AllergyWatch®

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

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

Volume 5, Number 2 March-April 2003

Four-Day Hymenoptera Immunotherapy Protocol Achieves Low Systemic Reaction Rate

FOR patients allergic to Hymenoptera venom, immunotherapy is effective in preventing future anaphylactic reactions to insect stings. Various high-dose rush protocols have been described to reach the maintenance dose of 100 µg in a matter of days, not weeks as in conventional immunotherapy. An 8-year experience with rush Hymenoptera venom immunotherapy is reported, including comparison with previously published studies.

The experience included 101, mainly high-risk, patients with allergy to bee, yellow jacket, or hornet venom. All patients underwent a 4-day rush immunotherapy regimen, in the hospital under strict observation. Injections started at very low concentrations, increasing in intervals of 60 minutes for a total of 17 injections, to reach the 100 µg maintenance dose. Immunotherapy consisted of honeybee venom in 52 patients and yellow jacket venom in 49. The rate and types of systemic reactions were analyzed.

Urticaria, swelling, and other local reactions occurred in several patients. Systemic reactions, generally mild to moderate, occurred in 6.9% of patients. Of the 8 systemic reactions encountered, 7 were to honeybee venom. None of the systemic reactions occurred in patients over age 50.

This experience supports the safety of a 4-day rush immunotherapy protocol for patients allergic to Hymenoptera venom. Even in a series of predominantly high-risk patients with a high rate of bee venom allergy, the systemic reaction rate was only about 7%, compared with an average 18% rate reported in the literature. Several factors may contribute to this low rate of systemic reactions, compared with previous studies.

COMMENT: *With stinging inset season nearly here, allergists will be seeing patients with Hymenoptera allergy who want desensitization "now." There are* ➤➤

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The American College of Allergy, Asthma & Immunology expresses its appreciation to Aventis Pharmaceuticals Inc.for its unrestricted grant in support of the publication of *AllergyWatch*®.

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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at least four basic treatment protocols: conventional (15 weeks); modified rush (6 weeks); rush (4 to 7 days, inpatient); and ultra-rush (2 days, inpatient). This is a report of a 4-day rush protocol in 101 patients, with a 6.9% rate of systemic reactions, none requiring epinephrine. More important, the authors review the literature on desensitization protocols and elucidate the reasons for the variability of safety data.
R. J. M.
Sturm G, Kränke B, Rudolph C, Aberer W: Rush Hymenoptera venom immunotherapy: a safe and practical protocol for high-risk patients.
J Allergy Clin Immunol 110:928-933, 2002. ♦♦

Very Low Peanut Doses Can Induce Allergic Reactions

SOME patients with peanut allergy will react to very low levels of peanut protein, to which they may be exposed accidentally or in processed food with "hidden" peanut content. More information is needed on the distribution of threshold doses in the population of patients with peanut allergy. This study evaluated individual threshold doses for peanut-allergic patients, including correlation with the severity of peanut-induced symptoms.

The study included 26 consenting patients with peanut allergy. All had a convincing history of symptomatic reactions to peanut, together with a specific IgE level of at least 0.7 kU/L or a 2+ or greater skin prick test response. Patients underwent double-blind, placebo-controlled challenges with increasing doses of peanut protein: from 30 µg to 1 g. The lowest dose resulting in a convincing allergic reaction was defined as the threshold dose.

All patients had a positive reaction to peanut challenge, including oral symptoms in 26 patients, GI symptoms in 14, and objective symptoms in 5. Six patients required oral antihistamines, and one required IV antihistamines and prednisolone. Reactions began within 30 minutes after peanut ingestion, although 2 patients developed additional symptoms after a 1- to 2-hour delay. Threshold doses were as low as 100 µg and as high as 1g. By the time the 3 mg dose of peanut protein was reached, one-half of patients had experienced an allergic reaction. Patients with more severe symptoms had lower threshold doses.

Very low doses of peanut protein can induce reactions in patients with peanut allergy, particularly in those with potentially life-threatening reactions. The results suggest that one-half of allergic patients will react to a dose of 3 mg, corresponding to about one-fiftieth of a peanut. The data will be useful in assessing the risk of allergic reactions to hidden peanut contamination.

COMMENT: *How much peanut protein is necessary to trigger an anaphylactic reaction in a sensitized patient? As one might expect, the severity of the historical reaction is inversely correlated with the provocative challenge dose. In this study of 26 patients, one-half reacted to 3 mg of peanut protein, and one-third to less than 0.5 mg. It doesn't take much!*
R. J. M.
Wensing M, Penninks AH, Hafle SL, et al:The distribution of individual threshold doses eliciting allergic reactions in a population with peanut allergy.
J Allergy Clin Immunol 110:915-920, 2002. ♦♦

Montelukast and Beclomethasone Provide Similar Asthma Control

INHALED corticosteroids (ICS) are commonly used as the initial controller medication for patients with persistent asthma. Several studies in adults with chronic asthma have shown significant improvements in asthma outcomes with a leukotriene receptor antagonist (LTRA) such as mon- ➤➤

tenlukast. The goals of treatment for chronic asthma are to reduce symptoms and prevent exacerbations, yet studies typically evaluate effects on airway function measures. This trial compared the effects of an ICS and an LTRA in patients with chronic asthma, focusing on days of asthma control.

The randomized, controlled, multicenter trial included 782 adult patients with asthma. All had had symptoms for at least 1 year; FEV_1 predicted was 50% to 85%, with average β-agonist use of more than 2 puffs/d. Patients were randomized to receive 6 weeks of treatment with montelukast, 10 mg/d; beclomethasone, 200 μg twice daily; or placebo. Percentage of days of asthma control was the main outcome measure; secondary outcome measures included FEV_1, asthma attacks, and rescue medication use.

Percentage of days with asthma control was about 41% with both montelukast and beclomethasone, compared with 27% with placebo. The percentage overlap in the distribution of this end point was 98% for the two active-treatment groups. Both treatments decreased in efficacy over time; the most common reason for asthma noncontrol was β-agonist use.

In terms of secondary outcomes, the LTRA was at least as effective as the ICS. Both were more effective than placebo in reducing asthma attacks, asthma flare-ups, and rescue corticosteroid use. Beclomethasone produced greater improvement in FEV_1 than montelukast, with a difference of 0.14 L. Both active treatments were better than placebo in improving this airway function measure. Both were well tolerated.

In percentage of asthma-free days and other clinically relevant measures, beclomethasone and montelukast provide similar disease control. Both medications improve asthma symptoms and airway function, although the ICS provides greater improvement in FEV_1. Montelukast is an effective alternative to beclomethasone for initial controller therapy of chronic asthma; more attention is needed to the clinical effects of asthma medications, rather than airway function tests.

COMMENT: *In an effort to determine the optimal initial monotherapy of asthma, this multicenter study compared the use of ICS and LTRA in asthmatics who would probably be classified as mild-moderate persistent, according to the new guidelines. Comparing the primary end-point of asthma control days and the secondary end-points of asthma flares and β-agonist and rescue steroid usage, there was no significant difference between ICS or LTRA. Inhaled corticosteroid did improve FEV_1 better than LTRA. Pulmonary function parameters have been the classic endpoints for measuring asthma control. This study and the CAMP study* (**N Engl J Med** 343:1054-1063, 2000) *both demonstrate that FEV_1 is probably not the optimal measurement for determining control in asthma. Until we find this optimal end-point, clinicians will still be faced with practical decisions about the best drugs for our patients with persistent asthma.*
S. M. F.

Israel E, Chervinsky PS, Friedman B, et al: Effects of montelukast and beclomethasone on airway function and asthma control.
J Allergy Clin Immunol 110:847-854, 2002. ♦♦

Postmenopausal Women Using Inhaled Corticosteroids Don't Have Reduced BMD

INHALED corticosteroids (ICS) are first-line anti-inflammatory therapy for patients with asthma. There is continuing concern about potential adverse effects of ICS on bone metabolism, particularly in postmenopausal women and other high-risk groups. The effects of long-term ICS therapy on bone mineral density (BMD) were studied in postmenopausal women.

From a larger population-based study, the researchers identified 106 postmenopausal women who had been exposed to corticosteroids only in the form of ICS. The women, mean age 58 years, had been using ICS for a mean of 8 years; mean dose was 853 μg. A random sample of 647 women with no history of corticosteroid exposure were studied as negative controls. A group of 49 women with a history of other corticosteroid exposure--ie, oral or intra-articular corticosteroids, in addition to ICS--were studied as positive controls. X-ray absorptiometry was performed to measure BMD of the distal forearm.

As expected, patients with a history of corticosteroid exposure had higher rates of allergy, asthma, and respiratory symptoms. Mean BMD values were not significantly different between the ICS-exposed women and the negative controls: about 0.43 g/cm^2 in both groups. In contrast, BMD was significantly reduced--to about 0.40 g/cm^2--in the women with other exposure to corticosteroids. More detailed analyses of the ICS group found no differences in BMD on stratification for cumulative ICS dose, duration of therapy, or dose above or below 1,000 μg.

Postmenopausal women with a history of ICS use have no significant decrement in forearm BMD, compared to nonexposed women. Even with years of exposure, no dose-response effect of ICS on BMD is apparent. Provided that the lowest effective dose of ICS is used, the associated risk of bone loss appears lower than that associated with traditional oral corticosteroid therapy.

COMMENT: *There is ongoing concern about the potential systemic effects of the inhaled corticosteroids we use to treat our patients with persistent asthma. These Swedish researchers used x-ray absorptiometry to measure BMD in postmenopausal women. The group receiving ICS had no significant difference in their BMD than a control group unexposed to corticosteroids. The positive control group of women who received corticosteroids--either oral or intra-articular, in addition to inhaled--did have lower BMD. This study measured BMD on the forearm, which is mostly cortical bone, and one can see corticosteroid-induced changes more rapidly in spinal trabecular bone. However, the mean duration of ICS was over 8 years, which should have been sufficient to detect a significant effect. It is reassuring to see studies with this result when we prescribe ICS.*
S. M. F.

Elmståhl S, Ekström H, Galvard H, et al: Is there an association between inhaled corticosteroids and bone density in postmenopausal women?
J Allergy Clin Immunol 111:91-96, 2003. ♦♦

Metacholine Can Induce Vocal Cord Adduction in Patients With VCD

PATIENTS with vocal cord dysfunction (VCD) have abnormal adduction of the vocal cords, most often during inspiration. The symptoms of VCD may be similar to those of asthma, sometimes leading to an incorrect diagnosis; the extent of overlap between asthma and VCD is uncertain. This study evaluated the response to methacholine challenge among patients with VCD.

The study included three groups of subjects with normal spirometry results: 10 patients with VCD, confirmed by direct laryngoscopy; 12 with exercise-induced asthma and a positive response to methacholine challenge testing; and 12 healthy controls. The VCD patients were 8 women and 2 men, average age 31 years. Spirometry was performed with analysis of flow-volume loops, which has been suggested as a useful test for VCD. In addition, direct laryngoscopy was performed immediately before and after a methacholine challenge test.

Four of the ten VCD patients showed vocal cord adduction on inspiration. In 2 of these patients, the vocal cords were adducted at initial examination and unchanged after methacholine challenge. The other 2 VCD patients showed acute inspiratory vocal cord adduction only after methacholine challenge. This finding did not occur in patients with exercise-induced asthma or in normal controls. The results of spirometry, including analysis of flow-volume loops, found no significant differences between VCD patients and those with exercise-induced asthma.

Methacholine challenge testing may induce acute vocal cord adduction in patients with VCD. In this group of patients, a positive response to methacholine may not indicate the presence of reactive airways disease. The results also suggest that flattening or truncation of the inspiratory flow volume loop is not a diagnostic sign of inspiratory vocal cord adduction.

COMMENT: *Vocal cord dysfunction is a common masquerader of asthma, and there is a misconception that an abnormal flow volume loop is a reliable way to confirm its presence. This study included 10 VCD patients, primarily young women who experienced symptoms with exercise. Methacholine challenge resulted in truncation of the inspiratory portion of the flow volume loop in 6 VCD subjects, 2 of whom had normal laryngoscopies postmethacholine. Therefore, although the flow volume loop may assist in evaluation of patients suspected of having VCD, it is neither a sensitive nor specific test for confirming the diagnosis. Direct visualization of the vocal cords during symptoms remains the gold standard.*

S. A. T.

Perkins PJ, Morris MJ: Vocal cord dysfunction induced by methacholine challenge testing.

Chest 122:1988-1993, 2002. ♦♦

How Do Pollutant Levels Affect Pediatric Asthma Visits?

PREVIOUS studies have linked ozone, small particulates, and other air pollutants to asthma exacerbations. However, experience at the authors' children's hospital suggests that asthma hospitalizations are low during the summer months, when air quality is poorest. The effects of outdoor air quality on pediatric asthma exacerbation rates were assessed.

The investigators reviewed the records of Cincinnati Children's' Hospital for a 7-month period, April through October, to identify emergency department and inpatient visits for pediatric asthma. The findings were compared against county air monitoring data, including concentrations of ozone, particulates under 10 μm (PM_{10}), pollens, and spores. Multiple regression analysis was performed to assess relationships between these levels and asthma visits 1 to 5 days later.

Visits for pediatric asthma were significantly related to daily pollen count, with a stronger effect for visits 1 to 3 days after the pollen count. As a predictor of asthma visits, PM_{10} counts were synergistic with pollen count. Ozone and fungal concentrations were not significant predictors. Asthma admissions were strongly related to pollen counts in the spring and summer months but not in the fall, although both asthma visits and pollen counts were high during the fall months.

The results show a significant effect of airborne pollen and small particulate levels on emergency department visits and hospital admissions for pediatric asthma. Ozone and fungal spore levels do not seem to affect the rate of asthma exacerbations in children.

COMMENT: *In this interesting study the authors document the importance of outdoor air quality on the course of pediatric asthma. In this as in previous studies, ozone did not appear to be an independent risk factor for asthma exacerbations. In an accompanying editorial, Dr. David Peden thoughtfully points out the genetic variability of asthma and response to exacerbating factors and also highlights the importance of nonallergic respirable particulates.*

A. M.

Lierl MB, Hornung RW: Relationship of outdoor air quality to pediatric asthma exacerbations.

Ann Allergy Asthma Immunol 90:28-33, 2003. ♦♦

Schools Show Significant Levels of Common Allergens

INCREASES in the prevalence of asthma among schoolchildren are disproportionately high among inner-city children. Although indoor allergens are known to play a role as asthma triggers, there are few data on the asthma risks associated with the school environment. Levels of common aeroallergens were measured in a sample of urban public schools.

The investigators measured allergen levels in dust samples from 12 Baltimore public elementary schools. Mean levels were 1.49 U/g for cockroach allergen Bla g, 0.38 μg/g for dust mite allergen Der f 1, 1.44 μg/g ➤➤

for dog allergen Can f 1, 1.66 for cat allergen Fel d 1, and 6.24 μg/g for mouse allergen Mus m 1. Levels of dog, cat, and dog allergens were significantly higher in carpeted rooms. Asthma prevalence rates at the schools varied from 11.8% to 20.8% and were significantly correlated with measured levels of cockroach allergen.

Common aeroallergens are readily detected in dust samples from inner-city schools with a high prevalence of asthma. The allergen levels are relatively low, suggesting that home exposures and other factors play a more important role in asthma sensitization and symptoms. However, keeping schools clean may help reduce allergen exposure for children with asthma.

COMMENT: *Our schoolrooms have long enjoyed the reputation of providing a sanctuary of safety for children. This study and others remind us that we must educate parents and administrators of the potential health hazards associated with schoolroom allergen exposure. In the accompanying editorial, Dr. Leikly raises many important issues, including "who will pay" for the costs involved with remediation.*
A. M.

Amr S, Bollinger ME, Myers M, et al: Environmental allergens and asthma in urban elementary schools.
Ann Allergy Asthma Immunol 90:34-40, 2003. ♦♦

What Is the Cytokine Profile of Patients With Chronic Urticaria?

UP to 40% of patients with chronic urticaria have a circulating IgG antibody that binds to the α subunit of the IgE receptor, leading to degranulation of basophils and cutaneous mast cells. Liberation of C5a may lead to histamine release, enhanced by complement activation. The cytokine profile of patients with chronic urticaria was studied to determine whether a Th1 or Th2 phenotype predominates.

Cytokine profiles were determined in sera from 60 patients with chronic urticaria and 51 controls. Interferon-γ was measured as an indicator of a Th1 phenotype and interleukin-4 (IL-4) and IL-5 as indicators of a Th2 phenotype. Mean IL-4 level was significantly higher in the chronic urticaria group than in healthy controls, 1.03 vs 0.20 pg/mL. However, there was no difference in IL-4 level between urticaria subjects and atopic controls, 0.52 pg/mL. None of the sera showed detectable IFN-γ or IL-5.

Further experiments were performed to measure responses of mast cells and basophils that were stimulated with sera capable of inducing histamine release. Sera that induced basophils to release histamine also induced the release of leukotriene and IL-4. Although CD4+ T cells from patients with chronic urticaria produced higher cytokine levels than CD4+ T cells from healthy controls, cytokine production by CD8+ lymphocytes was not significantly different.

Patients with chronic urticaria have basophil and mast cell activators in their serum that are involved in leukotriene and IL-4 production, in addition to histamine. The presence of IgE antibody receptor appears correlated with the capacity to induce release of IL-4. The findings in CD4+ lymphocytes support an immune basis for chronic urticaria. Rather than a Th1- or Th2-predominant profile, the cytokine measurements in patients with chronic urticaria suggest a Th0 profile or a mix of Th1 and Th2 cells.

COMMENT: *In patients with chronic urticaria, antibody to the IgE receptor is clearly correlated with the ability to induce IL-4 release. The data presented in this study support an immune basis for chronic urticaria. CD4+ lymphocytes from such patients are noted to be activated and release greater amounts of cytokine with nonspecific stimuli. We know this is likely operative in 30% to 40% of patients with chronic urticaria, but it would be more interesting to uncover the specific trigger that sets this in motion.*
E. J. B.

Ferrer M, Luquin E, Sanchez-Ibarrola A, et al: Secretion of cytokines, histamine and leukotrienes in chronic urticaria.
Int Arch Allergy Immunol 129:254-260, 2002. ♦♦

Mepolizumab Doesn't Eliminate Eosinophils From Airway

AN anti-interleukin-5 (IL-5) monoclonal antibody, mepolizumab, has been found to deplete eosinophils from the blood and sputum of patients with mild atopic asthma. Surprisingly, however, this antibody did not alter the response to inhaled allergen, raising questions about the eosinophil's role as the effector cell in asthma. Mepolizumab's effects on eosinophils in the airways, bone marrow, and blood of asthma patients were assessed.

Twenty-four patients with mild asthma were randomized to receive three IV doses of mepolizumab, 750 mg, or placebo over a 20-week period. Compared with baseline, mepolizumab treatment caused a median 55% reduction in airway eosinophils. Bone marrow eosinophils decreased by 52% and bone marrow eosinophils by 100%.

Nevertheless, bronchial mucosal staining for eosinophil major basic protein was unchanged. Neither was there any significant alteration in conventional clinical asthma measures, such as airway hyperresponsiveness, FEV_1, or peak flow.

Repeated therapy with mepolizumab reduces but does not eliminate eosinophils from the airway or bone marrow, despite a sharp reduction in blood eosinophils. There are also no reductions in clinical asthma measures. The authors call for further studies using more effective antieosinophil strategies.

COMMENT: *This study further supports the limited value of a monoclonal antibody against IL- 5 as an effective single-agent treatment for eosinophil-induced airway inflammation. The study does address the in vivo relevance of cytokine/growth factor redundancy and suggests that there are subpopulations of eosinophils with varying dependence on IL-5 for their survival and activity, further supporting the heterogeneity of the asthma syndrome.* ➤➤

G. D. M.

Flood-Page PT, Menzies-Gow AN, Kay B, Robinson DS: Eosinophil's role remains uncertain as anti-interleukin-5 only partially depletes numbers in asthmatic airway. **Am J Respir Crit Care Med** 167:199-204, 2002. ♦♦

Intranasal Allergen Produces Allergic Responses in Upper and Lower Airways

STUDIES have demonstrated an association between allergic rhinitis (AR) and asthma, and thus between allergic disease in the upper and lower airway. Primary sensitization to aeroallergens likely occurs in the nares, but questions remain about the regulation of local allergic responses. Animal models of allergic airway disease have generally relied on systemic sensitization. A mouse model of AR was developed to assess nasal, bronchial, and systemic responses to allergen stimulation.

Mice were sensitized to ovalbumin via isolated intranasal application or intraperitoneal injection. Allergic responses to a subsequent intranasal ovalbumin challenge were assessed. After the animals were killed, histologic examination of the upper and lower airways and assays of bronchoalveolar lavage fluid were performed.

Studies using intranasally applied dye confirmed intranasal particle deposition within the nares only. Systemic sensitization led to significant increases in specific IgG and IgE within 14 days. In the local sensitization group, these responses took 28 to 33 days to develop, depending on the allergen dose. On histologic examination, marked eosinophilic infiltration was present in both the upper and lower airways. Bronchoalveolar lavage fluid showed increased levels of interleukin-5 and polymorphonuclear infiltrates.

Local intranasal application of allergen produces allergic-type immune responses in the upper and lower airways of mice. The development and severity of these changes differ from those in animals systemically sensitized to the same allergen. The nasal environment at the time of allergen exposure may play a central role in subsequent responses in both the upper and lower airways; this mouse model may prove useful in further studies of induction and regulation of allergic responses, and of treatments for AR and asthma.

COMMENT: *The intimate relationship between AR and asthma is once again confirmed in this elegant murine model. A dose-dependent allergic response was demonstrated after intranasal sensitization with ovalbumin in these BALB/c mice. Besides increases of interleukin-5 in bronchoalveolar lavage fluid, dramatic increases in eosinophilic infiltration were found in both upper and lower airways after intra-nasal allergen challenge. Particular care was taken to limit allergen deposition to the nares and to ensure that there was no accidental intrapulmonary allergen exposure. These controls further strengthen the findings and reconfirm that allergen stimuli in the upper airway mediate inflammatory effects at the lower end of the airway as well.*

S. M. F.

McCusker C, Chicoine M, Hamid Q, Mazer B: Site-specific sensitization in a murine model of allergic rhinitis: role of the upper airway in lower airways disease. **J Allergy Clin Immunol** 110:891-898, 2002. ♦♦

Adrenal Effects of Budesonide Are Greater With DPI Than With pMDI

USING a dry-powder inhaler (DPI) for delivery of inhaled corticosteroids is associated with increased lung deposition and greater therapeutic effect than when a pressurized metered-dose inhaler (pMDI) is used. It is unclear whether this increased deposition leads to increased systemic absorption. The effects of inhaled budesonide on the hypothalamic-pituitary-adrenal axis were compared for asthmatic children using a DPI vs pMDI.

The study included 15 children using inhaled budesonide, 200 µg twice daily, for treatment of asthma. In random order, the children used the Turbuhaler DPI and the Nebuhaler pMDI with a 750 mL spacer for 1 month. Twenty-four-hour urine collections were obtained to assess the prevalence of adrenal suppression.

Mean baseline urinary cortisol:creatinine was similar between groups, 0.038 µg/mg. After 1 month of DPI therapy, urinary cortisol:creatinine was reduced by 27%. In contrast, there was no change from baseline after pMDI therapy.

Asthmatic children taking 400 µg/d of inhaled budesonide show significant adrenal suppression when the steroid is delivered via DPI. In contrast, no change in hypothalamic-pituitary-adrenal axis function is observed when the same children receive the same budesonide dose using a pMDI with spacer. The higher respiratory drug deposition achieved with a DPI may also lead to increased systemic absorption.

COMMENT: *This provocative study serves as a reminder to all clinicians that "low systemic bioavailability" does not imply* no *systemic bioavailability. The thoughtful accompanying editorial highlights the importance of understanding that increased hypothalamic-pituitary-adrenal axis suppression is likely associated with greater drug delivery to the peripheral airways. This is yet another reminder to always attempt to achieve the lowest effective dose of inhaled corticosteroids in children.*

A. M.

Goldberg S, Einot T, Algur N, et al: Adrenal suppression in asthmatic children receiving low-dose inhaled budesonide: comparison between dry powder inhaler and pressurized metered-dose inhaler attached to a spacer. **Ann Allergy Immunol** 89:566-571, 2002.

Do Intranasal Triamcinolone and Fluticasone Affect Growth in Children?

THERE is concern about the potential for adverse growth effects of inhaled and intranasal corti- ➤➤

costeroids in children with allergic rhinitis. Triamcinolone acetonide and fluticasone propionate aqueous nasal sprays have been found effective in controlling symptoms of allergic rhinitis in children; fluticasone reportedly causes suppression of the hypothalamic-pituitary-adrenal (HPA) axis, whereas triamcinolone does not. These two intranasal corticosteroids were compared for their effects on HPA axis function and short-term growth in children with allergic rhinitis.

The randomized, crossover trial included 59 children, mean age 7 years, with allergic rhinitis. They received two weeks of four different treatments: triamcinolone nasal spray, 110 and 220 µg; fluticasone nasal spray, 200 µg; and placebo. A 2-week washout period separated each treatment. Twelve-hour overnight urinary cortisol levels were measured to assess HPA axis function, and knemometry was performed to measure short-term lower-leg growth.

Forty-nine children completed all four treatments. Compared with placebo, mean growth velocity was reduced by approximately 20% with triamcinolone 110 µg and 22% with fluticasone 200 µg, compared to 33% with triamcinolone 220 µg. However, the difference did not meet specified criteria for clinical (or statistical) significance.

Fluticasone was associated with a significant change in cortisol level compared with placebo or the 220 µg dose of triamcinolone. The overnight urinary cortisol measurements showed more time-dependent variability than the knemometry results.

Intranasal triamcinolone and fluticasone do not significantly affect short-term bone growth in children with allergic rhinitis. However, 2 weeks of treatment with fluticasone causes significant suppression of the HPA axis, compared with triamcinolone or placebo.

COMMENT: *Intranasal corticosteroids remain a cornerstone of allergic rhinitis management in children. Although triamcinolone is acknowledged to have greater potential systemic bioavailability, no differences were noted in short-term growth velocity on comparison with the less-bioavailable fluticasone.*
A. M.

Skoner DP, Gentile D, Angelini B, et al: The effects of intranasal triamcinolone acetonide and intranasal fluticasone propionate on short-term bone growth and HPA axis in children with allergic rhinitis.
Ann Allergy Asthma Immunol 90:56-62, 2003. ♦♦

Thiomersal-Containing Vaccines Produce Low Blood Mercury Levels in Infants

THIOMERSAL is a preservative commonly used in vaccines, with antimicrobial effects resulting from the presence of small amounts of ethylmercury. The only reported adverse effects of thiomersal have been allergic reactions. The potential impact of thiomersal's mercury content on infants and young children undergoing vaccinations has received little research attention. Mercury levels were measured in the blood, urine, and stools of infants receiving vaccines.

The study sample comprised 40 infants receiving thiomersal-containing diphtheria-tetanus-pertussis vaccine, hepatitis B vaccine, and *Haemophilus influenzae* type b vaccines. Blood, urine, and stool samples were obtained at intervals from 3 to 28 days for measurement of mercury levels. The results were compared with those of 21 infants receiving thiomersal-free vaccines.

Mean total mercury dose for subjects receiving thiomersal-containing vaccines was 45.6 µg for 2 month-old-infants and 111.3 µg for 6-month-old infants. Measured blood mercury levels were very low: always less than 29 nmol/L, considered the safe mercury concentration in cord blood. Just 1 of the infants receiving thiomersal-free vaccines had measurable levels of mercury in the blood.

Mercury levels were low in urine but high in stool. The estimated blood half-life of ethylmercury in infants was estimated at less than 10 days, compared with 40 to 50 days for methylmercury in adults and breast-feeding infants.

Although thiomersal-containing vaccines produce elevated blood mercury levels in infants, the levels are far below those associated with toxic effects. Thiomersal-containing vaccines appear to carry very little risk in full-term infants, although they should not be used in very-low-birthweight preterm infants.

COMMENT: *The media and alternative medicine publications frequently report that exposure to mercury and its buildup within the body are associated with chronic ill health. Not a great deal is known about the harmful effects of mercury in infants and children receiving vaccines and at what level such harmful effects might occur. These authors show that, at between 12.5 and 25.0 µg of mercury per vaccine dose, blood levels are much lower than prescribed limits and the mercury is rapidly eliminated in stool.*
E. J. B.

Pichichero ME, Cernichiari E, Lopreiato J, Treanor J: Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study.
Lancet 360:1737-1341, 2002. ♦♦

Allergy Tests Can Diagnose Delayed Hypersensitivity to Penicillins

DELAYED reactions to penicillin can include maculopapular and urticarial rashes. Recent studies suggest that nonimmediate hypersensitivity reactions to systemic drugs occur through a type IV, cell-mediated mechanism. Patients with nonimmediate reactions to penicillins underwent a series of standard allergologic tests to evaluate the pathogenesis of these reactions.

The study included 259 patients reported nonimmediate reactions to penicillin. A careful history was obtained, followed by a protocol of skin-prick, intradermal, and patch tests with penicillin determinants, ampicillin, amoxicillin, or other implicated drugs. Challenge tests were performed in patients who reacted negatively to all of these tests or who had delayed intradermal test positivity and patch test negativity. ➤➤

Ninety-three percent of patients reported adverse reactions to aminopenicillins; maculopapular rashes were the most frequent manifestation. Immediate positive responses to skin testing occurred in just 3 patients. Patch tests and delayed intradermal tests to the culprit penicillins were positive in 94 patients: to aminopenicillins in 90 and to piperacillin in 4. All tests were negative in 154 patients, and challenges were performed in 125 of these: only 3 responded positively.

Nonimmediate reactions to penicillins, especially morbilliform rashes, can be diagnosed by means of patch and intradermal tests. In the current study, these tests diagnosed more than 50% of patients with maculopapular rashes as having delayed hypersensitivity. The presence of delayed hypersensitivity to penicillins does not appear to be affected by the time between the last clinical reaction and the time allergologic tests are performed.

COMMENT: *The tendency for penicillin to become rapidly haptenated into predictable intermediates has enabled the development of validated skin testing reagents for detecting penicillin-specific IgE. However, most adverse reactions to penicillin are not immediate, and these reagents have so far had limited utility beyond reassuring the doctor and patient that there is little risk of an immediate life-threatening reaction to penicillin. This uncontrolled Italian study attempts to define the usefulness of delayed intradermal and patch testing in patients with a history of delayed reactions to penicillin. In most cases the patch testing results matched the results of intradermal tests read at 48 and 72 hours, and only 3 of the 125 patients with negative skin and patch tests reacted on oral challenge. The results suggest that serious adverse reactions to penicillin are unlikely to occur in patients screened with these diagnostic techniques. However, controlled studies will be required before proper validation is complete.*
S. A. T.
Romano A, Viola M, Mondino C, et al: Diagnosing nonimmediate reactions to penicillins by in vivo tests.
Int Arch Allergy Immunol 129:169-174, 2002. ♦♦

Why the Autumn Increase in Childhood Asthma?

A sharp increase in health care utilization for asthma occurs during the fall months, suggesting a role of changes in allergen levels or other seasonal environmental factors. Data from a multicenter study of pediatric asthma were used to assess variables associated with seasonal patterns in asthma morbidity

The National Cooperative Inner-City Asthma Study (NCICAS) included 1,641 children with asthma from 8 research centers in Northern U.S. cities. The study population consisted largely of poor, minority children living in the inner-city. The children were followed up for 4 years after baseline assessment of skin test reactivity to allergens. Factors contributing to seasonal trends in asthma morbidity were assessed, including environmental tobacco smoke and air pollutants.

Asthma symptoms were highest in the fall, beginning in September; and lowest in the summer, July through August. Trends in unscheduled health visits and hospitalizations for asthma followed a similar seasonal pattern. The fall increases were little affected by the children's atopic status or by exposure to environmental tobacco smoke. Analysis of air pollution monitoring data suggested that seasonal patterns of sulfur dioxide were associated with asthma morbidity. No such association was noted for the other pollutants studied, such as ozone, nitrogen dioxide, or particulates smaller than 10 μm.

The data support the recognized seasonal pattern of increased asthma morbidity in the fall, with lowest levels during the summer. Of the potential contributing factors evaluated, only sulfur dioxide pollutant levels follow the same seasonal pattern. The findings are consistent with the theory that seasonal variation in asthma may be related to viral infections.

COMMENT: *Every first-year allergy fellow learns that asthmatic children are more prone to wheeze in the late fall and less likely to wheeze in the midsummer. The NCICAS data, involving 4- to 12-year-olds living in large Eastern and Midwestern inner-cities, confirm the existence of this pattern. A number of factors--eg, weather changes, allergy, pollution, viral infection--have been blamed but none has been confirmed as responsible. It appears that neither the atopic status of the child nor exposure to tobacco smoke in the home is a determining factor. The influence of viral infections was not studied.*
J. A. A.
Gergen PJ, Mitchell H, Lynn H, for the National Cooperative Inner-City Asthma Study (NCICAS): Understanding the seasonal pattern of childhood asthma: results from the National Cooperative Inner-City Asthma Study (NCICAS).
J Pediatr 141:631-636, 2002. ♦♦

Is Intranasal Amphotericin B Effective for Chronic Rhinosinusitis?

CHRONIC rhinosinusitis (CRS) is a common condition that is difficult to treat. The histologic findings in CRS include eosinophilia and fungi. Although the fungi alone cannot account for the presence of chronic inflammation in CRS, they might activate the immune system in sensitized patients. If so, then antifungal therapy might reduce the symptoms. A pilot study of intranasal amphotericin B for patients with CRS is reported.

The prospective, open-label trial included 51 patients with CRS that had not responded to other treatments. All patients received intranasal amphotericin B, 20 mL of a 100 μg/mL solution applied twice daily. Outcome assessment included symptom scores and endoscopic examination. Thirteen patients underwent CT scanning of the nose and sinuses before and after treatment.

Three-fourths of patients had reduction of symptoms after treatment with amphotericin B. According to the endoscopic score used in this study, 35% of patients achieved disease-free status while another 39% ➤➤

improved by one or more stages. In one-fourth of patients, antifungal therapy had no apparent effect. Pretreatment CT scans showed inflammatory mucosal thickening occluding the paranasal sinuses; posttreatment scans suggested significant reduction in this thickening.

Intranasal amphotericin B therapy appears safe and effective for the treatment of CRS. About three-fourths of patients show significant clinical improvement. Randomized, controlled trials are needed to establish the efficacy of this new approach to CRS treatment.

COMMENT: *Whether eosinophilia in the nose and sinuses of patients with CRS and nasal polyps is related to the presence of fungi in the nose is still debated. Some otolaryngologists believe the fungi cause the "allergic mucin," despite finding fungi in the noses of normal subjects as well. These "fungus-believers" here publish an* uncontrolled *study of intranasal amphotericin B: many CRS patients improved. It remains baffling why there hasn't been a properly controlled study.*
R. J. M.

Ponikau JU, Sherris DA, Kita H, Kern EB: Intranasal antifungal treatment in 51 patients with chronic rhinosinusitis.
J Allergy Clin Immunol 110:862-866, 2002. ◆◆

Early Exposure to Dust Mite Doesn't Predict Childhood Asthma

HOUSE dust mite (HDM) may play a key role as a primary cause of asthma and allergic disease. However, previous studies of the role of exposure to this allergen have included only limited one or two collections of household dust. Data from a birth cohort of newborns with high cord blood IgE were analyzed to assess the effects of HDM allergen exposure to asthma in childhood.

The study was based on an HMO cohort of 97 children with a cord blood IgE level of 0.56 IU/mL or higher at birth between 1987 and 1989. Exposure to HDM allergens was assessed using bedroom dust samples collected monthly through the first 2 years of life. When the children were 6 or 7 years old, 64 responded to a follow-up questionnaire regarding physician-diagnosed asthma. At the same time, the children underwent clinical examination, including skin-prick testing and methacholine challenge testing.

Ninety-three percent of planned house dust measurements were carried out. Nineteen of the children tested positive for bronchial hyperresponsiveness (BHR), although only 6 had received a physician diagnosis of asthma. Levels of HDM allergen were similar for children with vs without asthma and with vs without BHR. Children with skin test-confirmed sensitization to HDM were more likely to have a physician diagnosis of asthma, however.

In 6- to 7-year-old children, sensitization to HDM allergen is significantly associated with the presence of asthma. However, even with repeated measurements over a prolonged period, level of HDM exposure at home is unrelated to the development of asthma or BHR. Since the study included no allergen avoidance measures, the measured levels are probably a good indicator of "real-world" exposure to HDM.

COMMENT: *This is another in a series of papers resulting from a well-designed, epidemiologic study in suburban Detroit. The population's demographic characteristics are provided in other papers, but essentially the individuals are middle-class to upper middle-class, are predominantly Caucasian, and have elevated cord blood IgE. The predictive value of cord blood IgE in determining risk of atopic respiratory disease has been challenged. The findings of this study do not show any evidence of asthma or bronchial hyperreactivity in a population presumed to be at risk of asthma. Does this apply to all allergens, to all ethnic and economic groups, to populations at greater risk of respiratory disease, or to all atopic diseases? Good studies often result in as many questions as answers.*
D. K. L.

Carter PM, Peterson EL, Ownby DR, et al: Relationship of house-dust mite allergen exposure in children's bedrooms in infancy to bronchial hyperresponsiveness and asthma diagnosis by age 6 to 7.
Ann Allergy Asthma Immunol 90:41-44, 2003. ◆◆

Epinephrine and Albuterol Are Ineffective for Bronchiolitis in Infants

MOST infants hospitalized for acute viral bronchiolitis need only supportive treatment. This generally includes β_2-agonists such as albuterol, although recent reports have questioned the value of albuterol in this situation. Because of its effects on airway edema and mucus production, extended use of epinephrine might be of benefit. The effects of repeated nebulized epinephrine were compared with albuterol and placebo in infants with acute viral bronchiolitis.

The randomized, controlled trial included 149 infants hospitalized for acute viral bronchiolitis, characterized by a first episode of wheezing plus evidence of acute respiratory infection. Mean age was about 4 months. The infants were randomized to receive nebulized racemic epinephrine, 0.03 mL/kg/dose of a 2.25% solution; albuterol, 0.03 mL/kg/dose of a 5 mg/mL solution; or saline placebo. All treatments were administered once every 1 to 6 hours, at the discretion of the care providers. Length of hospital stay was compared among groups; times to normal hydration, oxygenation, and minimal respiratory distress were assessed as well.

The three groups were similar in terms of initial clinical characteristics and treatment. Mean length of stay was about 60 hours in all groups. Other outcomes were similar was well, including the findings at 1-week follow-up.

For infants with acute viral bronchiolitis, treatment with nebulized epinephrine or albuterol has no apparent benefit in terms of length of stay or other clinical outcomes. Neither is recommended for routine use in this group of hospitalized infants. Supportive therapy for viral bronchiolitis includes oxygen, fluids, and close observation. ➤➤

COMMENT: *In this Canadian study of infants with bronchiolitis (first-time wheezing in first year of life during the respiratory syncytial virus season associated with cough/coryza),* neither *inhaled albuterol nor epinephrine was better than saline placebo in reducing the time spent in the hospital. In my early years as a pediatrician, injectable epinephrine was occasionally used to help distinguish asthma from bronchiolitis. (Epinephrine did not help bronchiolitis.) In more recent times, it has become commonplace to treat all wheezing infants with, at least, inhaled bronchodilators. It appears we were correct in the first place: bronchodilators do not affect the clinical course of viral bronchiolitis.*
J. A. A.
Patel H, Platt RW, Pekeles GS, Ducharme FM: A randomized, controlled trial of the effectiveness of nebulized therapy with epinephrine compared with albuterol and saline in infants hospitalized for acute viral bronchiolitis.
J Pediatr 141:818-824, 2002. ♦♦

Inhaled Corticosteroids Bring Improvements in Children With Mild Asthma

SOME reports have suggested that inhaled corticosteroids should be used in young patients with even mild asthma, in an attempt to prevent pulmonary function abnormalities and airway remodeling. Because children with mild asthma have near-normal pulmonary function, these parameters cannot be used to assess the effects of inhaled corticosteroid therapy. The subjective and objective benefits of inhaled corticosteroids in children with mild asthma were assessed.

The study included 68 children, aged 5 to 10 years, with physician-diagnosed asthma but no recent systemic corticosteroid therapy. They were randomized to receive 12 weeks of treatment with fluticasone propionate, 250 µg twice daily, or placebo. Both treatments were administered using a metered-dose inhaler with spacer. Outcome measures included symptom scores, rescue medication use, parental evaluations. Pulmonary function tests, including methacholine challenge testing, were performed as well.

Children receiving fluticasone had a higher percentage of symptom-free days, odds ratio (OR) 1.93; and a higher percentage of rescue medication-free days, OR 3.08. Morning and evening peak expiratory flow and FEV_1% predicted were also higher in the fluticasone group. The other outcomes studied--including parental evaluations, absolute FEV_1, and methacholine PD_{20}--were not significantly different between groups.

For children with mild asthma, inhaled fluticasone is associated with significant improvement in some subjective and objective asthma parameters. The results strengthen the case for starting inhaled corticosteroids early in the course of asthma, before pulmonary function abnormalities develop. However, the findings show no significant change in several parameters, including bronchial hyperresponsiveness.

COMMENT: *This study continues the debate regarding the use of inhaled corticosteroids in young children (age 5 to 10) with step 2 mild persistent asthma. There were significant differences between groups (treatment vs placebo) in some objective airway measures but not others. Given the brief duration of the study (12 weeks) and the lack of significant effect on bronchial reactivity (PD_{20}), this study does little to resolve the controversy surrounding the relative value of chronic anti-inflammatory effect vs growth suppression risk in children receiving prolonged courses of inhaled corticosteroids.*
G. D. M.
Arets HGM, Kamps AWA, Brackel HJL, et al, on behalf of a multicentre study group: Children with mild asthma: do they benefit from inhaled corticosteroids?
Eur Respir J 20:1470-1475. ♦♦

More on Farms: Pro and Con

STUDIES from Europe have suggested that children raised on farms have lower rates of allergic disease. The relationship between living on a farm and allergy risk was assessed in New Zealand, where farms are larger and the climate is more temperate.

The case-control study included 293 children: 95 who lived on New Zealand farms and 198 who lived in a small town. Assessments included a parental questionnaire, dust sampling, and skin prick testing. Children who lived on a farm during their first year of life had a higher prevalence of hay fever; skin prick positivity and other allergic diseases were unaffected. Children who currently lived on a farm had higher rates of both hay fever and asthma, although this risk was mainly limited to skin prick-positive subjects. Endotoxin levels were lower on farms, but levels of Der p 1 were higher.

Children living on New Zealand farms have an elevated prevalence of hay fever and asthma. This relationship appears mainly among children with positive skin prick tests, possibly reflecting responses to the higher allergen loads found on farms. Like previous studies, the results suggest a possible protective effect of early-life exposure to animals.

COMMENT: *In contrast to studies from Europe, which have reported a reduced prevalence of allergy in farmers' children, these authors have found a greater prevalence of allergic disease in children raised in New Zealand farms. This increased risk of hay fever and asthma was largely among children with positive skin prick tests to prevalent allergens.*
E. J. B.
Wickens K, Lane JM, Fitzharris P, et al: Farm residence and exposures and the risk of allergic diseases in New Zealand children.
Allergy 57:1171-1179, 2002.

IN a previous study, the authors found a reduced rate of some allergic diseases among Finnish university students who grew up on farms. A further study was performed to assess the effects of childhood farm envi- ➤➤

ronment on current asthma and allergic sensitization.

The analysis included a clinical subsample of 296 participants in the original study: 29 who grew up in farm environments and 253 who did not. The rate of current asthma was about 3% for the farm group compared with 12% for the nonfarm group, odds ratio 0.22 (95% confidence interval 0.07 to 0.70). Subjects from farms also had a lower rate of sensitization to cat: 1.5% vs 13%, odds ratio 0.10 (95% confidence interval 0.02 to 0.47). Sensitization to other allergens also tended to be lower in the farm group. However, sensitization to house dust mite was higher in the farm group, odds ratio 5.43 (95% confidence interval 1.60 to 18.46).

Finnish university students who grew up on farms have lower rates of asthma and cat sensitization. The farm group also shows lower rates of IgE antibodies to most other allergens, the exception being house dust mite.

COMMENT: *This study adds to the mounting evidence that the farm environment protects against IgE-mediated disorders. There was a lower occurrence of asthma and of IgE antibodies to cat, as well as a trend toward lower levels of IgE antibodies to other allergens. The exception was IgE antibodies to house dust mite. The question related to why the latter is true remains an enigma.*
E. J. B.
Kilpeläinen M, Terho EO, Helenius H, Koskenvuo M: Childhood farm environment and asthma and sensitization in young adulthood.
Allergy 57:1130-1135, 2002. ♦♦

New Infant Mattresses Show Detectable Allergen Levels

EARLY-onset asthma has been linked to high levels of mite allergens in mattresses. Buying new mattresses for baby beds might be suggested as one way of avoiding allergen exposure. New mattresses were tested for levels of dust mite, dog, and cat allergens.

Dust samples were obtained from 90 infant mattresses purchased from 50 Dutch shops. Seventy-five of the mattresses tested contained at least some allergen. Some contained very high levels of allergen--up to 3.1 μg/g of Der p 1 and 46.5 μg/g of Der f 1--although the overall amount of dust in the mattresses was low. Allergen levels were higher in mattresses purchased without a plastic wrapping.

Significant levels of mite, dog, and cat allergen are detected in newly bought infant mattresses. Mattresses should be wrapped in plastic when purchased, then vacuumed before being placed on the child's bed.

COMMENT: *One would think that a newly purchased, never-slept-on mattress would not contain detectable levels of dust mites, but the current study suggests that this simply is not true. The study does not address the question of whether the mites found in new mattresses cause clinical symptoms in patients who encase them properly. However, advising a patient to purchase a new mattress that is wrapped in plastic and to vacuum thoroughly before encasing is relatively simple, inexpensive advice, given these results.*
S. A. T.
De Boer R: Allergens, Der p1, Der f 1, Fel d 1, and Can f 1, in newly bought mattresses for infants.
Clin Exp Allergy 32:1602-1605, 2002. ♦♦

Echinacea Shows No Benefit for Common Cold

ECHINACEA preparations have been claimed to be useful for the prevention and treatment of colds. Although some previous studies have shown positive results, most have had important methodologic shortcomings. A randomized, controlled trial was performed to evaluate the benefits of unrefined echinacea for treatment of colds.

The study included 148 university students with early symptoms of the common cold. One group received capsules containing a mix of unrefined echinacea herb and root, with instructions to take six doses on the first day of illness and three doses on subsequent days, for a total of 10 days. Patients in the placebo group received alfalfa capsules.

There were no differences in the severity or duration of symptoms between groups. The colds lasted about 6 days on average. Echinacea provided no benefit, even after controlling for the baseline severity and duration of symptoms, patient sex, date of enrollment, and use of other medications.

Unrefined echinacea is not an effective treatment for colds in healthy young adults, this randomized trial suggests. More research is needed to ascertain the true value of this widely used treatment.

COMMENT: *My patients are often hoping for a treatment that is not a "drug." Alternative medicine appeals strongly to this desire to avoid medication and is usually propelled by testimonials and personal experience. Physicians need to educate their patients about the need for science, to evaluate data without prejudice, and to promulgate studies such as this, since the media coverage of negative findings will likely be minimal.*
D. K. L.
Barrett BP, Brown RL, Locken K, et al: Treatment of the common cold with unrefined echinacea.
Ann Intern Med 137:939-946. ♦♦

REVIEWS OF NOTE

COMMENT: *This is a well-referenced review by authors with personal experience in evaluating and treating individuals with nonsteroidal anti-inflammatory drug hypersensitivity. Upper airway disease, asthma, anaphylaxis, angioedema, and urticaria are compared and contrasted. A simplified oral challenge/desensitization protocol, based on the Scripps Clinic experience, is provided. Suggestions are offered, based on available evidence, as to which conditions associated with nonsteroidal anti-inflammatory drugs will improve with desensitization. Practical information is the strength of this review.*
D. K. L.
Namazy JA, Simon RA: Sensitivity to nonsteroidal anti-inflammatory drugs.
Ann Allergy Asthma Immunol 89:542-550, 2002.

COMMENT: *President Bush has ordered the immediate vaccination against smallpox of about 500,000 military personnel. As well, he ordered a similar number of core health care workers in the United States to be vaccinated. To avert very significant adverse reactions, knowledge of atopic dermatitis and all of its clinical dimensions is paramount. This excellent review should be readily available to all allergists.*
E. J. B.
Leung DYM, Bieber T: Atopic dermatitis.
Lancet 361:151-161, 2003.

COMMENT: *The author provides a useful review of a topic of importance to all practicing allergists.*
A. M.
Osur SL: Viral respiratory infections in association with asthma and sinusitis: a review.
Ann Allergy Asthma Immunol 89:553-560, 2002.

COMMENT: *For over 30 years, allergic bronchopulmonary aspergillosis (ABPA) has fascinated clinicians and basic immunologists alike. It has answered "yes" to both ends of the "chicken-or-egg" question. This 8-page article provides a succinct review of the clinical features of ABPA.*
R. J. M.
Greenberger PA: Allergic bronchopulmonary aspergillosis.
J Allergy Clin Immunol 110:685-692, 2002.

COMMENT: *This very thorough review examines the association between cow's milk allergy and gastroesophageal reflux disease (GERD). One of the most interesting discussions in this article centers on identification and removal of milk from milk-allergic infants with GERD. Removal of dairy products may be the only form of treatment required to improve GERD; at the same time, antireflux medications may be ineffective. This article is a must-read for the allergist.*
A. L. L.
Salvatore S, Vandenplas Y: Gastroesophageal reflux and cow milk allergy: is there a link?
Pediatrics 110:972-984, 2002.

COMMENT: *Three statistics caught my attention as I read this broad review: (1) The annual influenza illness attack rate among children is 15% to 42%; (2) Healthy infants, up to 2 years of age, are at greater risk of an influenza-associated hospitalization than healthy 50- to 64-year-olds; (3) Despite recommendations to immunize all children with asthma, only 10% to 31% are given influenza shots each year.*
J. A. A.
American Academy of Pediatrics, Committee on Infectious Diseases: Reduction of the influenza burden in children.
Pediatrics 110:1246-1252, 2002.

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