# 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

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## Study Clarifies T-Cell Responses to Immunotherapy

SPECIFIC allergen immunotherapy is an effective treatment for seasonal allergic rhinitis. Some studies have suggested that allergen immunotherapy leads to decreased T-cell responses to allergen and/or a shift from a Th2 to Th1 response, while others have found that immunotherapy induces production of interleukin (IL)-10 by T cells. In mouse models, CD4+CD25+ T cells producing IL-10 have shown immunosuppressive properties. Patients receiving grass pollen immunotherapy were studied to assess the effects of treatment on IL-10 production and CD4+CD25+ T cells.

Peripheral blood mononuclear cells were obtained from 10 patients who had received at least 1.5 years of grass pollen immunotherapy, 12 atopic patients who had not received immunotherapy, and 11 nonatopic controls. After a 6-day cell *Phleum pratense* stimulation protocol, in vitro production of IL-10, IL-5, IL-4, and interferon-γ was assessed, along with measurement of CD4+CD25+ T cell numbers. Intracellular IL-10 analyses were performed as well.

Grass pollen immunotherapy was highly effective in reducing overall symptoms. Expression of Th2 cytokines was not significantly different between atopic patients who did and did not receive immunotherapy. However, production of IL-10 was significantly higher in the immunotherapy group: 116 pg/mL, compared with 30 pg/mL in the atopic controls. Numbers of CD4+CD25+ cells after allergen stimulation were also higher in atopic patients receiving immunotherapy. Intracellular IL-10 was detected only in T cells from patients in the immunotherapy group, almost exclusively CD4+CD25+ cells. T cell responsiveness to *P. pratense* was inhibited by treatment with exogenous IL-10.

Atopic patients receiving grass pollen immunotherapy demonstrate a population of T cells with an IL-10-expressing, CD4+CD25+ phenotype in response to allergen stimulation. Production of IL-10 does not appear to affect allergen-induced cell proliferation or Th2 cytokine expression; adding IL-10 does appear to reduce allergen-induced responses in vitro. The results ➤➤

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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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question whether induction of Th2-to-Th1 immune deviation is a critical feature of the response to immunotherapy.

**COMMENT:***The mechanisms of allergen immunotherapy are becoming more clear. Th2-to-Th1 deviation has been demonstrated in some models. Interluekin-10 has several potent anti-allergic properties, and can be produced by CD4+CD25+ regulatory T cells in human peripheral blood. This study shows that patients given allergen immunotherapy for grass pollen have higher numbers, compared to control atopic subjects, of these T cells that produce IL-10.*
*R. J. M.*
*Francis JN, Till SJ, Durham SR: Induction of IL-10+CD4+CD25+ T cells by grass pollen immunotherapy.*
**J Allergy Clin Immunol** 111:1255-1261, 2003. ♦♦

## A Lot More on Peanut Allergy

EFFECTIVE approaches to immunotherapy for peanut allergy are needed. An engineered recombinant peanut protein was evaluated for long-term desensitization in a mouse model of peanut allergy.

The investigation used heat-killed *Escherichia coli* that produced engineered Ara h1, Ara h2, and Ara h3 peanut proteins (HKE-MP123), modified to eliminate or reduce IgE binding. Peanut-allergic C3H/HeJ mice were given 3 weeks of treatment with low, medium, or high doses of HKE-MP123 protein, administered rectally; HKE-containing vector alone; or vehicle. Responses to peanut challenge were assessed 2, 6, and 10 weeks after the end of treatment.

Compared with sham-treated animals, symptom scores in response to the first peanut challenge were significantly reduced in all HKE-MP123 dose groups, as well as in mice receiving HKE-containing vector. At the 10-week posttreatment challenge, this protective effect persisted in the medium- and high-dose HKE-MP123 groups, which also showed a significant reduction in plasma histamine level. All HKE-MP123-treated groups--especially the high-dose group--had significantly reduced IgE levels. After the final challenge, splenocyte production of interleukin (IL)-4, IL-13, IL-5, and IL-10 was significantly decreased in mice receiving high-dose HKE-MP123, while production of interferon-γ and transforming growth factor-β was increased.

Treatment with an engineered recombinant peanut protein results in lasting down-regulation of peanut hypersensitivity in a mouse model. This protective effect appears to result from reduced antigen-specific Th2 responses, along with increased Th1 and T regulatory cytokine production. With further research, HKE-MP123 may offer an effective approach to desensitization for patients with peanut allergy.

**COMMENT:** *This investigation, using an engineered* E. coli *that produces recombinant peanut proteins, demonstrated a protective effect in peanut-sensitized mice. The mice receiving the highest dose of the engineered peanut proteins (HKE-MP123) not only tolerated intragastric peanut but also demonstrated Th1 cytokines even 8 weeks after administration of HKE-M123. This suggests a Th2-to-Th1 shift and down-regulation of peanut hypersensitivity in these animals. The report shows that progress toward a treatment for our peanut-allergic patients may be closer than we think. One obstacle is that subcutaneous administration produced large reactions; however, the product was well tolerated when administered rectally. Perhaps our peanut-allergic patients won't mind if it proves to be this effective in humans.*
*S. M. F.*
*Li X-M, Srivastava K, Grishin A, et al: Persistent protective effect of heat-killed* Escherichia coli *producing "engineered," recombinant peanut proteins in a murine model of peanut allergy.*
**J Allergy Clin Immunol** 112:159-167, 2003. ♦♦

RECENT studies have shown peanut allergy is not always a lifelong problem, with a significant proportion of children "outgrowing" their peanut allergy. However, allergic reactions remain a possibility even for patients with no response to a previous peanut challenge. The natural progression of peanut allergy among patients with previous peanut challenges was analyzed.

The analysis included 80 children with diagnosed peanut allergy and a peanut IgE level of 5 kU/L or less who had undergone an oral peanut challenge. Fifty-five percent of the patients passed their peanut challenge, including 60% of those in whom the diagnosis of peanut allergy was based on a positive skin prick test or peanut IgE level. Among patients with peanut IgE levels of 2 kU/L or less, 63% passed their peanut challenge. The patients who passed their peanut challenges included 3 with a history of anaphylactic reactions and 2 with initial peanut IgE levels of greater than 70 kU/L.

In response to a follow-up questionnaire, most patients had reintroduced peanut into their diet. However, many still checked food labels for the presence of peanut products, rarely ate peanuts, or had aversion to peanut. Two patients had suspected reactions to peanut after passing a food challenge.

Most patients with a history of peanut allergy and a peanut IgE level of 5 kU/L or less will outgrow their allergy, this follow-up study suggests. However, reactions to peanut may still occur even after the patient has passed a peanut challenge. Based on their findings, the authors recommend that peanut challenges be performed only after age 4 and in patients with a peanut IgE level of less than 2 kU/L. Even after passing a food challenge, patients should be advised to continue carrying epinephrine for another year or two, until they have demonstrated the consistent ability to tolerate eating peanuts.

**COMMENT:** *The peanut allergy experts from Baltimore and Arkansas present a continuation of their previous report, which concluded that 20% of children with peanut allergy outgrow their sensitivity (J Allergy Clin Immunol 107:367-374, 2001). They have now evaluated 84 patients with a history of peanut allergy and found that 55% with IgE RAST of 5 kU/L or less and 63% with levels of 2 kU/L or less tolerated an oral peanut challenge. The bottom line for the clinician is that an oral challenge with peanut under controlled conditions should be considered if the IgE RAST is 2 kU/L or less. However, injectable epinephrine should still be available for at least 2 years after a negative challenge, since there is still a remote chance of a reaction. Interestingly, after the negative challenge, many patients still reported an aversion to peanuts. Only 30% reported eating peanuts on a regular basis.*
*S. M. F.*

*Fleischer DM, Conover-Walker MK, Christie L, et al: The natural progression of peanut allergy: resolution and the possibility of recurrence.*
**J Allergy Clin Immunol** 112:183-189, 2003. ♦♦

MANY patients with atopic dermatitis (AD), particularly infants and children, have food allergies as well. Although skin prick tests are commonly performed as part of the diagnostic workup for AD, the results do not reliably predict the occurrence of allergen-mediated cutaneous reactions. The results of food atopy patch testing (APT) to peanut were compared with responses to skin prick tests and food challenges in patients with AD.

The study included 132 patients with AD, mean age 12 years. All patients were tested for peanut allergy using skin prick tests and APT. For APT, the test material consisted of two parts of whipped peanuts plus one part of petrolatum. The results of skin prick tests and APT were compared with responses to repeated open peanut challenges.

Responses to peanut challenge were positive in 9% of patients. The results of APT were positive in 19% of patients, while 12% had a positive skin prick test for peanut allergy. Patients with an eczematous response to peanut challenge were more likely to have a positive APT than those with an urticarial response. Skin prick test reactivity was higher in patients over 12 years old; in contrast, children under age 6 were more likely to have positive results on peanut APT.

In patients with AD, peanut APT may be a useful test for the presence of peanut allergy. This study finds a 75% rate of APT positivity in patients with challenge-confirmed peanut allergy. Especially in children, peanut APT may be a useful addition to standard tests for diagnosis of peanut allergy in AD.

**COMMENT:** *This unique study is the first to address food APT to peanut in AD patients. The study compares results between puncture and patch test responses to peanuts in AD patients. Atopy patch tests were more frequently positive in subjects with eczematous responses as opposed to urticarial reactions with the test challenge. Clearly, APT with peanut is a potentially useful investigative tool in this setting.*
*E. J. B.*

*Seidenari S, Giusti F, Bertoni L, Mantovani L: Combined skin prick and patch testing enhances identification of peanut-allergic patients with atopic dermatitis.* **Allergy** 58:495-499, 2003. ♦♦

ACCURATE diagnosis of peanut allergy is essential to enable proper avoidance and emergency treatment measures. Some children with atopy undergo skin prick testing to peanut, despite having no known history of peanut ingestion. If the test is positive, these children are usually advised to avoid peanuts, at least until a definitive challenge test is performed. This study examined the outcomes of children with a positive skin prick test to peanut but no previous peanut ingestion.

Review of pediatric allergy clinic records from 1994 to 2001 identified 47 children with a positive peanut ➤➤

skin prick test, wheal diameter at least 3 mm, and no previous history of peanut ingestion. Subsequent peanut challenges, performed as close as possible to school entry, were negative in 24 children and positive in 23. Mean largest wheal diameter was 6.3 mm in the children with negative challenges, compared to 10.3 mm in those with positive challenges. With a cutoff point of 5 mm or greater, a positive peanut skin prick test had a sensitivity and negative predictive value of 100%. However, specificity was 12.5% and positive predictive value 52.3%. Just 1 patient with a peanut-specific IgE level greater than 2.0 kU/L had a negative response to peanut challenge.

Nearly half of children with a positive skin prick test to peanut but no previous history of peanut exposure will have a positive response to peanut challenge. A positive skin prick test of 5 mm or greater is highly sensitive for the detection of peanut allergy, but positive predictive value is relatively low. More research is needed to investigate alternative challenge protocols for children with wheal diameters of 3 to 4 mm, perhaps in combination in low peanut-specific IgE levels.

**COMMENT:** *This report highlights the ongoing challenges of peanut allergy in children. We all recognize that a positive skin test does not imply clinical sensitivity in all settings, but many questions remain. For example, what is the response of patients with positive skin tests with exercise or during ingestion during the height of the pollen season?*
*A. M.*

*Kagan R, Hayami D, Joseph L, et al: The predictive value of a positive prick skin test to peanut in atopic, peanut-naÖve children.*
**Ann Allergy Asthma Immunol** 90:640-645, 2003. ♦♦

## Mite: Avoidance, Removal, and Clinical Benefits

REGULAR washing in hot water is commonly recommended to kill mites in clothing and bedding. However, little is known about the ability of warm or cold water washing to kill mites, or whether mites can be transferred from infested to uninfested garments during washing. The effects of various washing conditions on mite killing and mite transfer were investigated.

Residential washing machines were used to launder clothing and bedding in 6- to 8-pound loads. The items were washed in warm water, 36° to 38° C; or cold water, 22° to 27° C; with or without recommended amounts of laundry detergent or sodium hypochlorite bleach.

Experiments were designed to assess the ability of washing conditions to remove mites and mite allergen from infested items, and to determine whether mites can be transferred from infested to uninfested items during washing.

Sixty to eighty-three percent of live mites were removed by machine washing, whether in water alone, with detergent, or with detergent plus bleach. Some items retained more mites than others--eg, polyester blankets retained more mites than cotton blankets. With water alone or water plus detergent, washing removed 84% of Der f 1. When bleach was added, 98% of allergen was removed. However, mites were readily transferred during washing from infested to previously uninfested items.

Machine washing in warm or cold water, with detergent or detergent plus bleach, performs relatively well in removing mites and mite allergen from clothes and bedding. Repeated washings may be needed to further reduce mite infestation; bleach helps to eliminate mite allergen. Mites can be transferred from infested to uninfested items during washing.

**COMMENT:** *As part of our recommendations for environmental controls in households of allergic patients, we usually recommend frequent washing of bedding to remove dust mites. While previous studies have documented that very hot water (55° C [130° F]) can kill mites, this was a "real-world" study to determine is typical home washings in warm (36° to 38° C) or cold (22° to 27° C) water, with or without detergent or bleach, can reduce the mite load in clothing and bedding. Although both detergent and bleach washes helped reduce mites, it was surprising that mites can be transferred from mite-infested to uninfested garments during the wash. The physical action of the wash cycle for 12 minutes was more beneficial than just soaking the garments in either detergent or bleach for 1 hour. It appears that one of the keys to dust removal in the wash is agitation.*
*S. M. F.*

*Arlian LG, Vyszenski-Moher DL, Morgan MS: Mite and mite allergen removal during machine washing of laundry.* **J Allergy Clin Immunol** 111:1269-1273, 2003. ♦♦

MEASURES to reduce exposure to dust mite allergen are commonly recommended, but their effectiveness is unclear. A randomized trial was performed to examine the effectiveness of allergen-impermeable bed covers in reducing mite allergen exposure for adult asthma patients.

The double-blind trial included 1,122 adult asthma patients recruited from primary care practices. One group was assigned to receive a set of allergen- and vapor-impermeable Allergy Control barrier mattress, pillow, and quilt covers, while the control group received nonimpermeable, polyester-cotton covers. Morning peak expiratory flow rates were measured during a 4-week run-in period and after 6 months of using the assigned bed covers. From month 7 to 12, patients were placed on a phased inhaled-corticosteroid reduction program, and the percentage of patients who were able to discontinue steroid use was compared between groups. Mite allergen levels in mattress dust were measured in a subset of homes at baseline and after 6 and 12 months.

Sixty-five percent of patients in both groups were sensitized to dust-mite allergen. After 6 months, mite allergen levels in mattress dust were significantly lower in the active treatment group, geometric mean 0.58 vs 1.71 μg/g. However, the reduction in allergen levels was no longer significant after 12 months: 1.05 vs 1.64 ➤➤

μg/g, respectively.

After 6 months, both groups showed significant improvement in peak expiratory flow rates. With adjustment for differences in baseline characteristics, the difference in means for peak expiratory flow were not significantly different. In both groups, about 17% of patients were able to stop using inhaled corticosteroids. Mean reduction in steroid dose was not significantly different between groups, for all patients or for those with mite sensitization.

Used without other mite-control strategies, allergen-impermeable bed covers are not an effective clinical intervention for adult patients with asthma. Peak expiratory flow rates and corticosteroid use are not significantly influenced by the use of impermeable bed covers, even for patients with high mite-specific IgE levels and high exposure to mite allergen.

(next colum)

*Woodcock A, Forster L, Matthews E, et al, and the Medical Research Council General Practice Research Framework: Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma.*
**N Engl J Med** 349:225-236, 2003. ♦♦

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PATIENTS with allergic rhinitis are frequently advised to use allergen-impermeable bedding covers to reduce dust mite exposure, but the effectiveness of this intervention is unclear. The effects of impermeable bedding covers on signs and symptoms of allergic rhinitis were evaluated in a multicenter trial.

Two hundred seventy-nine children and adults with allergic rhinitis were randomized in double-blind fashion to receive impermeable or nonimpermeable covers for their mattress, pillow, and duvet or blanket. All patients had confirmed sensitization to dust mite; both groups were educated regarding general allergen-avoidance measures. Score on a rhinitis-specific visual analog scale was the main outcome of interest. Secondary outcomes included daily symptom score, results of nasal allergen provocation testing, and allergen levels in dust samples.

After 1 year, allergen levels in mattress dust samples were significantly lower for patients who used impermeable bedding covers. Allergen levels were reduced by about 70% in the impermeable-cover group, compared with a nonsignificant reduction of less than 20% in the control group. However, none of the clinical outcomes were significantly different between groups, both of which had significant reductions on the rhinitis visual analog scale.

Impermeable bedding covers do not appear to be an effective strategy for allergy control in patients with allergic rhinitis. Even though these covers reduce exposure to dust mite allergen, they do not affect rhinitis symptoms or other clinical outcomes.

**COMMENT:** *These two papers from the same issue of* The New England Journal of Medicine *have received widespread attention from the lay media, often with the wrong interpretation. Taken together, these studies show that mite-proof casings on pillows, mattress, and quilt/duvet, as a* single intervention*: (a) modestly reduce allergen exposure in the bed, but (b) do not significantly improve clinical outcomes in asthma or allergic rhinitis. Lest anyone suggest that casings are useless, a better interpretation is that, in the absence of other environmental protections (removal of carpet, pets, smoke, etc), casings alone cannot ensure good outcomes.*
*R. J. M.*
*Terreehorst I, Hak E, Oosting AJ, et al: Evaluation of impermeable covers for bedding in patients with allergic rhinitis.* **N Engl J Med** 349:237-246, 2003. ♦♦

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INFANTS who are genetically predisposed to allergy develop symptoms of atopic disease in response to various triggering factors. Exposure to house dust mite may be a particularly important risk factor for later development of asthma. Avoiding cow's milk appears to protect against food allergies and eczema in high-risk infants. A previous report suggested that measures to reduce exposure to allergens--including both food allergens and dust mite--reduce the risk of allergic disorders and sensitization through age 4. The long-term effects of allergen avoidance for genetically at-risk infants were evaluated when the children were 8 years old.

In 1990, a birth cohort of 120 infants at high risk of developing atopic disease were randomized to receive allergen avoidance measures, beginning at birth; or standard health care advice. In the prophylactic group, infants were either breast-fed with the mother on a low-allergen diet or received extensively hydrolyzed formula, while an acaricide and mattress covers were used to reduce dust mite levels. Final outcomes were assessed when the children were 8 years old, including a symptom questionnaire, skin prick testing, spirometry, and bronchial challenge testing.

Rates of current wheezing, the main study outcome, were 13.8% in the prophylactic group vs 27.4% in the control group. Avoidance measures during infancy were also associated with lower rates of nocturnal cough, 13.8% vs 32.3%. Defined as sensitization to one or more tested allergens, the atopy rate was 20.0% in the avoidance group vs 46.8% in the control group. Rates of sensitization to house dust mite were 10.9% vs 30.7%, respectively. With adjustment for potential confounders, the odds ratio for current wheezing for children who received allergen avoidance measures during infancy was 0.26.

For infants at high genetic risk of atopy, allergen avoidance during the first year of life seems to offer long-term protection against the development of asthma and other allergic diseases. These protective effects persist even many years after discontinuation of allergen avoidance. Early allergen avoidance reduces rates of childhood wheezing and dust mite sensitization, and may prevent asthma from developing in some children.

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**COMMENT:** *The initial hypothesis of this study was that allergen avoidance in infancy for genetically at-risk infants would reduce asthma and atopy and that the benefit would continue beyond the period of avoidance. Data from this report confirmed the second part of the hypothesis, showing benefit 7 years after discontinuation of avoidance measures. The study design did not permit discrimination between avoidance of food or dust mite allergen, or a combined effect.*
*E. J. B.*
*Arshad SH, Bateman B, Matthews SM: Primary prevention of asthma and atopy during childhood by allergen avoidance in infancy: a randomised controlled study.* **Thorax** 58:489-493, 2003. ♦♦

## Study Finds High Rate of Smoking among ED Patients with Acute Asthma

GIVEN the airway irritant effect of cigarette smoke and its links to respiratory disease, it would seem that patients with asthma should avoid smoking. However, clinical observations suggest that many patients seen in the emergency department (ED) for acute asthma attacks are current smokers. The prevalence of current smoking among adult patients with acute asthma seen in the ED was assessed.

The analysis included data on 1,847 patients, aged 18 to 54 years, seen for acute asthma at 64 North American EDs. In response to a structured interview, 35% of patients reported that they were current smokers, with a median smoking history of 10 pack-years. Another 23% were former smokers while 42% had never smoked. Asthma patients in their thirties had the highest rate of current smoking. Other factors independently associated with current smoking were white race, lower education, lower income, lack of private insurance, no recent history of inhaled steroid use, and no history of systemic steroid use. Of the current smokers, one-half acknowledged that smoking made their asthma symptoms worse. However, only 4% ascribed their current asthma attack to smoking.

More than one-third of adult patients seen in the ED for acute asthma attacks are current smokers. Certain factors are associated with an increased rate of smoking among asthma patients, including low income, low education, and lack of insurance. The ED may be an important setting for efforts to intervene in the problem of smoking among asthma patients.

**COMMENT:** *The fact that 35% of patients seen in emergency departments for acute asthma are current smokers is astounding. Less surprising is the association of smoking with lower household income and lack of insurance. Considering that this study included more than 1,800 patients at 64 sites in the United States and Canada, these observations are not unique to a few high-risk locations. While there is no proof that tobacco use causes ED visits, smoking is clearly bad for asthma, and this area deserves more of our attention.*
*S. A. T.*
*Silverman RA, Boudreaux ED, Woodruff PG, et al, on behalf of the Multicenter Airway Research Collaboration Investigators: Cigarette smoking among asthmatic adults presenting to 64 emergency departments.* **Chest** 123:1472-1479, 2003. ♦♦

## Cockroach Allergen Is Present in Suburban Homes Too

IN inner-city dwellings, cockroach allergen is highly prevalent and exposure is associated with allergic sensitization to cockroach. Few studies have looked at the prevalence of cockroach allergen and sensitization in other settings. Cockroach allergen exposure and sensitization were studied in children from middle-class homes.

The cross-sectional study included 339 school-age children recruited from three suburban and one urban pediatric practice in the Baltimore area. All children underwent skin testing for cockroach and other common allergens, and dust samples from their homes were analyzed for the same allergens. About one-half of the children were white, and more than half of households had an annual income of over $50,000. Approximately three-fourths of study homes were located in a suburban or rural area.

Forty-one percent of homes studied, and thirty percent of the suburban/rural homes, had kitchen Bla g 1 levels greater than 1 U/g in samples of kitchen dust. On inspection, only 5% of suburban/rural homes had evidence of cockroach infestation on inspection. Twenty-one percent of children from suburban/rural homes were sensitized to cockroach, compared with 35% of children from urban homes. A kitchen Bla g 1 level greater than 1 U/g was an independent risk factor for cockroach sensitization among suburban/urban children, as well as in the overall study sample--odds ratios 2.37 and 2.29, respectively. Other indoor allergens were also detected at significant levels, including dog, cat, and mite allergen. Exposure to dust mite did not affect the risk of sensitization to cockroach.

Exposure and sensitization to cockroach allergen are common among children from middle-class, suburban homes. A high level of cockroach allergen in the kitchen is a significant risk factor for cockroach sensitization. In this study, most homes with detectable cockroach allergen do not have apparent cockroach infestation.

**COMMENT:** *Cockroach allergen (Bla g 1) is prevalent in inner-city residences and has been associated with increased asthma. The group from Johns Hopkins reports significant cockroach allergen present in suburban middle-class homes as well. A remarkable number of households (41%) had Bla g 1 levels greater than 1 U/g, which is considered a significant risk factor for cockroach sensitization. Most of the cockroach allergen was found in kitchens. Measurements of other allergens found the highest levels of dog and cat dander in television rooms, although almost as much cat dander was found in bedrooms. The authors suggest that these homes may have occult cockroach infestations or the allergen may be tracked into the homes. Either* ➤➤

*way, indoor allergens continue to cause problems for children with asthma.*
*S. M. F.*
*Matsui EC, Wood RA, Rand C, et al: Cockroach allergen exposure and sensitization in suburban middle-class children with asthma.*
**J Allergy Clin Immunol** 112:87-92, 2003. ♦♦

## Study Looks at Laryngeal Edema Risk in Patients with Hereditary Angioedema

PATIENTS with C1 esterase inhibitor deficiency leading to hereditary angioedema are at risk of death from asphyxiation caused by laryngeal edema. Recurrent attacks of edema in these patients may occur as skin swellings or attacks of abdominal pain, in addition to episodes of upper airway obstruction. A large series of patients with larygneal edema caused by hereditary angioedema is reviewed.

The study included 123 patients with hereditary angioedema caused by C1 esterase inhibitor deficiency, seen between 1973 and 2001. Of these, 61 patients had a total of 596 episodes of laryngeal edema, with a range of 1 to 200 episodes per patient. Mean age at first episode of laryngeal edema was 26 years; 80% of laryngeal attacks occurred between 11 and 45 years of age. However, 15 of 19 patients aged 60 or older had episodes of laryngeal edema.

Whereas most patients had too many attacks of skin swelling and abdominal pain to count precisely, they were usually able to indicate the exact number of episodes of laryngeal edema. Approximate proportions of attacks were 70 episodes of skin swelling and 54 abdominal attacks for each episode of laryngeal edema. Only 4% of episodes of laryngeal edema occurred after direct or indirect local trauma; dental surgery and general anesthesia were among the precipitating factors.

Mean time from symptom onset to maximal laryngeal edema was about 8 hours. Laryngeal edema resolved without treatment in 342 episodes, while 208 were successfully treated using C1 esterase inhibitor concentrate. Of 32 patients started on danazole treatment to prevent laryngeal edema, 6 went on to have further laryngeal attacks. One child died of asphyxiation within 20 minutes after the onset of laryngeal edema.

About half of patients with hereditary angioedema caused by C1 esterase inhibitor deficiency will experience episodes of laryngeal edema. Such attacks may occur at any age, but the risk is highest in young adults. In adult patients, there is usually enough time after symptom onset to permit emergency treatment. These patients and their families need information on the warning signs and appropriate response to episodes of laryngeal edema.

**COMMENT:** *These interesting observations from Germany provide further insights into the natural history of angioedema. In the great majority of cases, laryngeal edema occurs in younger patients. Interestingly, the mean time to development of laryngeal edema from the onset of symptoms was 8 hours. Clearly the message for young patients is early detection to avoid asphyxiation!*
*A. M.*
*Bork K, Hardt J, Shickentanz K-H: Clinical studies of sudden upper airway obstruction in patients with hereditary angioedema due to C1 esterase inhibitor deficiency.*
**Arch Intern Med** 163:1229-1235, 2003. ♦♦

## Airway Obstruction Is Found in Most Cases of Fatal Asthma

ALTHOUGH not present in all cases, airway "plugging" with mucus exudates is thought to be a key pathologic feature of the lungs and airways of patients who die of asthma. This pathologic study examined the relative importance of luminal obstruction vs airway narrowing in fatal asthma.

The study included 275 airways from 93 patients who died of asthma in Auckland, New Zealand. Age at death ranged from 10 to 49 years; 59 patients were white and 34 Polynesian. Airway narrowing and luminal content were quantified in each airway, and in a sample of 28 airways from patients who died suddenly of nonpulmonary causes.

Although the percentage of luminal occlusion ranged from 4% to 100% in the airways from asthma patients, just 5 airways were less than 20% occluded. Luminal occlusion, occlusion by mucus, and occlusion by cells were all significantly greater in the asthmatic patients than controls. Older patients and those with larger airways had more pronounced airway narrowing. Airways with greater luminal content had a higher proportion of cells, with cells accounting for a higher proportion of small-airway exudates. Younger patients had more luminal mucus than older patients, and Polynesian patients had more than whites.

The airways of most patients who die of asthma show luminal obstruction by an exudate consisting of mucus and cells. Airway plugging appears to be an important contributor to fatal asthma in children and adults, whereas "dry airways" are likely a rare finding.

**COMMENT:** *These authors present a morphologic analysis of the nature of airway narrowing in fatal asthma among a large number of subjects in New Zealand. Substantial plugging occurred in the vast majority of asthma patients and was particularly striking in larger airways and in older patients. In brief, as the accompanying editorial points out, the outstanding pathologic feature of the asthmatic lung lies in the failure of clearance of bronchial secretions.*
*E. J. B.*
*Kuyper LM, Paré PD, Hogg JC, et al: Characterization of airway plugging in fatal asthma.*
**Am J Med** 115:6-11, 2003. ♦♦

## Lactobacillus Treatment in Infancy Reduces Atopic Eczema Risk Through Age 4

IN a previous randomized trial, perinatal administration of the probiotic *Lactobacillus rhamnosus* strain GG significantly reduced the risk of atopic eczema in high-risk infants through the first 2 years of life. Children from this study were followed up to age 4 to assess the persistence of the protective effect of probiotic treatment.

Of 132 children invited, 107 participated in the follow-up study at age 4 years. Questionnaire and clinical examination focused on the presence of atopic eczema, defined as itchy eczematous lesions with a typical location and relapsing or chronic course. Allergic rhinitis and asthma were assessed as well.

At age 4 years, atopic eczema was diagnosed in 26% of children receiving probiotic treatment with lactobacillus, compared with 46% receiving placebo. Risk of allergic rhinitis and asthma was not significantly different between groups. However, as a marker of bronchial inflammation, exhaled nitric oxide concentration was lower in the lactobacillus-treated group. Rates of positive skin-prick testing were also similar between groups.

Perinatal treatment with probiotic lactobacillus reduces the risk of atopic eczema through age 4 in high-risk children. The finding of higher exhaled nitric oxide in the placebo group raises the possibility that these children may have higher rates of underdiagnosed or subclinical respiratory allergic disease. Further study of probiotic treatment to prevent allergic disease is needed.

**COMMENT:** *Perinatal administration of the probiotic* L. rhamnosus *strain GG has been shown to reduce the incidence of atopic eczema in at-risk children during the first 2 years of life. (See* AllergyWatch *July/Aug 2001, p. 1.) This follow-up study suggests that the preventive effect of lactobacillus GG on atopic eczema extends beyond infancy.*
*E. J. B.*

*Kalliomäki M, Salminen S, Poussa T, et al: Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial.*
**Lancet** 361:1869-1871, 2003. ♦♦

## Do Inhaled Corticosteroids Affect Rate of $FEV_1$ Decline in COPD?

DEBATE continues over the effectiveness of inhaled corticosteroids for COPD. Current guidelines recommend inhaled corticosteroids for certain groups of patients with chronic obstructive pulmonary disease (COPD): symptomatic patients with a confirmed spirometric response to inhaled corticosteroids or those with moderate to severe COPD and repeated exacerbations requiring antibiotic or systemic corticosteroid therapy. A meta-analysis was performed to assess the long-term impact of inhaled corticosteroid therapy on the rate of $FEV_1$ decline in COPD patients.

The analysis included six randomized, placebo-controlled trials of inhaled corticosteroids for patients with COPD in which the rate of $FEV_1$ decline was a primary outcome measure. The studies included a total of 3,571 patients with follow-up periods of 24 to 54 months. The estimated difference in the rate of $FEV_1$ decline between placebo and inhaled corticosteroid therapy was nonsignificant: -5.0 mL/y (95% confidence interval -11.2 to 1.2 mL/y). Studies using higher doses of inhaled corticosteroid yielded greater effects on $FEV_1$.

Meta-analysis does not support the effectiveness of inhaled corticosteroids in slowing the rate of decline in $FEV_1$ among patients with COPD. The findings support current recommendations limiting inhaled corticosteroid therapy to specific groups of COPD patients; baseline $FEV_1$ does not appear to be an appropriate selection criterion.

**COMMENT:** *One more meta-analysis does not answer the question of the role of high-dose inhaled corticosteroids in patients with a major component of COPD. Two points need to be kept in mind when reviewing the literature on this topic. First, $FEV_1$ may not be nearly as important in the management of COPD as maximizing quality of life and minimizing exacerbations. Second, studies included in this and similar meta-analyses purposely eliminate subjects with any suggestions or possibility of asthma, and these are the very patients we see: those with COPD and some asthma. Therapeutic trials remain a valuable approach in individual patient management, despite the call for evidence-based medicine.*
*D. K. L.*

*Highland KB, Strange C, Heffner JE: Long-term effects of inhaled corticosteroids on $FEV_1$ in patients with chronic obstructive pulmonary disease: a meta-analysis.*
**Ann Intern Med** 138:969-973, 2003. ♦♦

## Recurrent vs Insidious Chronic Bird Fancier's Lung: Diagnostic Findings

PATIENTS who become hypersensitive to avian antigens may develop bird fancier's lung (BFL). The acute form of BFL is easily recognized. In contrast, chronic BFL may occur as recurrent, acute episodes or as slowly progressive respiratory disease with no acute episodes. The clinical and diagnostic findings of these recurrent and insidious forms of chronic BFL are reviewed.

The retrospective study included 32 patients with chronic BFL seen at a Japanese university hospital from 1992 to 2001. Fifteen patients were classified as having recurrent BFL while 17 had the insidious subtype. All clinical and diagnostic data were reviewed, including antibody measurements and chest imaging studies.

Mean age was 57 years for patients with recurrent BFL vs 64 years for those with insidious BFL. Most patients with recurrent BFL were pigeon breeders. In contrast, most patients with insidious BFL raised budgerigars, while the rest had only indirect con- ➤➤

tact with pigeons.

Eighty-seven percent of patients with recurrent BFL had specific antibodies against extracts of pigeon or budgerigar droppings, compared with 35% of those with insidious BFL. In both groups, nearly all patients were positive for antigen-induced lymphocyte proliferation. Pulmonary function test results were similar between groups, and both showed frequent involvement of the upper lung field on imaging studies. In all patients with insidious BFL, the diagnosis was established by laboratory-controlled inhalation testing.

The insidious form of chronic BFL poses a difficult diagnostic challenge. Because of the need to eliminate bird exposure in patients with BFL, it is essential to distinguish this condition from idiopathic pulmonary fibrosis. Recognition of insidious BFL requires a careful history and laboratory tests, including testing for antigen-induced lymphocyte proliferation and controlled inhalation challenges.

**COMMENT:** *A thorough environmental history is one of the distinguishing features of evaluation by an allergist/immunologist. The lack of "significant" bird exposure and acute respiratory episodes has previously led me to the false conclusion that hypersensitivity pneumonitis was not the cause of my patient's symptoms. This report shows that the serum precipitins, a test clinicians use to support the diagnosis of hypersensitivity pneumonitis, may be negative in up to two-thirds of affected patients with low-level exposure. We need to continue taking a thorough environmental history and remember that low-level, chronic exposure is a concern.*
*D. K. L.*

*Ohtani Y, Saiki S, Sumi Y, et al: Clinical features of recurrent and insidious chronic bird fancier's lung.*
**Ann Allergy Asthma Immunol** 90:604-610, 2003. ♦♦

## Hyperpolarized Helium-3 MRI Shows Postchallenge Ventilation Defects in Asthma Patients

EFFORTS to visualize intrapulmonary gas distribution in asthma patients have been hindered by the lack of an appropriate gaseous contrast agent. New MRI contrast agents such as xenon-129 and helium-3 provide a new approach to imaging lung ventilation without exposure to ionizing radiation. Hyperpolarized helium-3 (HHe3) MRI was evaluated for lung imaging in patients with asthma.

Asthma patients and healthy controls underwent chest MRI immediately after inhaling HHe3 gas. Baseline HHe3 MRI scans were performed in 19 asthma patients with $FEV_1$ values of 36% to 130% of predicted. After methacholine challenge or exercise,ventilation defects appeared as areas of lung with no or dramatically reduced HHe3 signal. The number of such defects was inversely correlated with the patients' $FEV_1$% of predicted value, r = 0.68. Patients with more severe disease tended to have a greater number and extent of lesions.

Three asthma patients underwent HHe3 MRI scanning before and after methacholine challenge testing. All showed new ventilation defects of varying size after receiving methacholine. In 6 patients with exercise-induced bronchospasm scanned after an exercise challenge, ventilation defects increased as $FEV_1$ decreased. With both methacholine and exercise challenge, defects increased significantly in number and size.

Performing MRI with HHe3 may provide a novel approach to imaging air distribution within the lung. In patients with asthma, these scans show increased ventilation defects after methacholine or exercise challenge, and may be useful in monitoring response to treatment. Hyperpolarized helium-3 is an inert gas that is nonradioactive and has no anesthetic activity; technical difficulties in producing and transporting the HHe3 gas remain to be overcome.

**COMMENT:** *Safe imaging of gas distribution in the lungs would be a very helpful diagnostic tool in asthma. I can think of many patients who have shortness of breath in the emergency department or the office, but in whom asthma is not certain. This paper shows remarkable ventilation images using MRI in subjects inhaling polarized helium-3, an inert gas that is not radioactive. The technique appears to safely provide vivid images of asthmatic bronchial obstruction. It is surprising how nonuniform the obstructions are, even in acute exercise-induced asthma.*
*R. J. M.*

*Samee S, Altes T, Powers P, et al: Imaging the lungs in asthmatic patients by using hyperpolarized helium-3 magnetic resonance: assessment of response to methacholine and exercise challenge.*
**J Allergy Clin Immunol** 111:1205-1211, 2003. ♦♦

## Nasal Air Samplers Show Lesser Reduction in Pet Allergen with Air Filter Use

EVEN though they are sensitized to cat or dog, many patients with asthma refuse to get rid of their pet. Air filtration units with a high-efficiency particulate arrest filter can greatly reduce pet allergen levels in the home, but previous trials have found no clinical benefit. Nasal air samplers were used to assess the effects of home air filtration units on personal exposure to cat allergen.

Five homes with cats were studied on 4 separate days under four conditions: with the cat present or absent and with a home air cleaner switched on or off. The median size of the study rooms was 54 $m^3$; all tests were performed with doors and windows closed. Nasal air samples were collected at baseline and at frequent intervals during 3 consecutive hours. A HALOgen assay was used to detect cat allergen-bearing particles and an enzyme-linked immunosorbent assay to measure Fel d 1 concentrations.

On days when the cat was in the room, using the air cleaner significantly reduced the level of inhaled Fel d 1. Halo counts decreased from 29.3 at baseline to ➤➤

11.8 at 1 hour, 10.0 at 2 hours, and 14.1 at 3 hours when the air cleaner was on, compared to no change when it was off. When the cat was not present, having the air cleaner on reduced allergen level marginally, but not significantly.

In rooms where cats are present, air filtration units can significantly reduce individual exposure to inhaled cat allergen. However, the extent of allergen reduction observed in this study, using nasal air samplers, is much less than that reported in previous studies using standard air samplers. The difference shown by nasal air samplers may reflect the wearer's close proximity to furniture or other reservoirs of pet allergen.

**COMMENT:** *When sensitization to cat allergen occurs in a symptomatic patient who lives with a cat, it is attractive to offer an alternative other than removing the pet from the home. Using a Honeywell air cleaner, this study showed a significant reduction in the amount of cat allergen reaching the patient's nose while the cat was in the room, although there was less clear benefit when the cat was out of the room. This treatment is clearly inferior to the undetectable levels of allergen achieved after removing the cat from the home, although it helps legitimize the expense of the air filters when the animal's presence is not negotiable.*
*S. A. T.*
*Gore RB, Bishop S, Durrell B, et al: Air filtration units in homes with cats: can they reduce personal exposure to cat allergen?* **Clin Exp Allergy** 33:765-769, 2003. ♦♦

## Low-Dose Budesonide/ Formoterol Performs Well in Mild to Moderate Asthma

FOR patients with moderate to severe asthma, a budesonide/formorterol combination (160/4.5 μg 2 inhalations bid) provides benefits similar to equivalent doses of the two drugs given via separate inhalers. A low-dose budesonide/formoterol combination (80/4.5 μg bid) was evaluated for safety and efficacy in patients with mild to moderate asthma.

The study included 467 patients with mild to moderate asthma, mean $FEV_1$ 82% predicted, that was not completely controlled on low-dose inhaled corticosteroid therapy. A 2-week run-in period consisted of treatment with budesonide 200 μg bid. They were then randomized to receive either the low-dose budesonide/formoterol combination or to have their budesonide dose increased to 200 μg bid.

Mean morning peak expiratory flow increased by 16.5 L/min with the budesonide/formoterol combination compared with 7.3 L/min with the higher dose of budesonide. The combination regimen also produced a greater increase in evening peak expiratory flow, symptom-free days, and asthma-control days. Risk of asthma exacerbations was reduced by about one-fourth in patients receiving the budesonide/formoterol combination. There was no significant difference in adverse events.

For patients with mild to moderate asthma, a combination of low-dose budesonide/formoterol provides better disease control than an increased dose of inhaled corticosteroid. As in more severe asthma, adding a long-acting $\beta_2$-agonist is superior to increasing the dose of inhaled corticosteroid for patients with symptomatic asthma.

**COMMENT:** *The merits of adding a long-acting inhaled β-adrenergic agonist to an inhaled steroid are well known. The inconvenience of administering multiple actuations of multiple inhalers has been successfully overcome, and the combined administration of fluticasone propionate and salmeterol in the product Advair has gained widespread acceptance in the United States and Europe. The combination of budesonide and formoterol in the Symbicort Turbuhaler is currently available in Europe, and FDA approval is being sought in the United States. This study focuses on mild-moderate asthma, and specifically addresses the effects of using a lower dose of budesonide in the combined product, compared to a higher dose of budesonide alone. As is the case with more severe asthma, the combined product was superior to the higher-dose inhaled corticosteroid alone.*
*S. A. T.*
*Lalloo UG, Malolepszy J, Kozma D, et al: Budesonide and formoterol in a single inhaler improves asthma control compared with increasing the dose of corticosteroid in adults with mild-to-moderate asthma.*
**Chest** 123:1480-1487, 2003. ♦♦

## Women Farmers Are Protected Against Pet- and Pollen-Related Airway Symptoms

PREVIOUS reports have suggested that children who grow up on farms are at lower risk of allergic and respiratory symptoms, perhaps via early childhood exposure to endotoxin. Farming has been linked to an increased risk of lower airway symptoms, including organic toxic dust syndrome. However, the effects of farming on upper airway symptoms (UAS) remain unclear: although farmers commonly experience nasal irritation, their rate of nasal allergy may be lower than in the general population. Rates of UAS induced by common allergens were compared for farmers vs nonfarmers.

The population-based study included 198 female farmers in one area of Finland, mainly dairy farmers; 50 women who lived on a farm but did not perform farm work; and 218 nonfarmers who did not live on a farm. All subjects completed a symptom questionnaire and underwent skin-prick testing to common allergens, including agricultural antigens. Rates of upper and lower airway symptoms were assessed, including adjustment for living on a farm as a child.

The women who worked as farmers had lower rates of UAS caused by pollen and pet antigens. However, 28% had UAS associated with farm work. Farmers had a higher rate of organic toxic dust syndromes and were somewhat more likely to use asthma medications. All airway symptoms were more frequent among sub- ➤➤

ject with positive skin test results. The risk of pollen- and pet-induced UAS decreased as the intensity and duration of animal husbandry increased, in dose-dependent fashion. The protective effect against pet-related symptoms was stronger in women who had grown up on a farm.

Female farmers are at reduced risk of pet- and pollen-induced UAS, which appears to be related to animal husbandry. However, the study also suggests that farmers are an increased risk of UAS induced by farming activities. The mechanisms of farming's protective effect against UAS induced by common allergens remain unclear, but the results suggest that the human immune system may have some flexibility in adulthood as well as childhood.

**COMMENT:** *The hygiene hypothesis for susceptibility to or protection from allergic/asthmatic diseases is predicated upon the early childhood programming of the Th1/Th2 balance away from an atopic slant. However, in this study of female farm workers and dwellers, adult exposure to the farming environment appears to protect against pollen- and pet-induced UAS. However, the farm environment appears to increase the risk of farm-antigen-associated UAS, possibly by including such ailments as hypersensitivity pneumonitis. This is an interesting article that extends the thinking about the hygiene hypothesis paradigm to suggest an impact on prophylactic effects of environment on adult immune systems as well.*
*G. D. M.*
*Koskela HO, Iivanainen KK, Remes ST, Pekkanen J: Pet- and pollen-induced upper airway symptoms in farmers and in nonfarmers.*
**Eur Respir J** 22:135-140, 2003. ♦♦

## Study Supports Safety of Long-Term Intranasal Budesonide for Children with Perennial Rhinitis

TOPICAL glucocorticosteroids are an effective treatment for perennial allergic rhinitis. However, there are concerns about the potential for adverse effects of long-term nasal glucocorticostercoid therapy in children. The long-term effects of intranasal budesonide on growth and other safety outcomes in children were assessed.

The open study included 78 children receiving intranasal budesonide, 200 μg twice daily via pressurized metered-dose inhaler, for symptomatic perennial rhinitis. The children ranged from 5 to 15 years old and had had symptoms for a mean of 4 years. Through 2 years of treatment, safety outcomes were regularly monitored, including growth, bone age, adrenal function, and ophthalmologic and rhinoscopic findings.

From baseline through the first year of treatment, the children's mean height increased from 150 to 155 cm. Growth did not differ significantly from that expected on standard growth charts. Bone age was also similar to reference standards, and there was no change in morning plasma cortisol and 24-hour urinary cortisol. Common adverse events included nasal dryness, blood-tinged secretions, and headache, but these effects were generally mild and transient.

For children with perennial rhinitis, long-term treatment with intranasal budesonide does not appear to adversely affect growth, bone age, or endogenous cortisol status. This treatment effectively reduces rhinitis symptoms with mild local side effects.

**COMMENT:** *While there are short-term data suggesting that intranasal corticosteroids impair growth to a modest degree, this study suggests that children progress normally on their growth charts while receiving intranasal budesonide for up to 2 years. The main weakness of the study is the lack of a placebo control group. This reflects a recent shift in the ethical standards applied to clinical research, and therefore will become commonplace in the future as we attempt to answer important questions regarding drug efficacy and safety.*
*S. A. T.*
*Möller C, Ahlström H, Henricson K-Å, et al: Safety of nasal budesonide in the long-term treatment of children with perennial rhinitis.*
**Clin Exp Allergy** 33:816-822, 2003. ♦♦

## Childhood Asthma Severity Affects Risk of Asthma in Adulthood

ALTHOUGH most reports that childhood asthma has a good prognosis, these studies have generally not considered the severity of asthma symptoms during childhood. The outcomes of patients with childhood asthma as adults were assessed, including the impact of childhood asthma severity.

The analysis included 403 adult subjects, age 42 years, who had been recruited for The Melbourne Epidemiological Study of Childhood Asthma at age 7. They represented 87% of subjects from the original cohort. The overall percentage of subjects with no recent asthma increased steadily during follow-up, from 20% at age 14 to 40% at age 42.

Clinical expression of asthma at age 42 varied depending on the subjects' asthma classification in childhood. The proportion with no recent asthma in adulthood was 66% among subjects with a childhood classification of mild bronchitis and wheezing, 57% for those with childhood bronchitis and wheezing, 29% for those with childhood asthma, and 11% for those with severe asthma. Conversely, proportions of subjects with persistent asthma increased with severity of childhood asthma. Adulthood lung function parameters were significantly reduced for subjects classified as having asthma or severe asthma in childhood.

Most children with persistent asthma will continue to have asthma symptoms and reduced pulmonary function as adults. In contrast, most children with intermittent asthma symptoms associated with respiratory infections will be free of asthma symptoms in adulthood.

**COMMENT:** *This interesting Australian study* ➤➤

*provides more retrospective analysis of the natural history of asthma. Clearly children with persistent asthma are more likely to have persistent asthma in adulthood. Interestingly, the children with mild intermittent asthma appeared to have normal pulmonary function test results in adulthood, without the availability of inhaled corticosteroids in early life.*

*A. M.*
*Horak E, Lannigan A, Roberts M, et al: Longitudinal study of childhood bronchitis with wheezing and asthma: outcome at age 42.*
**BMJ USA** 3:271-272, 2003.

## REVIEWS OF NOTE

**COMMENT:** *This is a useful review to help answer parents' and prospective parents' questions about what they should or should not do to reduce food allergy in their children. The authors divide the approaches into "proactive" (what you should do) and "prohibitionist" (who you should avoid) and provide the evidence or lack of evidence for a variety of measures.*
*D. K. L.*
*Fiocchi A, Martelli A, De Chiara A, et al: Primary dietary prevention of food allergy.*
**Ann Allergy Asthma Immunol** 91:3-13, 2003.

**COMMENT:** *This journal supplement is a report of a symposium held in 2002 in New York City on the subject of food allergy in children. The twelve articles, by as many authors, represent an easily read but comprehensive, up-to-date review of the subject. Particularly interesting are the reviews on GI manifestations by Dr. Sicherer, natural history by Dr. Wood, and daily coping strategies for patients and families by Anne Muñoz-Furlong.*
*J. A. A.*
*Pediatric food allergy.* **Pediatrics** 111:1591-1680, 2003 (supplement).

**COMMENT:** *This is an updated, systematic review of non-biotech anti-inflammatory agents applied to severe asthma. Methotrexate, gold, furosemide, heparin, cyclosporine, and troleandomycin are all reviewed with an emphasis on their utility as steroid-sparing agents.*
*S. A. T.*
*Niven AS, Argyros G: Alternate treatments in asthma.*
**Chest** 123:1254-1265, 2003.

**COMMENT:** *An excellent review of the basis behind the immunomodulatory and anti-inflammatory properties of intravenous immunoglobulin (IVIG).*
*E. J. B.*
*Simon HU, Späth PJ: IVIG--mechanisms of action.*
**Allergy** 58:543-552, 2003.

**COMMENT:** *Environmental issues in asthma remain important but controversial. Several interesting articles have been published recently, including those discussing the hygiene theory (we keep children too clean) and Dr. Ownby's study suggesting that pets in a newborn's home may protect against the development of asthma. This article reviews our present knowledge of "allergic asthma epidemics" and allergic exposures that exacerbate or lead to the development of asthma: eg, environmental tobacco smoke, dust mites, animal dander. In the final analysis, we are left with the imperative to either decrease or eliminate these known risk factors for asthma.*
*A. L. L.*
*Etzel RA: How environmental exposures influence the development and exacerbation of asthma.*
**Pediatrics** 112:233-239, 2003.

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