corticosteroid therapy. In a 1-week, doubling-dose design, the patients received six inhaled corticosteroids and matching placebos in four different doses. The medications and delivery devices tested were: beclomethasone dipropionate via chlorofluorocarbon metered-dose inhaler (CFC-MDI), budesonide via dry-powder inhaler (DPI), flunisolide via CFC-MDI, fluticasone propionate via DPI, fluticasone propionate via CFC-MDI, and triamcinolone acetonide via CFC-MDI. Various measures of the systemic effects of the inhaled corticosteroid preparations were evaluated, including hourly plasma cortisol, 12- and 24-hour urine cortisol, and morning blood osteocalcin.

The single best measure of systemic effects was the area under the concentration-time curve for hourly cortisol concentrations. Using this parameter, a significant dose-response effect was apparent for each medication-delivery device combination tested except fluticasone via DPI. At the 10% level of cortisol suppression, microgram doses producing an equisystemic effect were: 936 µg for flunisolide via CFC-MDI, 787 µg for triamcinolone via CFC-MDI, 548 µg for beclomethasone via CFC-MDI, 445 µg for budesonide via DPI, and 111 µg for fluticasone via CFC-MDI.

The findings suggest a useful new technique for comparing various inhaled corticosteroid preparations for their equisystemic effects in terms of cortisol suppression. Although this method requires frequent plas- ➤➤

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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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ma cortisol sampling and an overnight laboratory test, it is the most reliable measure of cortisol suppression tested. The technique will be used in a future ACRN study including assessment of respiratory efficacy outcomes.

COMMENT: *Comparisons of inhaled corticosteroid products have focused on the relative potency of molecules as an indicator of their efficacy and systemic bioavailability. It is increasingly appreciated that the delivery device (ie, CFC-MDI vs DPI) also affects these parameters. This study included direct, head-to-head comparisons of not only the different molecules but also of various delivery devices. The study used overnight cortisol suppression – assessed by 8:00 p.m. to 8:00 a.m. serum cortisol levels-as a rapid indicator of systemic bioavailability. This method may prove to be a better indicator of bioequivalence than currently used microgram comparisons. Such an improvement may be particularly important when considering changes from one delivery method to another with the same molecule.*
G. D. M.
Martin RJ, Szefler SJ, Chincilli VM, et al: Systemic effect comparisons of six inhaled corticosteroid preparations.
Am J Respir Crit Care Med 165:1377-1383, 2002. ♦♦

Liposome-Encapsulated Allergen Vaccination Reduces Asthma Symptoms

LIPOSOMES are naturally occurring lipids with low allergenic potential and a significant depot effect after subcutaneous injection. These characteristics make them potentially attractive as allergen carriers for allergy vaccination. The clinical efficacy and immunologic effects of liposome-encapsulated allergen vaccination were evaluated.

The 1-year study included 55 patients with mild to moderate asthma and confirmed allergy to *Dermatophagoides pteronyssinus*. Exclusion criteria included sensitization to other allergens and long-term corticosteroid therapy, and no topical corticosteroids were permitted during the study. Patients were randomized to receive regular injections with *D. pteronyssinus* encapsulated in active or placebo (empty) liposomes, average diameter 200 nm. Evaluations included immediate and late skin testing, allergen bronchial challenge testing, allergen-specific immunoglobulin levels, and symptom diary cards.

Fifty patients received the full 12 months of vaccinations. Evaluation of diary cards suggested that patients receiving active liposomes had significant improvement in the percentage of "healthy days": from 10.5% at baseline to 64.5% after vaccination. Nearly half of patients in the active-treatment group had a 60% or greater reduction in symptom and medication scores. By comparison, the placebo liposome group showed no improvement in symptoms or medication requirements. Vaccination with active liposomes was also associated with decreased skin and bronchial sensitivity to allergen, and with rapid and sustained increases in specific IgG, IgG_1, and particularly IgG_4. The liposome-encapsulated allergen was well-tolerated.

This randomized, controlled trial supports the efficacy of vaccination with liposome-encapsulated *D. pteronyssinus* for patients with allergic asthma. The results show significant reductions in symptoms, along with other evidence of clinical benefit. Because the study did not permit topical corticosteroid therapy or environmental control measures, the results support the positive effects of specific allergen vaccination.

COMMENT: *This is a fascinating study that is relevant to three very important questions. First, can allergy immunotherapy be effective against asthma? Second, how important might dust mites be in the pathogenesis of asthma? And third, can the therapeutic index of allergy immunotherapy be improved by physically altering the allergen in the vaccine, by liposome encapsulation? (Yes, sometimes very, and yes.)*
R. J. M.

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Basomba A, Tavar AI, de Rojas DHF, et al: Allergen vaccination with a liposome-encapsulated extract of Dermatophagoides pteronyssinus*: a randomized, double-blind, placebo-controlled trial in asthmatic patients.*
J Allergy Clin Immunol 109:943-948, 2002. ♦♦

Airway Remodeling in Asthma: What Are the Risk Factors and When Does It Start?

RECENT studies have demonstrated that chronic inflammation can lead to airway remodeling (AR) with irreversible loss of function in asthma patients. This very long-term study investigated risk factors for asthmatic AR from childhood through young adulthood. The analysis was based on a cohort of 1,037 children born in New Zealand during 1973. Respiratory questionnaires were administered at ages 9, 11, 13, 15, 18, 21, and 26 years; methacholine challenge testing and spirometry at 9, 11, 13, 15, and 21 years; and skin prick testing at 13 and 31 years. The results of these studies were analyzed as possible risk factors for AR, assessed in terms of the postbronchodilator FEV_1 vital capacity (VC) ratio in adulthood. Based on results in a group of normal subjects with no history of asthma or smoking, the lower limit of normal for FEV_1/VC ratio was set at the mean minus 1.96 standard deviation.

Based on this definition, 7.4% of subjects had a low postbronchodilator FEV_1/VC ratio at age 18, 6.4% at age 26, and 4.6% at both periods. The latter group of subjects had low pulmonary function results at all study times during childhood. The reduction in prebronchodilator ratio from age 9 to 26 was -12% in male subjects with persistently low postbronchodilator ratios compared with -6% in male subjects with normal postbronchodilator ratios. Corresponding figures for female subjects were -10.5% vs -5.5%.

Independent risk factors for a low postbronchodilator FEV_1/VC ratio included asthma, male sex, airway hyperresponsiveness, and low pulmonary function in childhood. In addition, a low postbronchodilator FEV_1 VC ratio was associated with a faster decline in lung function and decreased reversibility of airway obstruction.

A low postbronchodilator FEV_1/VC ratio could be a useful early predictor of AR in young asthma patients, the results suggest. The process of AR and impaired pulmonary function appears to commence in childhood and continue through early adulthood. Patients in whom the postbronchodilator FEV_1/VC ratio is persistently low at serial assessments 8 years apart may be at high risk for rapidly declining lung function.

COMMENT: *It is becoming more accepted that AR does occur in asthma and is a clinically relevant occurrence. However, little has been published regarding risk factors predisposing to the most severe remodeling, which results in irreversible loss of airway function. This paper describes a longitudinal case-control study from birth to 26 years, looking at factors predisposing to AR. A low postbronchodilator FEV_1/VC ratio at 18 and 26 years was used as evidence of AR. Between 6% and 7% of individual asthma patients showed evidence of AR at one or the other time point. Risk factors included male gender, airway hyperresponsiveness, and low lung function in childhood. This interesting work suggests that AR has early beginnings, and further begs the question of just how soon to intervene aggressively (ie, give inhaled corticosteroids) in children with asthma.*
G. D. M.

Rasmussen F, Taylor DR, Flannery EM, et al: Risk factors for airway remodeling in asthma manifested by a low postbronchodilator FEV_1 vital capacity ratio: a longitudinal population study from childhood to adulthood.
Am J Respir Crit Care Med 165:1480-1488, 2002. ♦♦

Study Cites 18% Prevalence of Physician-Diagnosed Asthma in Children

CHILDHOOD asthma is a common condition with a major impact on the lives of children. However, relatively little is known about the natural history of asthma in children-previous large studies of physician-diagnosed asthma have focused on inner-city children. A unique epidemiologic data base was used to evaluate physician-diagnosed asthma in a population-based cohort of schoolchildren.

The analysis included a 50% random sample all children enrolled in Rochester, Minn., public schools, kindergarten through twelfth grade. Data were obtained through the Rochester Epidemiology Project, which links all residents of Olmsted County, Minn., to their medical care providers in the community. This data base was used to gather information on all visits for asthma, reactive airway disease, asthmatic bronchitis, exercise-induced asthma, bronchospasm, and recurrent wheezing. The final analysis included complete school and medical data on 2,816 children.

At least one asthma diagnosis was recorded for 17.6% of children, with 16.0% having multiple diagnoses. The rate of asthma diagnosis was substantially higher for boys than girls, 21.0% vs 13.9%. The mean age at initial diagnosis of asthma was 6.1 years; children born in more recent years had a higher cumulative incidence of diagnosed asthma. Children of lower socioeconomic status had lower rates of asthma diagnosis, but asthma was unrelated to race. Based on analysis of children who had documented asthma within the 2 most recent years, the prevalence of current asthma was 12.9%: 15.3% in boys and 10.4% in girls.

One in six schoolchildren in the study community have physician-diagnosed asthma, the results suggest. This rate is similar to that found in previous studies of inner-city children and more than double that reported in the National Health Interview Survey. In contrast to previous reports, the findings suggest a higher rate of asthma diagnosis among children of higher socioeconomic status.

COMMENT: *Although this is a retrospective study, it is unique in that it is longitudinal and based on medical diagnoses from all the medical records in a northern Midwest county. The rates of "ever having a physician diagnosis of asthma" are comparable to those* ➤➤

found in a middle-class community in Michigan. Childhood asthma rates were lower among the socioeconomically disadvantaged.
J. A. A.
Yawn BP, Wollan P, Kurland M, Scanlon P: A longitudinal study of the prevalence of asthma in a community population of school-age children.
J Pediatr 140:576-581, 2002. ♦♦

Mast Cells "Microlocalize" in Smooth Muscle Cells in Asthma

PATIENTS with eosinophilic bronchitis have a corticosteroid-responsive cough and sputum eosinophilia, without evidence of variable airflow obstruction or airway hyperresponsiveness. Sputum histamine and prostaglandin D_2 are significantly higher in eosinophilic bronchitis than in asthma. This study compared the localization of mast cells within the airway wall between these two conditions.

The immunohistochemical study included bronchial biopsy specimens from three groups of subjects: 17 with asthma, 13 with eosinophilic bronchitis, and 11 normal controls. Median submucosal eosinophil counts were 9.5/mm² in the asthma group and 10.0/mm² in the eosinophilic bronchitis group, compared with 2.1/mm² in the control group. Submucosal T-lymphocyte counts were similar among groups, as were submucosal mast cell counts: 24/mm² in asthma patients, 28/mm² in eosinophilic bronchitis patients, and 17/mm² in controls. Smooth muscle cells were easily identified by their histologic appearance. The median number of tryptase-positive mast cells in airway smooth muscle was 5.1/mm² in the asthma group, compared with 0/mm² in both the eosinophilic bronchitis and control groups. The asthma patients showed a significant, inverse correlation between mast cell infiltration of the bronchial smooth muscle and bronchial responsiveness to methacholine. In general, none of the three groups showed T-cells or eosinophils in the airway smooth muscle. Within groups, the findings were similar for subjects with vs without atopy.

Patients with asthma have a much higher number of mast cells in the airway smooth muscle than either normal controls or patients with eosinophilic bronchitis. Smooth muscle infiltration by mast cells could play an important role in the pathophysiology of asthma. In contrast, mast cells may localize in the superficial airways of patients with eosinophilic bronchitis. The findings underscore the potential importance of microlocalization of inflammatory mediators.

COMMENT: *About 20 years ago, Dr. Charles Reed described the airway pathology in asthma as "chronic desquamating eosinophilic bronchitis." More recently, a disorder called eosinophilic bronchitis has been differentiated from asthma by its lack of variability in airflow obstruction and lack of airway hyperresponsiveness. Clinically it features sputum eosinophilia and a cough that is responsive to corticosteroids. On the basis of bronchial biopsies, these investigators show that mast cells are more highly localized in the airway smooth muscle of subjects with asthma than with eosinophilic bronchitis. They postulate that the "microlocalization" of mast cells is of fundamental importance in the causation of asthma.*
R. J. M.
Brightling CE, Bradding P, Symon FA, et al: Mast-cell infiltration of airway smooth muscle in asthma.
N Engl J Med 346:1699-1705-2002. ♦♦

Breast-Feeding Protects Against Asthma in Children of Asthmatic Mothers

A RECENT study suggested that the children of asthmatic mothers were more likely to develop childhood asthma if they were breast-fed exclusively during infancy. This raises questions about whether asthmatic mothers should breast-feed their infants. Data from a prospective birth cohort study were used to test the effect of maternal asthma on the relationship between breast-feeding and asthma.

The analysis included 2,602 children enrolled before 18 weeks' gestation in the Western Australia Pregnancy Cohort Study. Parents provided information on their history of respiratory illness, smoking, and general health, as well as on the method of infant feeding. Children were evaluated at the age of 6 years for the presence of current asthma, defined as a physician diagnosis of asthma plus wheezing within the past year.

Eighty-nine percent of children were breast-fed, with 48% being exclusively breast-fed for less than 4 months. Seventeen percent had current asthma at age 6 years; current asthma was also found in 15% of the mothers. Less than 4 months of exclusive breast-feeding was a significant risk factor for asthma: odds ratio 1.3, after adjustment for covariates. There was no evidence of an interaction between breast-feeding and maternal asthma.

Infants who are breast-fed exclusively for at least 4 months are at lower risk of asthma, these population-based data suggest. Breast-feeding is a significant protective factor, independent of maternal history of asthma or the child's atopic status. From a public health standpoint, breast-feeding should be recommended on the basis of its many health benefits, for asthmatic and nonasthmatic mothers alike.

COMMENT: *Development of asthma in childhood is associated with genetic and environmental factors, one of which seems to be the infant's diet. This prospective study of 2,600 children found that the risk of asthma was increased if nonhuman milk was introduced before the age of 4 months, whether or not the mother had a history of asthma.*
R. J. M.
Oddy WH, Peat JK, de Klerk NH: Maternal asthma, infant feeding, and the risk of asthma in childhood.
J Allergy Clin Immunol 110:65-67, 2002. ♦♦

Asthma in Olympic Swimmers: What Happens After They Stop Training?

OLYMPIC athletes have high rates of asthma, particularly endurance athletes such as cyclists, cross-country skiers, and swimmers. However, there have been no studies to determine whether signs of bronchial hyperresponsiveness and airway inflammation persist after these elite athletes retire from competition. This prospective follow-up study assessed the outcomes of asthma in Olympic swimmers.

In 1996, a complete evaluation was performed in 42 Finnish swimmers competing in an elite-level race. Most were members of the Finnish national swim team. The evaluation included symptom questionnaires, spirometry, histamine challenge testing, skin prick testing, and sputum examination. None of the athletes reported any respiratory tract infection in the month before the examination. In 2001, evaluations were repeated in 37 athletes. Changes in asthma indicators were compared for the 16 swimmers who continued intensive training during follow-up and the 26 who had stopped training.

Symptoms of exercise-induced bronchoconstriction were reported at baseline by 63% of subjects, and at follow-up by 81% of subjects who continued active swimming. For subjects who continued swimming, the rate of bronchial responsiveness remained stable: 44% at baseline and 50% at follow-up. For those who stopped swimming, the rate decreased from 31% at baseline to 12% at follow-up.

Based on these two findings, the rate of current asthma among active swimmers was 31% at baseline and 44% at follow-up. Fifty-six percent of subjects had atopy at the initial examination; at follow-up, atopy was present in 69% of active swimmers vs 46% of past swimmers. Rates of sputum eosinophilia among active swimmers were 6% at baseline vs 38% at follow-up.

The findings confirm high rates of bronchial hyperresponsiveness and asthma among elite swimmers. Swimmers who stop intensive training in the intervening years have reduction or even disappearance of bronchial hyperresponsiveness. In contrast, those who continue swimming may have worsening eosinophilic airway inflammation. Mild asthma associated with high-level swimming appears to be partially reversible.

COMMENT: *In this observational study, the Finnish researchers took advantage of the opportunity to evaluate their national swim team in 1996 and follow them for 5 years. The incidence of asthma in competitive swimmers is generally higher (33%) than for athletes in other sports (15%). Those athletes who stopped competing and reduced their swim time–from approximately 30 to 3 h/wk–had significantly reduced asthma and airway hyperreactivity. The authors discuss the possibility that disinfectants in pool water, such as chlorine, may be aggravating factors. However, it seems that the intense physical activity is more significant.*
S. M. F.

Helenius I, Rytilä P, Sarna S, et al: Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma: a 5-year prospective follow-up study of 42 highly trained swimmers. **J Allergy Clin Immunol** 109:962-968. ♦♦

Zafirlukast Reduces EIB, With or Without Loratadine

CURRENT asthma therapies do not provide adequate protection against exercise-induced bronchoconstriction (EIB). The authors previously demonstrated an additive effect of the H1-receptor antagonist loratadine and the leukotriene-receptor antagonist zafirlukast in preventing early and late asthmatic responses to bronchoprovocation. Here they evaluated the same drug combination for prevention of EIB.

The study included 16 nonsmoking patients with mild asthma, confirmed EIB, and histamine-induced airway hyperresponsiveness. The subjects were randomized to receive placebo, zafirlukast 80 mg twice daily, loratadine 10 mg twice daily, and a combination of zafirlukast and loratadine. One week later, they performed a standard 5-minute exercise challenge protocol. In double-blind crossover fashion, the effects of all four treatments were tested in all patients.

Exercise challenge produced a 21.6% mean maximum decline in FEV_1 after placebo and 22.8% after loratadine, compared with 13.9% after zafirlukast and 10.3% after loratadine/zafirlukast. In terms of area under the FEV_1 percentage change vs time curve, the mean protective effect was 57% with zafirlukast and 65% with zafirlukast/loratadine. On its own, loratadine offered no significant protection.

The leukotriene-receptor antagonist zafirlukast–on its own or in combination with loratadine-appears to have a significant protective effect against EIB in patients with mild asthma. On its own, the H1 receptor-antagonist does not offer significant protection. Other drug combinations, including bronchoconstrictor prostaglandin blockers, should be tested for protection against EIB.

COMMENT: *This study re-emphasizes the importance of leukotrienes as a trigger for EIB. At double the usual dosage of zafirlukast, there was impressive blockade of cycle ergometer exercise challenge after 1 week of therapy. The fact that loratadine did not influence the exercise challenge–alone or in addition to zafirlukast–suggests that histamine may not be an important mediator for EIB. This question was addressed in the accompanying editorial (*J Allergy Clin Immunol 109:771-773, 2002*), which points out that there may not have been sufficient mediator release with an exercise challenge of only 5 minutes. The exercise challenge model once again provides insight into the mechanism of asthma and available therapies.*
S. M. F.

Dahlén B, Roquet A, Inman MD, et al: Influence of zafirlukast and loratadine on exercise-induced bronchoconstriction.
J Allergy Clin Immunol 109:789-793, 2002. ♦♦

Upper and Lower Reactions to Fungi May Produce SAM Syndrome

PATIENTS with allergic fungal sinusitis (AFS) have fungal-specific IgE, intractable sinusitis, and nasal polyposis, sometimes leading to mucous plugging ➤➤

and chronic bacterial sinusitis. Since the first report in 1981, more than 100 case reports of AFS have appeared. It is thought to represent the upper airway manifestations of allergic bronchopulmonary mycosis (ABPM), a similar condition occurring in the lower airways of patients with atopic asthma. The authors report on the concomitant presence of AFS and ABPM in the same patient, for which they propose the term sinobronchial allergic mycosis (SAM) syndrome.

The findings in five patients with coexisting AFS and ABPM are summarized, including one new patient and four previously reported cases. The patients were 3 men and 2 women, age range 17 to 55 years. All had a history of asthma and chronic sinusitis. The sinusitis involved multiple sinuses; all patients but 1 had previously undergone sinus surgery. Skin tests showed an immediate reaction to fungal allergens, while blood testing revealed peripheral eosinophilia. Radiographic findings varied, usually including signs of bronchiectasis. However, the clinical features were similar to those observed in patients seen for isolated sinus or lung disease. All 5 patients had a good clinical response to corticosteroids.

The SAM syndrome refers to the simultaneous presence of AFS and ABPM, representing hypersensitivity reactions to fungi occurring at different locations within the airway. Patients with coexisting AFS and ABRM may present with symptoms of either disease or both; the initial response to corticosteroids is good, but the long-term prognosis is unclear. The potential association of these conditions with cystic fibrosis and mutations in the CFTR gene warrants further investigation.

COMMENT: *Sinobronchial allergic mycosis syndrome is an intriguing new syndrome. I have often wondered why more individuals with isolated fungal disease do not experience a spread throughout the entire respiratory tract. These investigators present both a case study and literature review of individuals with both ABRM and AFS. There is a suggestion that a CFTR gene mutation may be involved. Should we all look for both conditions in our patients with either condition and "sweat" them? I have a feeling we will be hearing more about the SAM syndrome.*
A. L. L.

Venarske DL, deShazo RD: Sinobronchial allergic mycosis: the SAM syndrome.
Chest 121:1670-1676, 2002. ♦♦

Computerized Voice Analysis Aids in Diagnosing Vocal Cord Dysfunction

PATIENTS with vocal cord dysfunction (VCD) experience airflow obstruction caused by adduction of the vocal cords on inspiration, with signs and symptoms mimicking those of asthma. With no known underlying abnormality, it has been suggested that VCD represents a type of conversion disorder. Currently, diagnosis requires characteristic findings on pulmonary function testing and laryngoscopy. This retrospective study reports on the use of computerized voice analysis in the diagnosis of VCD.

The investigators used the computerized Multidimensional Voice Program (MDVP) to analyze the voice patterns of 6 adolescents with suspected VCD. The patients were 4 females and 2 males, age range 11 to 17 years. All had a history of asthma or allergic-type reactions along with psychologic issues. Based on a single vocalization, the MDVP analyzed and displayed 33 different voice parameters, which can be displayed numerically or graphically. The data were analyzed by a speech-language pathologist. This information–along with the results of history, pulmonary function tests, and laryngoscopy–was used to make the diagnosis of VCD.

The MDVP analysis showed significant voice abnormalities in 5 of the 6 patients. Abnormal parameters in each case included the soft phonation index and variation in fundamental frequency. The sixth patient had normal results on MDVP, as well as on pulmonary function testing and laryngoscopy. One patient showed normalization of MDVP parameters after treatment for VCD.

The MDVP technique shows significant voice abnormalities in patients with VCD. Voice analysis may provide a useful new tool in evaluation of patients with this difficult-to-diagnose condition.

COMMENT: *Vocal cord dysfunction is increasingly recognized in a variety of age groups. The problem emulates symptoms of airway disease or occurs coincidently with asthma, complicating assessment of disease severity and treatment response. Diagnosis of VCD is often limited by the need for invasive techniques and to assess subjects during acute symptoms. This is a particular problem in children. Making a diagnosis by having patients phonate into a microphone for less than 3 seconds sounds too good to be true. This report gives new meaning to "Just say aaah."*
D. K. L.

Zelcer S, Henri C, Tewfik TL, et al: Multidimensional voice program analysis (MDVP) and the diagnosis of pediatric vocal cord dysfunction.
Ann Allergy Asthma Immunol 88:601-608, 2002. ♦♦

BCG Vaccination Shows Benefits in Korean Patients With Asthma

THERE is growing interest in the potential for manipulating the Th1/Th2 cytokine response as a treatment for asthma and other Th2-associated diseases. Experimental studies suggest that vaccination with bacille Calmette-Guérin (BCG) can inhibit airway eosinophilia and hyperresponsiveness. A clinical trial of BCG vaccination in adult asthma patients is reported.

The study included 43 Korean patients with moderate to severe perennial asthma. They were randomized to undergo percutaneous injection of BCG, 58.2 x 10^7 CFUs, or placebo. Spirometry and other assessments were performed before and at 4, 8, and 12 weeks after vaccination.

The two groups were similar in their rates of atopy, pollen sensitization, and rhinitis. However, the placebo group had higher rates of BCG vaccination scarring and previous antituberculosis drug treatment. In the BCG group, FEV_1 increased significantly, from 2.16 L at baseline to 2.43 at 4 weeks. There was no ➤➤

change in FEV_1 in the placebo group. Vaccination was also associated with significant increases in forced expiratory flow rate 25% to 75%, from 1.43 to 1.80 L/sec; and in morning peak expiratory flow rate, from 427 to 447 L/min. There was no significant change in asthma symptom scores at most times, although weekly medication scores were significantly decreased in the BCG group. Skin induration size increased from 7.55 mm before BCG vaccination to 10.5 at 12 weeks, compared with a significant decrease in the placebo group.

In patients with moderate to severe asthma, BCG vaccination may improve pulmonary function and reduce the need for asthma medication. These changes are associated with suppression of the Th2-type immune response. The authors note that their results in a Korean population–with high rates of BCG vaccination and mycobacterial exposure–may not be reproducible in Western countries.

COMMENT: *Modulation of allergic disease by manipulation of the Th1/Th2 balance has been repeatedly achieved in animals but not in humans. In this Asian population, BCG treatment seemed to increase Th1-like activity and improve moderate, persistent asthma. Other investigators have not had such success. This report encourages continued efforts to tilt the Th1/Th2 seesaw, particularly in more diverse patient populations.*
D. K. L.
Choi IS, Koh YI: Therapeutic effects of BCG vaccination in adult asthmatic patients: a randomized, controlled trial.
Ann Allergy Asthma Immunol 88:584-591, 2002. ♦♦

Topical Test for Dust Mite Sensitivity in Atopic Dermatitis

THERE is ongoing debate over the contribution of environmental allergens–particularly the house dust mite *Dermatophagoides pteronyssinus* (Dp)–to the pathogenesis of atopic dermatitis (AD). Allergen avoidance is difficult to achieve and has yielded mixed results even under controlled conditions. A topical allergen provocation technique was evaluated for clinical assessment of Dp hypersensitivity in patients with AD.

Twenty patients with AD underwent topical challenge with Dp and control skin prick test solutions, applied to the cubital fossae twice daily for 4 days. Allergen-specific serum IgE levels were strongly positive in 16 of the 20 patients. However, just 6 patients showed increased AD severity and pruritus at cubital fossa sites where Dp solution was topically applied, compared with control sites.

Seven patients had immediate but transient contact urticaria reactions after their first application of Dp. Patients with a positive in vivo challenge response also showed greater peripheral blood mononuclear cell proliferation in response to Dp in the presence of fresh, autologous serum.

Topical challenge with Dp skin prick testing solution produces a delayed dermatitic response in about one-third of patients with AD. The same group of patients show a strong in vitro response to Dp in a peripheral blood mononuclear cell proliferation assay. Topical application of mite allergen might help to identify AD patients who are likely to respond to dust mite avoidance measures.

COMMENT: *A majority of people with AD have specific allergies, but it is often unclear what role the allergies play in flares of dermatitis. Do allergens exert their effect systemically (eg, foods), topically (eg, pets, dust mites), or both? This study found that, of AD patients who tested positive for dust mite allergy, about one-third reacted to topical application of dust mite extract. This simple test might direct recommendations for strict environmental control and immunotherapy to those AD patients who are most likely to benefit.*
R. J. M.
Shah D, Hales J, Cooper D, Camp R: Recognition of pathogenically relevant house dust mite hypersensitivity in adults with atopic dermatitis: a new approach?
J Allergy Clin Immunol 109:1012-1018. ♦♦

Immune Serum Globulin Vaccination Reduces Respiratory Infections And Asthma

IN 1996, a food worker in an Israeli army base developed hepatitis A. In response, the entire exposed population–all 2,835 soldiers on the base–were vaccinated with (ISG), 2 mL IM. This enabled assessment of the effects of ISG vaccination on the rates of asthma attacks and respiratory infections.

In the 3 months after vaccination, there were 7 cases of asthma exacerbation in the vaccinated soldiers, compared with 35 cases in the population of the same base 1 year previously. The rate ratio for asthma after vaccination was 0.2 (95% confidence interval 0.09 to 0.45). Vaccination with ISG was also associated with significant reductions in sinusitis, rate ratio 0.34 (95% confidence interval 0.2 to 0.58); and in pneumonia, rate ratio 0.41 (95% confidence interval 0.17 to 0.99).

The results of this "natural clinical trial" suggest that vaccination with ISG may reduce the risk of respiratory infections and asthma. The finding that ISG reduces respiratory infections is not surprising; the effect on asthma risk may be related to reduction in attacks triggered by bacteria or viruses.

COMMENT: *These observations are extremely provocative and could potentially change our attitude toward prevention of respiratory infections and subsequent asthma. Since there are many potential confounding variables, this work will need to be reproduced in nonmilitary settings.*
A. M.
Mimouni D, Gdalevich M, Mimouni K, et al: Incidental asthma prevention by immune serum globulin.
Ann Allergy Asthma Immunol 89:99-100, 2002. ♦♦

High Rate of Antibodies to *Stachybotrys chartarum*

STACHYBOTRYS chartarum is a widely distributed fungus, commonly found in water-damaged homes. Previous studies have suggested that this organism has disease-causing potential in humans, often ➤➤

through a nonimmunologic mechanism. The prevalence of serum antibodies against *S. chartarum* was evaluated in a general population sample.

The study included 139 plasma samples, obtained from blood donor units scheduled to be discarded. Enzyme immunoassays identified IgG directed against *S. chartarum* in 49% of samples tested. Another 9% of sera contained IgE against *S. chartarum*. Extracts of *S. chartarum* spores and mycelia identified two IgE-binding proteins at 34 and 52 kDa.

A surprisingly high percentage of healthy blood donors show IgG or IgE antibodies against *S. chartarum*. Many questions remain regarding the contribution of the widespread fungus-which has toxic as well as immunologic potential-to asthma and allergy in the population.

COMMENT: *There is much we need to learn about* Stachybotrys. *This study indicates that there is immunologic reactivity toward this ubiquitous fungus in healthy subjects. Further investigation will be needed to determine a cause-and-effect relationship between exposure and human disease.*
A. M.
Barnes C, Buckley S, Pacheco F, Portnoy J: IgE-reactive proteins from Stachybotrys chartarum.
Ann Allergy Asthma Immunol 89:29-33, 2002. ♦♦

Is Rofecoxib Safe for Patients With NSAID-Induced Skin Reactions?

PREVIOUS studies have suggested that the selective cyclo-oxygenase (COX)-2 inhibitors celecoxib and rofecoxib are well-tolerated by patients with aspirin-sensitive asthma. This study evaluated the safety of rofecoxib in patients with cutaneous reactions to nonsteroidal anti-inflammatory drugs (NSAIDs).

The study included 15 patients with a history of NSAID intolerance and cutaneous reactions in response to single-blind, placebo-controlled, oral challenges with NSAIDs. The patients were 9 men and 6 women, mean age 31 years. Forty-seven percent of patients reacted to aspirin; 40% to nimesulide, a COX-2 inhibitor with minor inhibition of COX-1; and 13% to diclofenac. The reactions included urticaria in 53% of patients, facial angioedema in 40%, and nonurticarial rash in 7%.

The patients then received a further challenge with rofecoxib, 12.5 and 25 mg. All patients tolerated rofecoxib well. Ten showed tolerance to other NSAIDs in the protocol.

In placebo-controlled challenges, patients with NSAID-induced cutaneous reactions do not react to the selective COX-2 inhibitor rofecoxib. Rofecoxib does not cross-react with aspirin or other NSAIDs, and appears safe in the patient group studied.

COMMENT: *This report gives us further reassurance that rofecoxib is safe in aspirin- and NSAID-sensitive patients. It is important to recognize that this study involved patients with only cutaneous reactions. Further studies will be required before COX-2 inhibitors can be routinely recommended in these patients.*
A. M.
Quiralte J, S·enz de San Pedro B, Florido JFF: Safety of selective cyclooxygenase-2 inhibitor rofecoxib in patients with NSAID-induced cutaneous reactions.
Ann Allergy Asthma Immunol 89:63-66, 2002. ♦♦

Latex Avoidance for High-Risk Children: 5-Year Follow-Up Results

RECENT years have seen increased recognition and research of latex as a cause of IgE-mediated allergic reactions. Although primary and secondary preventive measures have been proposed, few studies have evaluated their efficacy. The long-term effects of a latex-avoidance program for a group of high-risk children were evaluated.

The study included 131 children with shunted hydrocephalus, most often associated with spina bifida. Based on a thorough screening evaluation, 41 children were found to be sensitized to latex. Patients and parents were instructed in latex avoidance and supplied with an emergency kit, which included an oral antihistamine, a soluble corticosteroid, and an epinephrine inhaler and autoinjector. After 5 years, 100 patients were available for re-evaluation, including a specific questionnaire to assess the extent of latex prophylaxis.

Of the 70 patients who did not have latex-specific IgE at baseline, 64 still tested negative at follow-up. Of 30 patients with initially positive radioallergosorbent test (RAST) results, 9 had become RAST-negative and another 11 had a reduction of at least one RAST class. Just 34 patients–mainly those who tested positive for latex sensitivity–had observed both private and medical latex prophylaxis. During follow-up, 47% of these patients showed improvement while another 27% remained negative. Among previously sensitized patients, the rate of increased latex-specific IgE was just 9%.

The secondary prevention program evaluated in this study reduces latex-specific IgE in a group of high-risk children. Medical prophylaxis appears more important than home prophylaxis. Induction of latex-specific IgE appears to occur mainly during early childhood, underscoring the need for effective primary prevention efforts.

COMMENT: *During the peak of the latex allergy epidemic, we had very little knowledge of the natural history of the disease. In this study, nearly half of the patients with latex RAST class III or less in 1995 had a negative RAST in 2000. Only 3 of 29 patients with a positive RAST in 1995 had their titers increase over the 5-year study period. This study confirms several smaller reports suggesting that latex avoidance usually results in a decline in latex-specific IgE. The fact that medical prophylaxis is more important than latex avoidance at home is not surprising and will help us in counseling latex-allergic patients.*
S. A. T.
Reider N, Kretz B, Menardi G, et al: Outcome of a latex avoidance program in a high-risk population for latex allergy-a five-year follow-up study.
Clin Exp Allergy 32:708-713. ♦♦

Avoidance Program Reduces Mite Sensitization in High-Risk Children

AS the prevalence of asthma and allergy continues to rise, there is growing interest in methods of primary prevention. House dust mite sensitization plays a central role in asthma pathogenesis. The effects of a dust mite avoidance program on the development of sensitization in school-age children were evaluated.

The multicenter trial included 242 children, aged 5 to 7 years, in three European countries. All enrolled children had a family history of atopy and a positive skin test response to aeroallergens, but not to house dust mite. Children randomized to the prophylactic group received environmental measures to reduce exposure to dust mite, including impermeable mattress covers and advice to remove carpets and pets, increase ventilation, etc. Those assigned to the control group received nonspecific advice. Evaluation at 12 months' follow-up included skin-prick testing and a symptom questionnaire.

Compliance with the use of mattress covers and increased ventilation was high. Relatively few families removed carpets, and more gained pets than gave them up. Dust mite sensitization occurred in 2.56% of children in the prophylactic group compared with 9.38% in the control group. The number of cases needed to treat to prevent 1 case of sensitization was 15. On logistic regression analysis, prophylactic measures were an independent predictor of mite sensitization status, odds ratio 0.14 (95% confidence interval 0.03 to 0.79).

Dust mite avoidance measures may help to reduce the rate of mite sensitization among school-age children. The use of mite-impermeable mattress covers may offer a particularly simple means of reducing the sensitization rate.

COMMENT: *Although the benefits of reducing indoor allergen exposure in sensitized patients have been well-shown, the effects of empiric reduction of allergen exposure in skin test-negative patients are less clear. For example, we really do not know what to tell atopic patients who share their beds with cats and have negative skin tests to cat. This study is the first to examine primary prevention of dust mite sensitization in school-age children, and the preliminary results are promising. We hope the authors will successfully extend the observation period for several more years, both to confirm the results and to see if dust mite avoidance affects the incidence of asthma in these children.*
S. A. T.
Arshad SH, Bojarskas J, Tsitoura S, et al, and the SPACE study group:Outcome of a latex avoidance program in a high-risk population for latex allergy-a five-year follow-up study.
Clin Exp Allergy 32:843-849, 2002. ♦♦

Early Measles and Other Childhood Infections Don't Reduce Atopy Risk

THE so-called hygiene hypothesis seeks to ascribe the rising prevalence of allergic disease to reduced childhood exposure to infections and other environmental stimuli. If this is so, early exposure to common childhood infections should reduce the risk of allergy. The effects of age at exposure to measles, rubella, varicella, and mumps on subsequent atopy risk were analyzed.

The study included 889 pregnant Danish women participating in a nationwide maternal-child health study. All subjects had available school health records providing detailed information on history of measles, rubella, varicella, and mumps. Current atopic status was assessed by serum testing for specific IgE against common inhalant allergens.

Serum samples showed evidence of atopy in 29% of women. The rate of atopy was significantly increased for women whose school records showed asthma occurring before age 7 years: odds ratio 1.46 (95% confidence interval 1.01 to 2.09). The other childhood infections showed no association with current atopic status. However, subjects with a higher number of infections during the first 2 years of life had higher atopy rates.

Common childhood infections do not have any protective effect against the development of atopy later in life, regardless of age at the time of infection. Early exposure to measles may actually increase the risk of atopy. This study, based on uniquely detailed records of childhood history of infections, overcomes many of the limitations of previous studies evaluating the hygiene hypothesis.

COMMENT: *Controversy continues to shroud the "hygiene hypothesis," which suggests the absence of exposure to infections in childhood causes the immune system to retain the Th2 profile, resulting in increased allergy. This well-done study is one of several that fail to support this hypothesis. In fact, the authors found an increased risk of atopy in individuals who had measles during the first year of life. It seems the tide is moving out on the hygiene hypothesis.*
E. J. B.
Bager P, Westergaard T, Rostgaard K, et al: Age at childhood infections and risk of atopy.
Thorax 57:379-382, 2002. ♦♦

Indoor Settings Show Detectable Levels of Pigeon Allergen

EXPOSURE to pigeons can cause allergic disease, not only among pigeon breeders but also among people exposed to wild pigeons. Pigeons are widespread in cities. This study evaluated the presence of pigeon allergens in homes and public buildings in an urban area.

The study included a total of 115 dust samples collected from various settings in the Chicago area, including a pigeon-infested school building, pigeon coops, and the homes of people who kept pigeons or indoor birds. Samples were also obtained from hospitals and from homes without indoor birds. Levels of pigeon allergen were measured using a direct competitive enzyme-linked immunosorbent assay.

Samples from pigeon coops showed the highest level of pigeon allergens, with median activity of 11.2% compared with pigeon droppings. The pigeon-infested building showed a median activity of 7.4%; one sample ➤➤

taken from an area underneath pigeon roots showed activity of 62.3%. High allergen levels were also detected on the floor and windowsills of a classroom where the teacher developed hypersensitivity pneumonitis. The samples from home and hospital settings showed low levels of pigeon allergen on average. However, 52% of these samples–58% from homes without indoor birds and 37% from hospitals–had pigeon allergen levels above the limit of detection.

The findings show significant levels of pigeon allergens from various urban settings, including schools, hospitals, and homes where no domestic birds are kept. Further research is needed to assess the possible health effects of exposure to pigeon allergen. In addition, new techniques of measuring pigeon allergens in indoor settings are needed.

COMMENT: *Occasionally, patients present with symptoms suggesting hypersensitivity pneumonitis, but the medical history is not supportive. This preliminary study gives us food for thought in some of these diagnostic dilemmas. In homes and facilities devoid of birds, 52% had pigeon allergen concentrations above the detection level. Since there is remarkable shared antigenicity between avian species, further studies will be required to determine the clinical implications of this study.*
E. J. B.
Curtis L, Lee B-S, Cai D, et al: Pigeon allergens in indoor environments: a preliminary study.
Allergy 57:627-631, 2002. ♦♦

Previous Operations Greatly Increase Risk of Latex Sensitization in Children

CERTAIN groups of children are at high risk of latex allergy and sensitization. The risk of latex-induced anaphylaxis could be reduced by preoperative screening. The prevalence of latex allergy and sensitization were assessed in a large group of children undergoing surgery.

The prospective study included a total of 1,263 children undergoing elective surgery with general anesthesia at an international referral center. All underwent measurement of total and latex-specific IgE and latex skin testing. Children with typical symptoms or latex allergy plus either a positive latex skin test or increased latex-specific IgE were classified as latex allergic; those with increased latex-specific IgE only were classified as latex sensitized.

The patients were 743 boys and 520 girls, median age 6 years; just 23.5% of patients were undergoing their first surgical procedure. Although 10 patients initially reported reactions to latex, this was ruled out by interview and skin testing in 4 patients. The remaining 6 patients were confirmed as having latex allergy, for a prevalence of 0.47%. Another 50 patients had latex sensitization, for a prevalence of 4.0%. During the study period, repeat operations were performed in 1 patient with latex allergy and 7 with latex sensitization. In all repeat surgeries, the rate of latex seroconversion was 2.1%, with all patients having more than three previous operations before study enrollment. Any previous surgery greatly increased the risk of latex sensitization, odds ratio 13.51. In this group of surgical patients, the odds of latex sensitization increased by 16% per year of age.

The study provides up-to-date information on the prevalence of latex allergy and sensitization among children undergoing surgery. The risk is particularly high in children with a history of previous surgeries; for children undergoing repeat operations, the rate of latex seroconversion is 2%. The findings have important implications for the use of primary prophylaxis against latex in pediatric surgical patients.

COMMENT: *This large, prospective study of unselected children going to surgery in a well-known U.K. children's hospital is important because it gives current (1999) risk assessment for latex allergy. Latex allergy (history of previous symptoms plus positive in vitro IgE/skin test): 0.05%; latex sensitization (positive in vitro IgE/skin test but no history of latex reactions): 4.0%. As expected, latex sensitization was more likely in atopic children with a history of rhinitis and/or with kiwi, banana, or peanut food allergy. An important finding is that a history of even* one *previous surgery increased the risk of latex sensitization by 13-fold.*
J. A. A.
Hourihane JO'B, Allard JM, Wade AM, et al: Impact of repeated surgical procedures on the incidence and prevalence of latex allergy: a prospective study of 1263 children. **J Pediatr** 140:479-482. ♦♦

Feather Pillows Aren't Contaminated With Dust Mite Allergen

PEOPLE with allergies or asthma commonly believe that feather pillows and comforters serve as breeding sites for dust mites and other allergens. However, no studies have examined the presence of dust mite allergen feathers, before or after industrial processing, or the accumulation of allergen in feather pillows during daily use.

Levels of mite allergen were measured in 8 batches of raw, unprocessed feathers from different manufacturers and in 16 batches of processed feathers. All but one of the unprocessed feather samples contained dust mite allergen, with a mean combined Der p 1 and Der f 1 level of 524 ng/g. However, none of the processed feather samples contained detectable levels of mite allergen.

An allergen transfer study was performed in the bedrooms of five volunteers, who used new feather pillows for 3 months. Baseline dust samples showed significant levels of dust mite allergen in 4 of the 5 bedrooms, with more than 2,000 ng/g of Der p 1 and Der f 1. However, the new pillows were not found to contain detectable levels of dust mite allergen after 90 days in use. This was so whether or not a pillow cover was used.

Industrially processed features do not contain measurable levels of dust mite allergen. Furthermore, new feather pillows do not accumulate dust mite allergen, even after 3 months of use in a room contaminated with mite allergen. ➤➤

COMMENT: *Another myth dispelled–feather pillows are not a risk for allergen exposure. Common sense will never supplant scientific, clinical studies. We need always to distinguish between things we do because of convention vs recommendations based on science.*
D. K. L.
Dryer AL, Chandler MJ, Hamilton RG: Dust-mite allergen removal from feathers by commercial processing. **Ann Allergy Asthma Immunol** 88:576-577, 2002. ♦♦

Cold Symptoms After Flying Aren't Related to Recirculated Air

AIRPLANE cabins have several characteristics that might increase the risk of infectious disease transmission: they are confined spaces with limited ventilation and recirculated air. Today's aircraft use filtered, recirculated air to reduce the work demands on the plane's engines. The possible association between recirculated air and symptoms of upper respiratory infections (URIs) after air travel was evaluated.

A "natural experiment" was conducted in 1,100 subjects who flew from San Francisco to Denver over a 3-month period in 1999. The passengers completed a questionnaire before the flight, then were interviewed by telephone 5 to 7 days afterward. The development of URI symptoms was compared for 516 subjects whose flights used 100% fresh air vs 584 subjects whose flights used approximately 50% recirculated air.

Rates of URI symptoms after the flights were similar between groups. Rates of self-reported colds were 21% for passengers on fresh-air flights and 19% for those on recirculated-air flights. Rates of self-reported "colds and a runny nose" were 11% and 10%, respectively. Three percent of both groups reported an aggregation of eight different cold symptoms.

For passengers on commercial flights lasting about 2 hours, the use of recirculated air in the aircraft cabin does not increase the rate of URI symptoms. However, the study shows a high rate of self-reported symptoms whether or not recirculated air is used. This may be related to other factors such as stress, sleep loss, or crowding.

COMMENT: *Patients often report increased respiratory symptoms after flying in commercial airplanes. Reassuringly, the study demonstrates that, in flights of 2 hours or less, respiratory symptoms are not related to the use of recirculated air. Recirculation of cabin air is an increasingly common practice to improve fuel efficiency. A striking observation from the data is that one-third of passenger report URI-like symptoms during the week following a commercial flight. We can all take a deep breath when flying, but we need to continue looking for an explanation of respiratory symptoms when we land.*
D. K. L.
Zitter JN, Mazonson PD, Miller DP, et al: Aircraft cabin air recirculation and symptoms of the common cold. **JAMA** 288:483-486, 2002. ♦♦

Hay Fever Linked to Increased Rate of Panic Attacks

THE apparent increase in allergic disease remains unexplained. Recent studies in clinical samples have suggested increased rates of anxiety and depressive disorders among patients with allergies, including those with hay fever. The association between hay fever and mental disorders was assessed in a general population sample.

The analysis included data from 3,032 respondents to the Midlife Development in the United States Survey. The survey included a series of diagnostic-specific scales for common mental disorders, including major depression, panic attacks, generalized anxiety disorder, and alcohol/substance use disorders. The relationship of these diagnoses with various physical illnesses was assessed.

About 14% of the respondents reported hay fever. The rate of self-reported hay fever was significantly higher among subjects with major depression or panic attacks, compared to those without these mental disorders. After controlling for other factors, panic attack was the only factor significantly associated with self-reported hay fever: odds ratio 1.8 (95% confidence interval 1.2 to 2.6).

The findings suggest a significant association between panic attacks and hay fever in the general population. The mechanism of this association warrants further study. Unlike studies in clinical samples, the results show no significant association between allergy and depressive disorders.

COMMENT: *A number of observations may be explained by the association of panic disorder and allergic rhinitis. For example, the linkage of allergy and Westernized lifestyle, the increasing prevalence of allergic rhinitis, the impact of rhinitis on quality of life, and the occurrence of vocal cord dysfunction and laryngeal complaints in subjects with rhinitis. The relationship of panic disorder and allergy should be further investigated. Allergists/immunologists may need to add knowledge of psychiatry to their repertoire.*
D. K. L.
Goodwin RD: Self-reported hay fever and panic attacks in the community.
Ann Allergy Asthma Immunol 88:556-559, 2002. ♦♦

REVIEWS OF NOTE

Buckley RH: Primary cellular immunodeficiencies. **J Allergy Clin Immunol** 109:747-757, 2002.

COMMENT: *Dr. Buckley presents a wonderful, well-illustrated review of T-cell defects. This should be required reading for anyone facing a Board exam, or for those of us confused by RAG1, ZAP70, and Jak3.*
S. M. F.

Solomon WR: Airborne pollen: a brief life. **J Allergy Clin Immunol** 109:895-900, 2002.

COMMENT: *For most doctors of medicine, botany is but a distant memory from an undergraduate biology course. For allergists plants have more relevance, but probably very few of us are conversant with the cellular events in pollination, which are elegantly described by Dr. Solomon in this review. His description of plants' species-specific rejection of "foreign" pollens–end even their own pollens!–is thought provoking.*
R. J. M.

Sutherland MF, Suphioglu C, Rolland JM, O'Hehir RE: Latex allergy: towards immunotherapy for health care workers. **Clin Exp Allergy** 32:667-673, 2002.

COMMENT: *This is a nice review of the available literature investigating immunotherapy strategies for latex allergy. The techniques reviewed include traditional immunotherapy, peptide immunotherapy, hypoallergenic mutants, and DNA vaccination.*
S. A. T.

Waldman SA: Does potency predict clinical efficacy? Illustration through an antihistamine model. Ann **Allergy Asthma Immunol** 89:7-12, 2002.

COMMENT: *This is a brief review article packed with useful information. Definitions and examples are provided to distinguish between potency, efficacy, and effectiveness-terms often confused in the medical literature. Examples of antihistamine studies are used to reinforce the limitations of applying data from one experimental system to another. Thus the review provides insight into general pharmacologic concepts and simultaneously informs the reader about antihistamine potency and efficacy.*
D. K. L.

Rodrigo GJ, Rodrigo C: The role of anticholinergics in acute asthma treatment: an evidence-based evaluation. **Chest** 121:1977-1987, 2002.

COMMENT: *This is a good review of the most recent evidence for the use of anticholinergics in the treatment of an asthma exacerbation. The thorough review outlines studies in both adults and children. The article concludes with a concise list of the beneficial effects of anticholinergics.*
A. L. L.

Alsaeedi A, Sin DD, McAlister FA: The effects of inhaled corticosteroids in chronic obstructive pulmonary disease: a systematic review of randomized placebo-controlled trials. **Am J Med** 113:59-65, 2002.

COMMENT: *Although chronic obstructive pulmonary disease does not generally fall into the purview of allergists, many of our adult patients with asthma have elements of COPD superimposed on their asthma. The present review will assist in justifying inhaled steroid treatment in this group of patients.*
E. J. B.

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