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AllergyWatch®

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

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

Volume 16, Number 2 March - April 2014

What's the Risk of Death from Food Allergy? Lower Than You Might Think

FOOD allergies are the most common cause of anaphylaxis, which is potentially fatal. However, the true risk of death from anaphylactic reactions to foods is unclear. This information may have important implications for patient management and policy.

A systematic review of the literature from 1946 to 2012 identified 13 studies of various types reporting a total of 240 deaths from food allergy anaphylaxis. The data were pooled for meta-analysis, including estimation of the incidence of fatal food anaphylaxis in the population at risk.

The studies were of mixed quality. There was high heterogeneity in the results, likely reflecting variations in food allergy prevalence and data collection methods. The 240 deaths occurred over an estimated 165 million food-allergic person-years. Assuming a 3% prevalence of food allergy, the estimated incidence of fatal food anaphylaxis was 1.81 per million person-years.

In sensitivity analyses using different food allergy prevalence rates, the incidence of fatal anaphylaxis ranged from 1.35 to 2.71 per million person-years. From age 0 to 19 years, the estimated incidence of food allergy anaphylaxis was higher, 3.25 per million person-years. Rates of death from food allergy were much lower than the age-specific risks of death from any type of accident.

Available data suggest that deaths from anaphylactic reactions to foods are "very rare," the investigators conclude. For most patients, food allergies will have little impact on overall mortality risk. Allergen avoidance and anaphylaxis management strategies are still essential, but the results may offer some perspective and reassurance for patients and families affected by food allergies. ➤➤

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The American College of Allergy, Asthma & Immunology expresses its appreciation to MERCK for its 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
- Pediatric Allergy and Immunology

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COMMENT: *Food allergy fatalities are tragic and horrible events. They motivate us to emphasize to our patients and/or their parents the importance of strict avoidance and anaphylaxis action plans. In fact, in the past few years, as the prevalence of food allergy has increased, the standard of care has gradually evolved toward prescribing at least two epinephrine auto-injectors for every patient, in case one injection is not sufficient to prevent a poor outcome. Are we contributing to a somewhat distorted perspective on the true risk of death from this disease? This European review concludes that the risk of death from ingesting food is less than 1:100,000. Stated another way, this risk is much lower than the risk of dying in a car accident and slightly lower than the risk of being murdered, but still higher than the risk of being fatally struck by lightning.*
S.A.T.

Umasunthar T, Leonardi-Bee J, Hodes M, et al: Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and meta-analysis.
Clin Exp Allergy. 2013;43:1333-1341. ♦♦

Anti-IL-13 Blocks Late Response to Inhaled Allergen Challenge

THE T-helper 2 (Th2) cytokine interleukin-13 (IL-13) is thought to be involved in regulating inflammatory responses to allergen, which suggests a possible therapeutic role of IL-13 blockade. In a previous study, the anti-IL-13 monoclonal antibody lebrikizumab improved prebronchodilator FEV_1 in patients with uncontrolled, moderate to severe asthma. This phase 2 study evaluated the effects of lebrikizumab on response to allergen challenge in mild asthma.

Twenty-nine patients with mild allergic asthma underwent allergen and methacholine challenge, followed by 12 weeks of treatment with lebrikizumab, 5 mg/kg sc every 4 weeks, or placebo. At 13 weeks, allergen and methacholine challenge were repeated. The main outcome of interest was the late asthmatic response (LAR), defined as area under the curve of FEV_1 from 2 to 8 hours after allergen challenge.

At 13 weeks, patients in the lebrikizumab group had a 48% reduction in LAR compared to the placebo group, although the difference was not statistically significant. In exploratory analyses, lebrikizumab appeared to have larger effects on LAR in patients with higher baseline levels of peripheral blood eosinophils, serum IgE, or periostin. Lebrikizumab showed significant effects on systemic markers of Th2 inflammation, including about a one-fourth reduction in serum IgE chemokine ligands 13 and 17. Lebrikizumab treatment was well tolerated, with no serious adverse events.

Lebrikizumab may reduce the LAR response to allergen challenge in patients with mild asthma. Certain markers of increased Th2 airway inflammation may be associated with a greater LAR effect of anti-IL-13 therapy. The authors discuss the implications for further studies of lebrikizumab as a novel therapeutic agent for asthma.

COMMENT: *Developing therapeutic agents that target the Th2 cytokine pathway has so far been a laborious process that has not resulted in approved medications for asthma. Blocking the effects of IL-13 in asthmatic subjects is currently being explored. In this study, there was an impressive reduction in the allergen-induced fall in FEV_1 from 5 to 8 hours postchallenge. These results are comparable to those of previous anti-IgE allergen challenge studies, and superior to the effect of anti-IL-5 on late allergen challenge. Whether the efficacy of this therapeutic approach is superior to currently available treatments for chronic asthma is unknown, although targeting IL-13 does appear promising. Stay tuned!*
S.A.T.

Scheerens H, Arron JR, Zheng Y, et al: The effects of lebrikizumab in patients with mild asthma following whole lung allergen challenge.
Clin Exp Allergy. 2012;44:38-46. ♦♦

Parental Allergy Increases Risk for Both Allergic and Nonallergic Rhinitis

CHILDREN whose parents have asthma or allergic rhinitis (AR) are at increased risk of developing AR. Many children and adults have rhinitis without sensitization, but little is known about the risk factors for this condition. This study evaluated parental allergic disease as a risk factor for AR and nonallergic rhinitis (NAR) in children.

The researchers analyzed data on 2,413 children from a Swedish population-based birth cohort study, including questionnaire responses and measurement of IgE to inhalant allergens. Evidence of allergic disease in parents--including hay fever, asthma, eczema, pollen, and pet allergy--was evaluated for association with AR and NAR in the children at age 8 years. Cluster analysis was performed to assess possible latent phenotypes of heredity that are likely associated with AR and NAR in offspring.

The results showed AR in 13.8% of children at age 8 years and NAR in another 6.4%. Children whose parents had hay fever only were twice as likely to develop AR: odds ratio 2.2. In contrast, asthma or eczema alone did not affect offspring AR risk.

Children whose parents had two or more allergy-related diseases were more likely to develop NAR. On cluster analysis, AR was present in 37.5% of offspring when both parents had hay fever and pollen allergy. The rate of NAR was highest, 11.0%, when one parent had hay fever, pollen allergy, and eczema.

Allergic disease in the parents appears to contribute to the risk of both NAR and AR in children. Maternal and paternal allergy have similar and significant effects. Parental hay fever may be the strongest hereditary risk factor for AR in offspring; risk is even greater when both parents have hay fever or asthma.

COMMENT: *Nonallergic rhinitis is a common and heterogeneous disorder that we evaluate and treat in our practices every day. Yet very little is known about its pathophysiology or natural history. In this large population-based birth cohort study, about 14% of 8-year-olds had AR and 6% had NAR. Interestingly, parental history of allergic rhinitis was a risk factor for both AR and NAR. It is not known whether children with NAR have local nasal IgE, whether their condition will evolve into AR, or whether they will remain symptomatic from their NAR. Nevertheless, the findings help to validate what we see in clinical practice. This may be a circumstance where checking a nasal smear for eosinophils can help direct therapy.*
S.A.T.
Westman M, Kull I, Lind T, et al: The link between parental allergy and offspring allergic and nonallergic rhinitis.
Allergy. 2013;68:1571-1578. ♦♦

Other Indoor Exposures Modify Endotoxin's Effects on Asthma

EXPOSURE to endotoxin may contribute to the development of allergic diseases, but little is known about its effects on asthma morbidity among urban children with established asthma. Certain pollutants may modify the effects of endotoxin on airway inflammatory markers, but it is unknown whether this extends to asthma symptoms or morbidity in "real world" settings.

The investigators made repeated clinical assessments over 1 year in 146 children and adolescents with persistent asthma in Baltimore City. The participants' median age was 11 years; 57% were male and more than 90% were African American. Airborne nicotine, endotoxin, and nitrogen dioxide levels were measured at home visits conducted at the same times as clinical assessments. The effects of pollutant exposures on the association between endotoxin exposure and asthma outcomes were assessed, including stratified and interaction analyses.

The relationship between home endotoxin exposure and asthma outcomes was affected by both air nicotine and nitrogen dioxide levels. For children with no exposure to nicotine at home, higher exposure to endotoxin was associated with fewer acute visits and oral corticosteroid bursts. In contrast, when nicotine was detected at home, endotoxin was associated with higher rates of both outcomes.

Higher endotoxin was associated with more acute care visits for children living in homes with NO_2 levels of less than 20 ppb, but fewer acute visits for children whose homes had higher NO_2 concentrations. There was a similar interaction between endotoxin and NO_2 in terms of asthma symptoms.

For urban children with asthma, associations of home endotoxin exposure with disease morbidity are influenced by levels of indoor nicotine and nitrogen dioxide. Depending on these other exposures, endotoxin can have opposite effects on asthma-related outcomes. The authors discuss the possible implications for developing effective approaches to environmental control for asthmatic children.

COMMENT: *This rigorous evaluation of the indoor effects of inhaled irritants reinforces that multiple components of the air we breathe may have discordant effects. The data are a clear message that there are a lot of "moving parts" that drive airway hyperreactivity. Also see accompanying editorial (Am J Respir Crit Care Med. 2013;188:1181-1183).*
B.E.C.
Matsui EC, Hansel NN, Aloe C, et al: Indoor pollutant exposures modify the effect of airborne endotoxin on asthma in urban children.
Am J Respir Crit Care Med.2013;188:1210-1215. ♦♦

Genotype Doesn't Affect Loss of Response to Salmeterol, But NO Level Does

β_2-AGONISTS play a key role in the management of exercise-induced bronchoconstriction (EIB), but patients may develop tolerance to the bronchoprotective effect. Previous studies have reported Arg16Gly polymorphisms of the β_2-adrenergic receptor that affect receptor downregulation and responses to regular ➤➤

β_2-agonist use. This study evaluated the effects of Arg16Gly polymorphisms on the bronchoprotective effect of salmeterol in EIB.

The prospective cohort study included 26 adults with EIB who were not receiving controller therapy: 12 with the Arg16Arg genotype and 14 with the Gly16Gly genotype. Patients performed exercise challenges before and after 2 weeks of treatment with salmeterol, 50 μg twice daily. The relationship between genotype and loss of bronchoprotection (LOB) with salmeterol was assessed. The effects of baseline functional and inflammatory variables were evaluated as well.

The maximum reduction in FEV_1 on exercise challenge was 27.9% at baseline. 8.1% after the first dose of salmeterol, and 22.8% after salmeterol treatment. There was no significant difference in LOB with salmeterol between the Arg16Arg and Gly16Gly genotype groups.

However, baseline exhaled nitric oxide was significantly related to LOB. Participants with exhaled NO levels greater than 50 ppb had a mean 74% LOB after salmeterol treatment, compared to a 7% gain in bronchoprotective effect for those with exhaled NO less than 25 ppb. Other baseline factors, including FEV_1 and degree of EIB, showed no association.

The Arg16Gly polymorphism of the β_2-adrenergic receptor does not affect LOB to salmeterol in patients with EIB. However, high exhaled NO levels at baseline are associated with marked LOB after 2 weeks on salmeterol. These findings suggest it may be better to avoid long-acting β_2-agonist use in EIB patients with high exhaled NO, until their underlying airway inflammation is better controlled.

COMMENT: *Here are more data to suggest that the Arg16Gly polymorphism does not influence the bronchoprotective effects of regular salmeterol use. However, the results are not clearly applicable to clinical practice, as inhaled corticosteroid was not used concurrently. The unexpected but important observation centers on the loss of bronchoprotective effect in exercise for patients who have high exhaled nitric oxide levels. This finding supports the importance of NO in evaluating patients with EIB.*
B.E.C.
Bonini M, Permaul P, Kulkarni T, et al: Loss of salmeterol bronchoprotection against exercise in relation to ADRB2 Arg16Gly polymorphism and exhaled nitric oxide.
Am J Respir Crit Care Med. 2013;188:1407-1412. ♦♦

Corticosteroid-Resistant Asthma Linked to Microbiome Differences

CLINICAL responses to corticosteroid treatment for asthma vary considerably. Airway microbiome studies suggest that patients with asthma have increased bacterial burden and diversity, and that the composition and diversity of the microbiome may be correlated with bronchial hyperresponsiveness. This study assessed the relationship between airway microbiome and corticosteroid hyperresponsiveness in asthma.

The airway microbiome was analyzed by 16S RNA gene sequencing of bronchoalveolar lavage (BAL) specimens from 39 asthmatic patients and 12 healthy controls. Based on nonresponse to a 1-week prednisone burst, 29 patients were classified as corticosteroid-resistant (CR). Additional studies in asthma patients included stimulation of BAL macrophages with pathogenic and commensal organisms and real-time polymerase chain reaction assays for corticosteroid-regulated gene expression and activation of cellular p38 mitogen-activated protein kinase (MAPK).

At the level of phylum, the specimens from corticosteroid-sensitive (CS) and CR asthma patients did not differ in terms of richness, evenness, diversity, or community composition. However, there were significant differences at the genus level, with 14 patients with CR asthma showing "unique bacterial expansions."

Corticosteroid-resistant asthma specimens preincubated with *Haemophilus parainfluenzae*--a potential pathogen found only in the CR asthma group--resulted in activation of p38 MAPK, increased interleukin-8, expression of mitogen-activated kinase phosphatase 1 mRNA expression, and inhibition of corticosteroid responses. These changes were not observed on stimulation with the commensal organism *Prevotella melaninogenica*. Corticosteroid sensitivity was restored by inhibition of transforming growth factor-β-associated kinase-1, an upstream activator of MAPK.

The results show significant differences in the airway microbiome in about half of patients with CR asthma. In these patients, expanded populations of specific gram-negative bacteria trigger TAK1/MAPK1 activation and corticoid resistance. The study identifies TAK1 activation as a potentially useful new treatment approach in CR asthma.

COMMENT: *The current study expands our knowledge base into the "next universe" of the lower airway. This direction probably started with the observation by Bisgaard et al that positive hypopharyngeal cultures in neonates predict asthma development (N Engl J Med. 2007;357:1487-1495). The data are a major contribution to understanding the programming of airway inflammation and response to therapy. Also see the accompanying editorial (Am J Respir Crit Care Med. 2013;188:1178-1180).*
B.E.C.
Goleva E, Jackson LP, Harris JK, et al: The effects of airway microbiome on corticosteroid responsiveness in asthma.
Am J Respir Crit Care Med. 2013;188:1193-1201. ♦♦

Reactivity to Egg Allergens Differs by Age

NEW molecular techniques such as component-resolved diagnosis may provide useful information on the severity of egg allergy and the likelihood of resolution. So far, few studies have examined differences in reactivity to major egg allergens among children in different age groups.

The researchers investigated 27 children with a convincing history of egg allergy and an egg white-specific ➤➤

IgE level of 0.35 kU_A/L or higher. The children were divided into three age groups: younger than 12 months, 12 to 23 months, and 24 months or older. These age groups were assessed for differences in reactivity toward ovalbumin, ovomucoid, and ovotransferrin on immunoblotting and enzyme-linked immunosorbent assay.

On immunoblotting, all infants younger than 12 months showed IgE reactivity to ovalbumin, but not to the other two proteins. Between 1 and 2 years, all children showed reactivity to ovomucoid as well as ovalbumin, and 3 of 8 had IgE binding to ovotransferrin. At age 2 years and older, all patients had reactivity to ovalbumin, 5 out of 12 to ovomucoid, and 8 out of 12 to ovotransferrin. For both ovalbumin and ovotransferrin, specific IgE binding increased with age.

The results show differing patterns of IgE reactivity to egg allergens for infants and young children during the first few years of life. The study may be relevant to the development of guidelines for management of egg allergy in infants.

COMMENT: *Recently, molecular diagnostic testing encompassing component-resolved diagnosis or epitope mapping has been developed to characterize the presence, severity and probability of resolution of egg allergy. This study demonstrates that IgE reactivity to egg proteins differs with age. Ovalbumin binding is demonstrated by immunoblotting in all children less than 12 months of age, while binding to ovalbumin and ovotransferrin increase with age. Ultimately, component testing may allow allergists to determine the sensitivity, severity, and likelihood of resolution of egg allergy as well as the safety of oral challenge.*
C.C.R.

Kim J, Lee H, Park M-R, et al: Special consideration is required for the component-resolved diagnosis of egg allergy in children.
Ann Allergy Asthma Immunol. 2014;112;53-57. ♦♦

Is Omalizumab Effective for Chronic Intractable Urticaria?

RANDOMIZED trials support the effectiveness of anti-IgE therapy with omalizumab for patients with chronic urticaria. This paper presents a real-world experience with omalizumab for patients with severe, refractory chronic urticaria.

The open-label study included 68 patients with severe urticaria--7-day urticaria activity (UAS-7) score of 30 or higher--with a suboptimal response to previous treatments. The patients were treated at allergy departments in Toronto and Quebec City. The diagnosis was chronic spontaneous urticaria in 61 patients, cold urticaria in 6, and urticarial vasculitis in 1. All received omalizumab at a dosage of 150 mg per month, and were followed for up to 25 months.

For Toronto patients, mean UAS-7 score decreased from 32.2 before omalizumab treatment to 5.7 after the last dose. Complete responses, UAS-7 score of 0, were obtained in 79% of patients; another 18% had improvement but not remission. For the Quebec City patients, mean UAS-7 score decreased from 24.4 to 2.2, while the quantitative medication score decreased from 13.3 to 3.0. All 6 patients with cold urticaria became asymptomatic on omalizumab, with significant improvement on cold stimulation tolerance testing.

This experience shows good outcomes with omalizumab 150 mg in patients with severe chronic urticaria that has not responded to other treatments. Omalizumab is well tolerated and provides lasting symptomatic improvement, with many complete remissions. The authors suggest maintenance dose schedules of 6 to 12 weeks.

COMMENT: *A randomized double-blind study has demonstrated that omalizumab, given at 150 and 300 mg monthly doses, is efficacious for intractable urticaria in patients on high- dose antihistamine. These reports from two Canadian centers using the 150 mg dose document remission rates of 69% to 79% at up to 25 months of follow-up. That includes patients with chronic spontaneous urticaria, cold urticaria, and urticarial vasculitis who were steroid dependent. There were no significant adverse effects. Omalizumab provides safe and effective (though expensive) therapy for steroid-dependent chronic, intractable urticaria, with the prospect of remission.*
C.C.R.

Sussman G, Hébert J, Barron C, et al: Real-life experiences with omalizumab for the treatment of chronic urticaria.
Ann Allergy Asthma Immunol. 2014;112:170-174. ♦♦

Sulfasalazine: A New Option for Chronic Idiopathic Urticaria?

LITTLE is known about possible alternative treatments for chronic idiopathic urticaria (CIU) that does not respond to antihistamines. Sulfasalazine is a potentially effective agent, with approved uses for rheumatoid arthritis and inflammatory bowel disease and a known safety record. The authors report their experience with sulfasalazine for treatment of CIU.

The retrospective analysis included 39 CIU patients treated with sulfasalazine at one allergy center between 2007 and 2012. Eight patients were excluded because of missing data. Of the remaining 31 patients, the median age was 45 years and 61% were women. All were receiving an antihistamine at the time they started sulfasalazine; about two-thirds were taking 3 or more medications for CIU.

Symptom improvement occurred within 3 months after starting sulfasalazine in 83.9% of patients, and 51.6% became symptom-free within 6 months. After tapering sulfasalazine, 35.4% of patients had complete symptom relief. Sulfasalazine treatment failed in 16.1% of patients, and 19.4% developed hematologic abnormalities requiring treatment modification. Two patients had serious adverse events necessitating drug discontinuation: one case of drug-induced leukopenia and one of rhabdomyolysis.

This experience supports the efficacy of sulfasalazine for CIU patients who do not respond to antihista-➤➤

mines. Response rates are good, and some patients remain asymptomatic after drug tapering. Close monitoring for adverse events is essential.

COMMENT: *The treatment of patients with refractory CIU is difficult. In an effort to reduce oral corticosteroid use, alternative medications are often considered. The authors performed a chart review of patients treated with sulfasalazine. Of 39 patients, 83% had symptom improvement within 3 months. More than half became asymptomatic within 6 months of treatment, and over a third remained asymptomatic after sulfasalazine taper. Two patients had severe adverse effects. The study was limited by the absence of a placebo group; safety was comparable to cyclosporine. The authors' recommendations include the need for laboratory monitoring.*
V.H.-T.
Orden RA, Timble H, Saini SS: Efficacy and safety of sulfasalazine in patients with chronic idiopathic urticaria.
Ann Allergy Asthma Immunol. 2014;112:64-70. ♦♦

Encouraging Results with Peanut Oral Immunotherapy

THERE is growing interest in oral immunotherapy for desensitization in children with peanut allergy. A phase 1 trial showed good tolerability. The authors report a randomized, crossover trial of OIT for peanut-allergic children.

The STOP II trial included 85 children, aged 7 to 16 years, with immediate hypersensitivity reactions to peanut and positive results on skin-prick testing and double-blind placebo-controlled food challenge. They were randomly assigned to active OIT with peanut flour, at protein doses of 2 to 800 mg/d; or standard care, ie, peanut avoidance.

Desensitization, defined as negative results on a 1,400 mg peanut challenge, was assessed after 6 months of treatment. After 6 months, controls received OIT. Immunologic responses and quality of life were measured as well.

In OIT group, 62% of children achieved desensitization, compared to none of the control group. Eighty-four percent of children receiving OIT were able to tolerate peanut ingestion of 800 mg/d--about five peanuts. The median increase in peanut threshold after OIT was 1,345 mg: more than 25 times the baseline value.

In the second phase of the study, the desensitization rate after OIT was 54%, with 91% of patients tolerating ingestion of 800 mg/d. Immunologic measures were consistent with desensitization, and quality of life scores were improved. Side effects were generally mild, mainly consisting of gastrointestinal symptoms. Oral pruritus occurred after 6.3% of doses and wheezing after 0.41%. Epinephrine was required after 0.01% of doses.

This OIT regimen induces a high desensitization rate and increase in peanut threshold in peanut-allergic children. Treatment appears safe and well tolerated, and leads to improvements in quality of life. Pending further studies in wider populations, peanut OIT should only be attempted in specialist settings.

COMMENT: *This study adds to the growing body of evidence that systematically investigates OIT for peanut-sensitive individuals. The results are impressive and should not be dismissed. On the other hand, they should not be generalized until important questions are answered. Subject selection, dosing, and establishment of permanent tolerance are but a few questions needed to be answered. Indeed, the authors as well as the accompanying editorial agree that further studies are needed before this treatment is marketable.*
S.F.W.
Anagnostou K, Islam S, King Y, et al: Assessing the efficacy of oral immunotherapy for the desensitisation of peanut allergy in children (STOP II): a phase 2 randomised controlled trial.
Lancet 30 January 2014(Article in Press DOI: 10.1016/S0140-6736(13)62301-6). ♦♦

Oral Immunotherapy for Children with Severe Reactions to Milk

STRICT allergen avoidance cannot eliminate the risk of serious reactions to inadvertent exposure in children with cow's milk allergy. A handful of studies have reported promising results with oral immunotherapy (OIT). A single-center experience with OIT for children with cow's milk allergy is presented.

The authors report on 280 children older than 4 years with IgE-mediated cow's milk allergy. Even high-risk children with a history of anaphylaxis were eligible for milk OIT. The children's median age was 7.5 years; 60% were boys and 64% had an asthma diagnosis.

Carried out in a highly controlled setting, OIT consisted of three rounds of induction 4 weeks apart. Reaction thresholds were determined on the first day, and a tolerated starting dose under the threshold was confirmed on the second and third days. On the fourth day, children received the home treatment, which was continued until the next round of treatment.

The children received a median initial starting dose of 52.5 mg of cow's milk protein. Five failed OIT during the first week, and another 15 were still in treatment. Of the remaining 260 patients, 61.5% tolerated 7,200 mg of cow's milk protein and 85.4% were consuming at least 180 mg per day. Injectable epinephrine was needed in 15.7% of patients and 0.075% of doses. On multivariate analysis, factors associated with tolerating a full dose of cow's milk protein included a starting dose greater than 30 mg, odds ratio (OR) 4.6; no need for epinephrine during induction or home treatment OR 5.2 and 2.6; and absence of nonanaphylactic-type symptoms, OR 15.6.

The authors report good outcomes of an OIT program for children with cow's milk allergy, not excluding high-risk patients. A large majority of children receiving OIT derive protection against accidental exposures to cow's milk. The study identifies several factors associated with achievement of full consumption of cow's milk protein.

COMMENT: *Many studies of OIT have shown protective effects in children with food allergies. This* ➤➤

study looked at a large cohort of children with cow's milk allergy, including many with a history of anaphylaxis--who are often excluded from OIT studies. All patients had positive skin prick test to cow's milk and were older than 4 years. Although 15% required epinephrine treatment for a reaction, the results were promising, with most children being protected against accidental exposure. Even in the most severe group, 21% were able to consume 180 mg of cow's milk protein. The question remains whether the patients develop tolerance once the cow's milk protein is discontinued from the diet.

V.H.-T.

Levy MB, Elizur A, Goldberg MR, et al: Clinical predictors of favorable outcomes in an oral immunotherapy program for IgE-mediated cow's milk allergy.

Ann Allergy Asthma Immunol. 2014;112:58-63. ♦♦

Omalizumab May Facilitate Oral Peanut Desensitization

FOR peanut and other food allergens, effective oral desensitization protocols have been reported. However, there is a risk of potentially severe reactions, perhaps especially in patients with high peanut-specific IgE levels. The authors evaluated the use of omalizumab before and after rapid oral desensitization for peanut allergy.

The study included 13 children, median 10 years, undergoing oral peanut desensitization. The children were considered at high risk for developing significant peanut-induced allergic reactions; median peanut-specific IgE level was 229 kU_A/L and total IgE level 621 kU/L. On initial double-blind placebo-controlled food challenge, all patients reacted to a peanut flour dose of 100 mg or lower.

The children were pretreated with omalizumab, every 2 or 4 weeks for 12 weeks before desensitization; then continued omalizumab throughout the 8-week protocol. All successfully tolerated the 11 doses given during the first day of desensitization--including the maximum 500 mg of peanut flour--with minimal or no rescue therapy.

All but 1 patient reached the 4,000 mg/d maximum maintenance dose of peanut flour in a median of 8 weeks. Omalizumab was stopped at that time; the children continued on the 4,000 mg/d dose of peanut flour. After 10 to 12 additional weeks, all patients tolerated an 8,000 mg peanut flour challenge. Six children had mild or no allergic reactions, 5 had grade 2 reactions, and 2 had grade 3 reactions. All reactions responded to treatment.

Omalizumab may promote successful oral peanut desensitization in children with high-risk peanut allergy. If confirmed in future double-blind, placebo-controlled trials, this anti-IgE therapy approach could help to extend the use of oral desensitization for clinically significant peanut allergy.

COMMENT: *Oral peanut desensitization has been shown to help build tolerance in children at risk for anaphylaxis to peanut protein. Previous studies of oral peanut desensitization report severe reactions in up to 25% of patients. This relatively small study of children with very severe peanut allergy impressively shows that pretreatment with omalizumab before desensitization enabled safer oral challenges. Treated children had fewer and less severe reactions, with sustained tolerance for up to 20 peanuts daily even after discontinuing omalizumab. There are still many unanswered questions: What is the best dose of omalizumab? How long should we pretreat? How long do the patients need to continue daily peanut ingestion? Stay tuned; the authors state that larger, placebo-controlled trials are in the works.*

S.M.F.

Schneider LC, Rachid R, LeBovidge J, et al: A pilot study of omalizumab to facilitate rapid oral desensitization in high-risk peanut-allergic patients.

J Allergy Clin Immunol. 2013;132:1368-1374. ♦♦

Breast-Feeding and Atopic Disease: Too Much of a Good Thing?

THE effects of breast-feeding on the risk of allergic diseases in children remain unclear. Although some studies show a protective effect, others report an increased risk or no association. The relationship between breast-feeding and risk of atopic dermatitis (AD) was assessed in a large population of Korean children.

The study included 10,383 infants and children up to 13 years old living in Seoul in 2008. Parents completed questionnaires regarding current AD and environmental factors. Questions regarding AD were based on International Study of Asthma and Allergies in Childhood diagnostic criteria. Associations were adjusted for age, sex, maternal education, household smoking, moving to a new home within 1 year after birth, and parental history of allergies.

On adjusted analysis, age and maternal education were inversely related to AD risk in the child. For children aged 5 years or younger, risk of AD increased along with duration of breast-feeding: odds ratio 1.21 for children breast-fed for 6 to 12 months and 1.44 for those breast-fed for longer than 12 months, compared to non-breast-fed children.

The association was independent of parental history of atopic diseases. Breast-feeding was unrelated to AD in children older than 5 years.

Prolonged breast-feeding may be associated with an increased risk of AD in young children. The association is independent of potential confounding factors, and is not significant after age 5. The authors note some important limitations of their cross-sectional study.

COMMENT: *A question frequently asked in our office is whether we can make recommendations regarding infants and their risk of atopic disease. Some studies have shown protection against atopy in children who have been breast-fed. However, this study found that prolonged breast-feeding (more than 12 months) was associated with AD in children less than 5 years old. This was true regardless of parental history of* ➤➤

atopy. This study was based on questionnaires in a large number of children up to 13 years old in Korea. Because of this, one limitation was recall bias; it was also not clear whether breast-feeding was partial or exclusive. Further studies are needed to better understand whether we should recommend a specific amount of time for breast-feeding with regard to atopic disease.
V.H.-T.
Hong S, Choi W-J, Kwon H-J, et al: Effect of prolonged breast-feeding on risk of atopic dermatitis in early childhood.
Asthma Allergy Proc 2014;35:66-70. ♦♦

Smoking and Childhood Asthma--Spit Out the Truth

INFORMATION on tobacco exposure is important in managing children with asthma, including assessment of future exacerbation risk. Caregiver reports of secondhand smoke exposure don't always agree with objective measures. This study examined the relationship between caregiver-reported and cotinine-assessed exposure to tobacco smoke among children hospitalized for asthma.

The prospective study included 775 children, aged 1 to 16 years, admitted to a children's hospital for asthma or bronchodilator-responsive wheezing. Caregivers were asked about tobacco exposure at home, in secondary residences, or in cars. In addition, cotinine levels were measured in serum and saliva samples from the children. Associations between tobacco exposure and the children's 1-year readmission rate were assessed.

Six hundred nineteen children had complete information on tobacco exposure. The mean age was 6.43 years; 57% of children were African American and 76% were on Medicaid. Overall 1-year rate of readmission for asthma or wheezing was 17%.

Compared to a reported tobacco exposure rate of 35.1%, measured rates were 56.1% in serum and 76.9% in saliva. Caregiver reports of tobacco exposure were unrelated to readmission risk, but risk was significantly elevated for children with cotinine detected in serum or saliva: adjusted odds ratio 1.59 and 2.35, respectively.

Cotinine was detected in serum from 39.1% and in saliva from 69.9% of children whose caregivers denied tobacco exposure. In contrast, detection rates in children with reported tobacco exposures were 87.6% and 97.7%, respectively.

In children hospitalized for asthma, 1-year readmission risk is unrelated to caregiver-reported tobacco exposure. However, readmission risk is significantly higher for children with detectable cotinine in serum or saliva samples. These objective measures may help to guide specific interventions, such as parental counseling, before the child is discharged from the hospital.

COMMENT: *In a study of 619 hospitalized children admitted for asthma, the tobacco exposure rates were about 35%, 56%, and 77% by report, serum, and saliva measures, respectively. Interestingly, caregiver report of any tobacco exposure was not associated with readmission, but detectable serum or salivary cotinine were. And, "curiouser and curiouser," among children whose caregivers reported no tobacco exposure, 39% had detectable serum cotinine and 70% had detectable salivary cotinine! Perhaps we need to consider using salivary cotinine levels as a risk stratification tool that will help develop targeted interventions to prevent readmission.*
C.D.
Howrylak JA, Spanier AJ, Huang B, et al: Cotinine in children admitted for asthma and readmission.
Pediatrics. 2014;133:e355-e362. ♦♦

Do Inhaled Corticosteroids Increase Pneumonia Risk in Asthma?

CLINICAL trials of chronic obstructive pulmonary disease have suggested that inhaled corticosteroid (ICS) treatment is associated with an increased risk of pneumonia. It is unclear whether ICS therapy for asthma carries a similar risk. This question was addressed using a large UK primary care database.

From The Health Improvement Network database, the researchers identified 6,857 patients with asthma and pneumonia or lower respiratory tract infection (LRTI), along with 36,312 age- and sex-matched controls. The dosage and type of ICS therapy were analyzed for association with the risk of pneumonia or LRTI.

Case patients were more likely to have a prescription for ICS within the past 90 days, compared to controls: adjusted odds ratio (OR) 1.24. There was evidence of a dose-response relationship, with a twofold increase in the risk of pneumonia or LRTI for patients receiving an ICS dose of 1,000 μg or greater: adjusted OR 2.04, compared to asthma patients with no ICS prescription in the past 90 days.

The findings support an association between ICS therapy and pneumonia or LRTI risk in patients with asthma. Risk is higher for asthma patients receiving higher doses of ICS. "Pneumonia should be considered as a possible side effect of inhaled corticosteroids," the researchers write.

COMMENT: *Previous studies have indicated that ICS may increase the risk of pneumonia in patients with chronic obstructive pulmonary disease. These authors evaluated a large UK database to see if ICS use in asthma increases risk of pneumonia. They found a modest increase in risk of pneumonia with ICS, although the association was not present for all types of ICS. A dose-response effect was also shown. The study has several limitations, including absence of radiographic documentation of pneumonia and no data on ICS adherence and actual dosing. Although it provides yet another reason to limit ICS to the minimally effective dose, further studies are required to determine if the association with pneumonia is truly valid.*
D.A.K.
McKeever T, Harrison TW, Hubbard R, Shaw D: Inhaled corticosteroids and the risk of pneumonia in people with asthma: a case-control study.
Chest. 2014;144:1788-1794. ♦♦

Vitamin D and COPD: A Negative Study!

CROSS-sectional studies have reported that most patients with chronic obstructive pulmonary disease (COPD) have vitamin D deficiency, but there are few longitudinal studies of this issue. Long-term follow-up data were used to assess the relationship between vitamin D status and exacerbation risk in COPD.

The study included 356 patients from the Global Initiative for Chronic Obstructive Lung Disease. All had stage II to IV disease and were free from exacerbations for at least 4 weeks at baseline. Serum 25-hydroxyvitamin D level was evaluated for association with COPD exacerbations and mortality at 2 years' follow-up.

Mean baseline 25-hydroxyvitamin D level was 15.5 ng/dL, with 77% of patients classified as having vitamin D deficiency (less than 20 ng/dL). Exacerbation risk was not significantly different for patients in various vitamin D status groups: 29.8% with severe deficiency, 47.2% with moderate deficiency, and 16.3% with insufficiency. Nor were exacerbation rates significantly lower (6.7%) in patients with desirable 25-hydroxyvitamin D levels (greater than 30 mg/dL). The results were similar for patients taking vitamin D supplements or in analyses using different cutoffs or competing risk models.

Serum 25-hydroxyvitamin D levels are unrelated to the risk of exacerbations over time in patients with COPD. Vitamin D status also appears unrelated to mortality.

COMMENT: *Vitamin D deficiency seems to be associated with just about any disease these days. Several cross-sectional studies have suggested an association with vitamin D deficiency and severity of COPD. These authors performed a prospective study of 356 patients with COPD and followed them for 2 years, tracking both moderate-severe exacerbations and mortality. No association was found between any severity of vitamin D deficiency and COPD exacerbations or mortality. Thus it appears that there may be at least one thing that vitamin D deficiency does not impact!*
D.A.K.

Puhan MA, Siebling L, Frei A, et al: No association of 25-hydroxyvitamin D with exacerbations in primary care patients with COPD.
Chest. 2014;145:37-43. ♦♦

Exploring the Immunopathology of Neutrophilic Asthma

DIFFERENT inflammatory phenotypes of asthma have been identified and linked to transcriptional profiles in the airways. It is unknown how the histone acetyltransferases (HATs) and histone deacetylases (HDACs), which regulate gene expression, are involved in the different inflammatory phenotypes. This study compared HAT and HDAC expression and activity in neutrophilic asthma (NA) versus other inflammatory phenotypes.

The study used peripheral blood and induced sputum samples from 52 adult asthma patients and 9 healthy controls. Based on sputum inflammatory cell counts, 9 patients were classified as having NA, 21 as having eosinophilic asthma, and 22 as having paucigranulocytic asthma. In blood monocytes, HAT and HDAC activity were inversely associated with each other.

Compared to eosinophilic asthma, the NA phenotype was associated with increased monocyte HAT activity, decreased HDAC activity, and an increased HAT:HDAC ratio. Gene expression of EP300, KAT2B, CREBBP, or HDACs 1, 2 and 3 in monocytes from asthma patients or the inflammatory phenotype groups were not significantly different. Activity of HAT/HDAC was also unaffected by inhaled corticosteroid therapy, asthma control, or asthma severity. Sputum macrophage expression of KAT2B was greater in eosinophilic asthma than in the paucigranulocytic phenotype.

The NA inflammatory phenotype is associated with increased HAT activity and decreased HDAC activity in blood monocytes. The findings add to previous evidence linking differences in inflammatory gene transcription profile to the systemic manifestations of NA. This line of research could help in understanding the mechanisms of asthma and in developing new therapeutic targets.

COMMENT: *While eosinophilic asthma has been studied extensively, less is known about NA. This study focused on enzymes involved in regulating chromatin structure: HATs and HDACs. A reduction in HDAC and an increase in HAT activity can potentiate inflammatory gene transcription and has been shown in prior studies of asthma. Neutrophilic asthma was associated with elevated levels of HAT and decreased HDAC. However, gene expression for HATs and HDACs did not differ between asthma phenotypes. Prior studies have shown that patients with reduced HDAC activity are less sensitive to corticosteroids. This could potentially explain why patients with NA often require higher doses of inhaled corticosteroids.*
D.A.K.

Gunawardhana LP, Gibson PG, Simpson JL, et al: Activity and expression of histone acetylases and deacetylases in inflammatory phenotypes of asthma.
Clin Exp Allergy. 2013;44:47-57. ♦♦

Probiotics to Prevent Asthma and Allergies? Evidence Remains Weak

IT'S still unclear whether probiotics, through their effect on the microbiome, can influence the risk of allergic disease. Most previous studies have focused on high-risk infants. The effects of probiotic milk consumption on the risk of allergic diseases in early childhood were evaluated in a large, population-based cohort of pregnant women.

The analysis included data on 40,614 children from the Norwegian Mother and Child Cohort Study. Intake of probiotic milk products during pregnancy and infancy was evaluated for associations with parent-reported atopic eczema, rhinoconjunctivitis, and asthma in the children.

Maternal consumption of probiotic milk during pregnancy was associated with significant but small reductions in atopic eczema at 6 months and rhinocon-➤➤

junctivitis at 18 to 36 months. Adjusted relative risks were 0.94 and 0.87, respectively; the associations were unaffected by maternal history of allergy. Consumption of probiotic milk by the mother during pregnancy and by the infant after age 6 months was related to a reduced risk of rhinoconjunctivitis: adjusted relative risk 0.80. However, probiotic consumption had no effect on the risk of asthma in the children at age 36 months. The results were similar on sensitivity analyses.

This large, population-based cohort study suggests that consumption of probiotic milk products by mothers and infants may lead to reductions in atopic eczema and rhinoconjunctivitis during early childhood. However, probiotic consumption is unrelated to the risk of asthma at age 3 years. The authors emphasize that most children in their study were not at increased genetic risk for asthma and allergies.

PERTURBATIONS of the infant gut microbiota occur before the development of atopic dermatitis, regarded as the first step in the "atopic march" leading to allergic rhinitis and asthma. This suggests that giving probiotics during pregnancy or infancy may help to prevent allergic diseases. The growing body of research evidence on this topic is analyzed in a systematic review and meta-analysis.

The review identified 20 randomized trials involving probiotic administration to pregnant women or to infants during the first year of life. The meta-analysis included pooled data on 4,866 children. The main outcome of interest was physician-diagnosed asthma; wheezing and lower respiratory tract infection were analyzed as secondary outcomes.

The types and duration of probiotic therapy used in the studies varied, as did the length of follow-up. The trials included median follow-up of 24 months, with only 5 of 20 following the children beyond age 6. None of the studies was powered to assess asthma as the primary outcome. Overall, asthma developed in 10.7% of infants, wheezing in 33.3%, and lower respiratory tract infection in 13.9%.

Nine trials provided data on asthma in 3,257 infants, with no significant reduction in asthma risk with probiotics. Neither were probiotics associated with a reduction in wheezing, based on 1,949 infants in 9 trials; or lower respiratory tract infection, based on 1,364 infants in 6 trials. Most of the studies had high or unclear risk of bias.

Based on a substantial number of randomized trials, the meta-analysis finds no significant effect of probiotics in preventing childhood asthma and wheezing. The authors conclude that current evidence is "insufficient" to recommend probiotics to prevent asthma and allergic disease. They call for "additional basic research and adequately powered long-term clinical trials."

COMMENT: *The first of these two papers prospectively followed a birth cohort in Norway and found that consumption of probiotic milk during pregnancy was associated with a slightly reduced risk of atopic eczema in the infants. When both the mother and infant consumed probiotic milk, there was a reduced risk of rhinoconjunctivitis. However, there was no reduction in asthma risk when either the mother or the child or both consumed the probiotic milk.*

The second study was a meta-analysis of 20 trials, which found that probiotics administered to pregnant mothers or infants did not have a protective effect against the development of childhood asthma. One of the reasons for our current quandary on probiotics is that many of these studies use different organisms; the timing of administration varies and the target populations are inconstant as well. Atopic families are searching for ways to help prevent the development of allergic disease in their children. Although probiotics may offer some hope, there are minimal data supporting firm recommendations at this time.

S.M.F.

Bertelsen RJ, Brantsæter AL, Magnus MC, et al: Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systemic review and meta-analysis.
J Allergy Clin Immunol. 2014;133:165-171.
Azad MB, Coneys JG, Kozyrskyj AL, et al: Probiotic supplementation during pregnancy or infancy for the prevention of asthma and wheeze: systematic review and meta-analysis.
BMJ. 2013;347:f6471.

♦♦

Maternal Distress May Be a Risk Factor for Wheezing

INTRAUTERINE exposures causing abnormal development of the fetal lung and immune system may increase the risk of asthma in offspring. One such possible exposure is maternal psychologic distress during pregnancy. This hypothesis was examined in a population-based cohort study, including evaluation of paternal psychologic distress to address the issue of confounding.

The analysis included 4,848 children in Rotterdam enrolled in the "Generation R Study." The Brief Symptom Inventory was used to assess maternal and paternal psychologic distress during the second trimester of pregnancy and 3 years after delivery, as well as maternal distress at 2 and 6 months after delivery. The occurrence of wheezing in the children from age 1 to 4 years was evaluated by questionnaires; physician-diagnosed asthma was assessed at age 6 years.

Maternal psychologic distress during pregnancy was associated with increased rates of wheezing in the child at age 1 to 4 years. Odds ratios were 1.60 for overall distress, 1.60 for depression, and 1.39 for anxiety. Maternal distress in the second trimester was also related to number of wheezing episodes and patterns of wheezing. There was a borderline significant association with physician-diagnosed asthma at age 6. Paternal psychologic distress during pregnancy showed no association with wheezing or asthma in the children; the same was true for both maternal and paternal distress after delivery.

Psychologic distress in the mother during pregnancy may be a risk factor for wheezing in children through the first 6 years of life. This association is indepen-➤➤

dent of the father's distress during pregnancy, or distress in either parent after birth. Although more study is needed, the results suggest a possible "intrauterine programming effect" linking maternal psychologic distress to childhood respiratory morbidity.

COMMENT: *Maternal physiology clearly influences the developing fetus in utero. This large population-based cohort study from the Netherlands suggests that maternal psychologic distress during pregnancy increases the children's risk of developing wheezing during the first 6 years of life. Interestingly, paternal psychology either prenatally or after delivery and maternal postpartum psychology aren't correlated with increased risk. The authors suggest that prenatal hypothalamic-pituitary-adrenal axis or changes in immunomodulation could explain this intrauterine programming effect. Is this something else new moms can worry about?*
S.M.F.

Guxens M, Sonnenschein-van der Voot AMM, Tiemeier H, et al: Parental psychological distress during pregnancy and wheezing in preschool children: The Generation R Study.
J Allergy Clin Immunol. 2014;133:59-67. ♦♦

Good Outcomes 5 Years after Bronchial Thermoplasty

BRONCHIAL thermoplasty (BT) has emerged as a new option for patients with moderate to severe persistent asthma. The Asthma Intervention Research 2 (AIR2) trial reported improved asthma control 2 years after BT. The current study reports 5-year safety and durability outcomes of BT for severe persistent asthma.

Five-year follow-up data were available for 162 of 190 patients undergoing BT in the AIR2 trial. From year 1 through 5, compared to the pretreatment year, patients had an average 44% reduction in severe exacerbations and a 78% reduction in emergency department visits. Respiratory adverse events and hospitalizations remained the same in years 2 through 5, compared to year 1.

Average daily inhaled corticosteroid dose decreased by 18%, yet prebronchodilator FEV_1 values were stable through all 5 years of follow-up. High-resolution computed tomography scans found no significant airway structure changes attributable to BT.

These follow-up data support the long-term safety and durability of BT for patients. Improvements in asthma control are maintained through 5 years, including reduced rates of severe exacerbations and ED visits. The investigators conclude that BT should be considered for patients with severe asthma that persists despite treatment with inhaled corticosteroids and long-acting β_2-agonists.

COMMENT: *Bronchial thermoplasty is a relatively new, nonpharmacologic option for patients with difficult-to-manage persistent asthma. This report, from an extension of the AIR2 study, shows an impressive sustained improvement in exacerbations, hospitalizations, and ED visits in patients with severe persistent asthma receiving BT. The improvements continued over the 5-year posttreatment period, with 28% of patients reducing their inhaled corticosteroid dose by at least half. The CT imaging safety data were also impressive. Limitations of the study include the fact that the control group was not followed, so true efficacy is difficult to evaluate.*
S.M.F.

Wechsler ME, Laviolette M, Rubin AS, et al: Bronchial thermoplasty: Long-term safety and effectiveness in patients with severe persistent asthma.
J Allergy Clin Immunol. 2013;132:1295-1302. ♦♦

CLINICAL TIDBITS

Food Protein in Mattress Dust: An Important Source of Allergen Exposure?

HIGH exposure to peanut allergen in the home environment may be an important risk factor for cutaneous sensitization. This study measured peanut allergens in dust from various areas of the home and related it to household peanut consumption.

Dust samples were collected from 21 German homes, and peanut levels were measured using an enzyme-linked immunosorbent assay. Peanut was detectable in samples from bed sheets in 91% of homes, and from the eating area in 76%. Levels of peanut in the eating area, but not on sheets, were correlated with the frequency of household peanut consumption.

Peanut remained detectable in most households even when participants did not consume peanut at home for 4 weeks. In homes with low levels at baseline, peanut levels increased 48 hours after consumption of roasted peanut snacks.

Peanut allergen is detected in dust from the eating area and bed of homes, and may be related to household peanut consumption. The results suggest that environmental peanut exposure could contribute to sensitization risk via the skin or airway.

FOOD allergies caused by allergen exposure via the skin or airway have been mainly reported in occupational settings and in experimental studies. This study measured levels of various food allergens in home mattress dust.

Mattress dust samples were obtained from the homes of 143 Norwegian adolescents with asthma. All but 3 samples contained some type of food allergen: fish allergen in 46%, peanut in 31%, milk in 39%, and egg in 22%. All allergens were more commonly found in samples from smaller homes. Milk, peanut, and egg allergen were two to three times more likely to be detected when the bedroom and kitchen were on the same floor.

Food allergens are very commonly detected in mattress dust samples, especially in smaller homes and when the bedroom is located near the kitchen. The researchers write, "Due to the amount of time children spent in the bedroom, mattress dust may be an important source of exposure to food allergens." ➤➤

COMMENT: *We tend to assume that the skyrocketing prevalence of food allergy is due to sensitization from ingestion of the food, although exposure via skin or respiratory mucosal contact may also be important. These two European studies report significant levels of food allergen in house dust. In the German study by Trendelenburg and colleagues, levels were higher in smaller homes where the bedroom was closer to the kitchen. In the Norwegian study by Bertelsen et al, peanut protein in dust correlated with frequency of peanut consumption--even in bedroom dust 48 hours later! Further study is necessary to evaluate whether food exposure in dust contributes to either food sensitization or chronic symptoms in sensitized patients.*
S.A.T.

Trendelenburg V, Ahrens B, Wehrmann A-K, et al: Peanut allergen in house dust of eating area in bed--a risk factor for peanut sensitization?
Allergy. 2013;68:1460-1462.

Bertelsen RJ, Faeste CK, Granum B, et al: Food allergens in mattress dust in Norwegian homes--a potentially important source of allergen exposure.
Clin Exp Allergy. 2014;44:142-149. ♦♦

Do Children on IVIG Reach Protective Pneumococcal Antibody Levels?

CHILDREN with primary immunodeficiencies (PID) are treated with intravenous immunoglobulin (IVIG) to reduce the frequency and severity of infections. There are few data on the effective levels of protective, serospecific antibodies in these patients. This study measured total IgG and peak/trough levels of specific antipneumococcal antibodies (PnPsAbs) in PID patients receiving IVIG.

The prospective, multicenter study included 22 children with PID receiving 7 consecutive IVIG infusions. For total IgG, mean trough level was 7.77 g/L and mean peak level 13.93 g/L. For the PnPsAbs, trough and peak geometric mean concentrations and distribution curves varied widely by serotype. However, 89% to 100% of children had trough levels of 0.2 μg/mL or greater--likely protective against invasive pneumococcal infection--for most serotypes.

For some serotypes, antibody levels reached the levels observed in adults. Trough geometric mean PnPsAb concentrations appeared to reflect the contents of the IVIG product used.

The results show protective levels of antibodies against most pathogenic pneumococcal serotypes in children with PID receiving IVIG. The correlation with PnPsAb contents suggests an opportunity to adapt IVIG products and dosing based on epidemiology.

COMMENT: *This study measured antibodies against pneumococcal serotypes in 22 children with primary immunodeficiency diseases treated with seven consecutive infusions of IVIG (mean monthly dose 0.4 g/kg). Protective levels against invasive pneumococcal infection (above or equal to 0.2 mg/mL) were achieved at trough level in 89% to 100% of patients for all serotypes except 4, 9V, and 12F and at peak level in 93% to 100% of patients. For several serotypes, trough levels reached adult levels (greater than or equal to 1.0 to 1.3 mg/mL). Apart from demonstrating a linear relationship between serotype-specific PnPsAbs in patients and the administered IVIG product, these findings raise the additional question of the need to monitor these levels--both in IVIG batches and in patients.*
C.D.

Tuerlinckx D, Florkin B, Ferster A, et al: Pneumococcal antibody levels in children with PID receiving immunoglobulin.
Pediatrics. 2014;133:e 154-e162. ♦♦

REVIEWS OF NOTE

COMMENT: *Asthma treatment is evolving. This review looked at studies that used biologic therapy in the treatment of asthma. Many drugs are currently being studied. The possibility of using biologic therapy for the individual's particular asthma phenotype is exciting. The use of these medications after conventional therapy failure for patients with moderate to severe asthma is likely. The authors suggest that their use may explain how biomarkers may predict response to therapeutic agents.*
V.H.-T.

Bice JB, Leechawengwongs E, Montanaro A: Biologic targeted therapy in allergic asthma.
Ann Allergy Asthma Immunol. 2014;112:108-115. ♦♦

COMMENT: *This is an important review regarding the use of antibiotics in respiratory infections in patients with chronic airway obstruction.*
B.E.C.

Miravitilles M, Anzueto A: Antibiotics for acute and chronic respiratory infection in patients with chronic obstructive pulmonary disease.
Am J Respir Crit Care Med. 2013;188:1052-1-57. ♦♦

COMMENT: *This is an excellent review of an interesting subgroup of our patients. Long-term patterns of intense exercise appear to result in airway problems such as asthma at a rate far higher than in the general population. The authors suggest that airway dysfunction be considered an occupational hazard in elite athletes.*
S.A.T.

Price OJ, Ansley L, Menzies-Gow A, et al: Airway dysfunction in elite athletes--an occupational lung disease?
Allergy. 2013;68:1343-1352. ♦♦