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FEATURE ARTICLES

Particulate Exposure during Mid-Gestation Affects Asthma Risk in Boys

The adverse respiratory health effects of air pollution may begin even before birth. The influence of in utero exposure to ambient fine particulate matter ($PM_{2.5}$) may depend on the timing of exposure and may be sex specific. This study used advanced statistical models to clarify the effects of prenatal exposure to $PM_{2.5}$ on the risk of asthma development in a cohort of urban children.

The study included 736 full-term children in the Boston area, born to mothers enrolled in a pregnancy cohort study between 2002 and 2009. Most of the mothers were Hispanic or black, with 12 or fewer years of education. Eighty percent did not smoke during pregnancy.

The mothers' weekly exposure to $PM_{2.5}$ was estimated using a previously validated, satellite-based spatiotemporal resolved model. Distributed lag models were used to assess the relationship between average $PM_{2.5}$ levels during pregnancy and onset of physician-diagnosed asthma before age 6 in the children. The association was compared for boys versus girls.

Higher exposure to $PM_{2.5}$ at 16 to 25 weeks' gestation was associated with a higher risk of childhood asthma. The association was significant after adjustment for child age and sex and for maternal race/ethnicity, education, smoking, stress, atopy, and obesity before pregnancy.

Asthma was diagnosed in 18% of boys versus 12% of girls. On sex-stratified analysis, the association between $PM_{2.5}$ exposure and childhood asthma was significant only for boys.

Higher prenatal exposure to $PM_{2.5}$ during midgestation is associated with a higher risk of childhood asthma specifically in boys, the new analysis suggests. The authors note that the "sensitive window" identified in their study cor- • • •

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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
- Journal of Asthama
- 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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responds to the late pseudoglandular and canalicular phases of fetal lung development. Further study of the vulnerable exposure periods may help to better understand how in utero pollutant exposure affects childhood asthma risk.

COMMENT: This study allows greater insight into another determinant for the persistence of wheezing, especially in prepubertal males. The mechanism underlying the association with prenatal exposure to particulate pollution is thought to involve oxidative stress pathways with proinflammatory cytokine induction. These are supportive data regarding the early gestational effects of air pollution, and have significant public health implications.

B.E.C.

Leon Hsu HH, Mathilda Chiu YH, Coull BA, et al: Prenatal particulate air pollution and asthma onset in urban children: identifying sensitive windows and sex differences.
Am J Resp Crit Care Med. 2015;192:1052-1059.

Keywords: asthma (child), air pollution, maternal exposure, primary prevention

FOCUS ON THE MICROBIOME

Microbiome May Help Determine Asthma Phenotype

Previous studies have suggested that variations in the clinical features of mild to moderate asthma may be related to differences in the airway microbiome. This study looked for similar associations between airway microbiota and disease features in severe asthma.

The study included 40 patients enrolled in the Bronchoscopic Exploratory Research Study of Biomarkers in Corticosteroid-refractory Asthma (BOBCAT) study. Microbiome profiling of bronchial brushings was performed using 16S ribosomal RNA-based techniques, and associations with clinical and inflammatory findings were assessed. The researchers also compared differences in the microbiota for 7 patients with severe asthma versus 7 healthy controls and 41 patients with mild to moderate asthma.

Several features of severe asthma were related to the airway microbiome, including body mass index (BMI), change in Asthma Control Questionnaire (ACQ) scores, sputum total leukocytes, and bronchial biopsy eosinophils. Proteobacteria were associated with worsening ACQ scores and sputum total leukocytes, while Bacteroidetes/Firmicutes were associated with BMI.

By comparison, the presence of Actinobacteria was associated with stable or improving ACQ scores and with bronchial epithelial gene expression of the steroid-responsiveness marker FK506 binding protein (FKBP5). Biopsy eosinophil counts were generally negatively correlated with Proteobacteria. None of the microbiota studied were associated with a Th2-related epithelial gene expression signature, although Proteobacteria were related to expression of Th17-related genes.

Severe asthma was associated with significant enrichment of Actinobacteria, compared to normal subjects or those with mild to moderate asthma. However, the largest single difference was a 7.8-fold increase in a *Klebsiella* species in the severe asthma group.

Specific microbiota may modulate inflammatory processes in severe asthma, the associations suggest. The airway microbiome in patients with severe asthma differs from that reported in patients with • • •

mild to moderate asthma treated with inhaled corticosteroids. Further studies are needed, including "mechanism-oriented investigations of specific microbial targets."

COMMENT: Analyzing data from the BOBCAT study, these researchers found that bronchial bacterial flora contribute to various phenotypes in patients with severe asthma. Of particular interest, patients with high BMI tended to have Bacteroidetes and Firmicutes phyla. Proteobacteria were more closely associated with non-Th2, neutrophilic inflammation. Although there was no clear-cut association of bacterial composition with type 2 inflammation, Actinobacteria were correlated with better asthma control and expression of FKBP5. The microbiome does influence asthmatics' inflammatory responses. We need to be on the lookout as more studies investigate this mechanism.

S.M.F.

Huang YJ, Nariya S, Harris JM, et al: The airway microbiome in patients with severe asthma: associations with disease features and severity.

J Allergy Clin Immunol. 2015;136:874-884.

Keywords: asthma (severe), microbiome, biomarkers

Home Microbiome Differs for Children with Asthma

Microbial exposures have repeatedly been shown to influence the development of asthma and other atopic diseases. Little is known about the microbial communities associated with specific environments associated with asthma risk, such as low-income urban homes. This pilot study compared the home microbiota of urban children with and without asthma.

The investigators performed 16S rRNA-based phylogenetic analysis of dust samples from the homes of low-income children in the greater Kansas City area: 14 asthmatic and 5 nonasthmatic children. The analysis sought to identify differences in the overall microbiome between groups, along with any species that were more abundant in the homes of asthmatic children.

At the genus level, there was no difference in bacterial richness, but a significant difference in the overall bacterial profile between groups. All of the top 12 operational taxonomic units (OTUs) with significant abundance differences were increased in the homes of children with asthma. All of these OTUs belonged to one of five phyla; nearly half of the significant abundance differences were for Cyanobacteria or Proteobacteria. One OTU in the phylum Firmicutes and two in Proteobacteria were increased in the homes of nonasthmatic children.

The results suggest a characteristic microbiota in the homes of low-income urban children with asthma, with an abundance of Cyanobacteria and Proteobacteria. Further studies are needed to characterize microbial exposures in the home and how they influence human health and disease risks.

COMMENT: The Hygiene Hypothesis postulates that microbial exposures affect the development of atopic conditions encompassing asthma, allergic rhinitis, and atopic dermatitis. This intriguing study demonstrates that house dust has an identifiable microbiota that is altered in the homes of patients with asthma, leading to a specific enhancement of Cyanobacteria and Proteobacteria. The implications are that altered microbial flora in home house dust may affect the development of asthma and other atopic conditions.

C.C.R.

Ciaccio CE, Barnes CF, Kennedy K, et al: Home dust microbiota is disordered in homes of low-income asthmatic children.

J Asthma. 2015;52:873-880.

Keywords: asthma (child), hygiene hypothesis, microbiome

Animals and Asthma Risk:The Hygiene Hypothesis Is Alive and Well

Questions remain about the effects of early exposure to pets and the risk of developing childhood asthma. Studies of exposure to farm animals have been more consistent than studies of pets. The effects of dog and farm animal exposure on childhood asthma were assessed using Swedish national registry data.

The analysis included more than 1 million children born in asthma from 2001 through 2010. Birth registry data were linked to other records including data and farm registration, asthma diagnosis and medications, and potential confounders for parents and children. Outcomes of interest were current diagnosis of asthma at age 6 for school-aged children and incident asthma at age 1 to 5 for preschool-aged children. Follow-up data were analyzed from 2007 to 2012.

Exposure to dogs was recorded for 14.2% of preschool-aged children and 8.2% of school-aged children. Rates of farm animal exposure were 0.5% and 0.3%, respectively. In the preschool-aged cohort, 5.0% of children had an asthmatic event before baseline. During follow-up there were 28,511 cases of asthma during 906,071 years at risk, for an incidence rate of 3.1 cases per 1,000 years at risk. In the school-aged cohort, 4.2% of children had an asthmatic event during the seventh year of life.

Dog exposure during the first year of life was associated with a lower risk of asthma in school-aged children, odds ratio 0.87; and in preschool-aged children aged 3 years or older, hazard ratio 0.90. There was no effect in children under age 3. Farm animal exposure was associated with a reduced risk of asthma in both groups: OR 0.48 in preschool children and HR 0.69 in school-aged children.

These nationwide data suggest a reduced risk of asthma in 6-year-olds with a history of exposure to dogs and farm animals. The associations remain significant after considering parental asthma or whether the child was first-born. The evidence may be useful in discussing whether and when

infants and young children should be exposed to animals.

COMMENT: These data from a large, 10-year Swedish birth cohort shows that children exposed to either dogs or farm animals or both had significant reduction in their risk of developing asthma at age 6. Exposure to farm animals was minimal (0.5%), but 14% of children were exposed to dogs. The risk reduction was greater for farm animal exposure than for dogs. The authors suggest there may be a rationale for advising parents about when to expose children to animals. Once again, we have data supporting the Hygiene Hypothesis.

S.M.F.

Fall T, Lundholm C, Ortqvist AK, et al: Early exposure to dogs and farm animals and the risk of childhood asthma.
JAMA Pediatr. 2015;169:e153219.

Keywords: animals, asthma (child), hygiene hypothesis

Basophil Assay Predicts Reactions during VIT

Honeybee venom immunotherapy (VIT) is associated with a high risk of systemic reactions (SRs), compared to wasp VIT. Some previous studies have suggested that the basophil CD63 allergen response might be a useful indicator of SRs during VIT. This study evaluated the CD63 activation test as a risk marker for SRs during the buildup phase of honeybee VIT.

The prospective single-center study included 93 patients undergoing ultra-rush honeybee VIT. Basophil CD63 response and other immunologic variables were evaluated for association with adverse SRs. Basophil response was assessed in terms of CD63 up-regulation to single allergen concentrations, or various dose-response curve metrics. Patient- and sting-specific factors were evaluated as well.

Mild SRs occurred in 24.7% of patients and severe SRs in 14.0%. The buildup phase was halted in 5 of 13 patients with severe SRs. Measures of high basophil allergen sensitivity were the only factor independently associated with severe SRs or the need to stop the buildup phase. Other factors associated with severe SRs were time of less than 5 minutes after sting to symptom onset and lower specific IgE to rApi m 1.

Baseline tryptase, associated with SRs to wasp VIT, was not a significant factor in honeybee VIT. None of the factors evaluated were related to mild SRs.

For patients undergoing the buildup phase of honeybee VIT, high basophil allergen sensitivity phenotype is a strong, independent predictor of the risk of severe SRs. Measuring the basophil CD63 allergen before the start of honeybee VIT may help in identifying patients at high risks of severe systemic SRs. Further studies including longitudinal follow-up are needed.

COMMENT: Wouldn't it be great if we had a clue as to which of our patients receiving hymenoptera venom were at risk of SRs during the buildup phase to honeybee VIT? This study found that high basophil allergen sensitivity, as measured by basophil CD63 response, was an indicator of high risk for severe SRs during the buildup phase. This is not the first study to suggest the importance of basophils in SRs during immunotherapy (also see Kosnik M, Silar M, Bajrovic N, et al: Allergy 2005;60:1401-1406).

J.J.O.

Korošec P, Žiberna K, Šilar M, et al: Immunological and clinical factors associated with adverse systemic reactions during the build-up phase of honeybee venom immunotherapy.
Clin Exp Allergy. 2015;45:1579-1589.

Keywords: immunotherapy, systemic reactions, venom allergy

FOCUS ON ASTHMA BIOMARKERS

Should We Be Checking Peripheral Blood Eosinophils in Asthma?

Elevated sputum eosinophil counts predict asthma exacerbations and inhaled corticosteroid responsiveness, but this measure is not readily available in primary care. Blood eosinophil count was evaluated as an outcome predictor in a large cohort of asthma patients.

The analysis included data on more than 130,000 primary care patients with asthma, age range 12 to 80 years. All had continuous medical records including 1 year before and 1 year after their most recent blood eosinophil measurement. Exacerbation rates and asthma control were compared for patients at different blood eosinophil counts, with a cutoff point of 400 cells/μL. Analyses were adjusted for age, sex, body mass index, smoking, and comorbidity.

The blood eosinophil count was greater than 400 cells/μL for 16 percent of patients. This group was at increased risk of severe exacerbations and acute respiratory events—adjusted rate ratio 1.42 and 1.28, respectively, compared to those with counts of 400 cells/μL or less. Elevated blood eosinophil count was also associated with lower odds of overall asthma control, based on limited reliever use, no asthma-related hospital visits or admissions, and no oral steroids or antibiotics—odds ratio 0.74. Above the reference level of 200 cells per μL, incremental increases in blood eosinophil count were associated with progressive increases in exacerbation rates.

A blood eosinophil count greater than 400 cells/μL identifies a group of asthma patients at increased risk of exacerbations and worse asthma control. Between 200 and 400 cells/μL, there is a "count-response" association with adverse asthma outcomes. Full blood counts with differential might be a useful routine assessment in patients with asthma, the authors suggest.

COMMENT: Prior studies have demonstrated that elevated sputum eosinophil counts are a reliable surrogate of the level of asthmatic inflammation and correlate with outcomes including exacerbation. However, this measure is difficult to obtain and is limited to specialized centers. Thus, more recent data showing that peripheral blood eosinophil counts • • •

may also provide a useful measure have been quite heartening. In several small studies, elevated blood eosinophil counts have been associated with reduction in FEV_1 as well as asthma exacerbations. This fascinating article by Price and colleagues explores this surrogate of asthma inflammation over a yearlong period, relying upon a historical cohort of over 130,000 asthmatic patients via anonymized medical record data. Almost 21% of patients had elevated blood eosinophil counts (over 400 cells/μL), and this population experienced more severe exacerbations as well as poorer asthma control. The authors suggest that peripheral blood eosinophil count may be of use in the routine care of asthma patients, as it may add predictive value in their risk assessment.

J.J.O.

Price DB, Rigazio A, Campbell JD, et al: Blood eosinophil count and prospective annual asthma disease burden: a UK cohort study.
Lancet Respir Med. 2015;3:849-858.

Keywords: asthma (adult), biomarkers, eosinophils

Do Biomarker Profiles Correlate with Reversibility or Disease Control?

Adult asthma patients with high reversibility after bronchodilator administration have a distinct set of clinical characteristics, including increased oral corticosteroid use and health care utilization. This study compared biomarker profiles and disease control in patients with moderate to severe asthma and high vs low reversibility (HR versus LR).

The analysis included 622 patients with moderate to severe asthma, drawn from two completed clinical trials. Of these, 237 patients were classified as HR (20% or greater change in postbronchodilator FEV_1) and 385 as LR. Biomarkers associated with Th2-high and Th2-low phenotypes were assessed (blood eosinophil count, serum IgE, and exhaled nitric oxide), along with Asthma Control Questionnaire scores associated with not well controlled (between 1.5 and 2.143) and very poorly controlled disease (over 2.143).

In both the HR and LR groups, most patients had Th2-low biomarker profiles and very poor disease control. Regardless of HR versus LR status, Th2 biomarkers were not a good indicator of disease control. The HR patients were more likely to have Th2-high biomarker profiles: 40.1% versus 29.4%. High reversibility was also associated with lower lung function, FEV_1 63.5% versus 67.9% predicted; and a higher rate of atopy, 93.7% versus 86.5%.

Among patients with moderate to severe asthma, HR is associated with reduced lung function and a greater frequency of the Th2-high biomarker profile. Yet most patients in this clinical trial sample have the Th2-low profile, while the Th2-high profile is not associated with worse disease control. Conventional Th2 biomarkers are "reasonably stable" indicators of inflammatory status in patients receiving stable treatment for moderate to severe asthma.

COMMENT: Having high reversibility following bronchodilator is a distinctive physiologic characteristic of certain subtypes of severe asthma. This study of moderate to severe asthmatics examined biomarkers in patients with HR and LR and their relationship to asthma control. Blood eosinophil counts, IgE levels, and exhaled NO were used to identify Th2 biomarkers. Patients with HR were more likely to have this inflammatory signature than those with LR. Unfortunately, disease control did not correlate with Th2 biomarker status and most patients had Th2-low biomarker profiles. Factors other than Th2 inflammation may be driving disease activity in the majority of patients with moderate to severe asthma.

D.A.K.

Busse WW, Holgate ST, Wenzel SW, et al: Biomarker profiles in asthma with high vs low airway reversibility and poor disease control.
Chest. 2015;148:1489-1496.

Keywords: asthma (adult), biomarkers, bronchodilators

FOXP3 May Help Predict Severity of Food Allergy and Asthma

Allergic diseases may involve an imbalance between T regulatory lymphocytes (Tregs) and Th2 effector cells. The transcription factor forkhead box p3 *(FOXP3)* is the main gene responsible for Treg development and function. However, the effects of changes in *FOXP3* mRNA expression on the phenotype and severity of allergic diseases remains unclear. This study compared *FOXP3* mRNA expression in children with and without asthma and/or food allergy.

The study included 15 children with atopic asthma and IgE-dependent food allergy, 27 with atopic asthma alone, 20 with IgE-dependent food allergy alone, and 20 nonatopic controls. For all allergic groups, *FOXP3* expression was significantly lower than in controls: 2.2 versus 4.2. The lowest level of gene expression, 1.9, was found in children with both asthma and food allergy.

Children with higher *FOXP3* mRNA expression had milder asthma or a lesser allergic reaction to food challenge. In addition, *FOXP3* expression increased significantly after positive food challenge.

Children with asthma and food allergy have lower levels of *FOXP3* expression compared to healthy controls. Among children with allergic diseases, lower *FOXP3* expression is associated with a more severe clinical course. The results also suggest that *FOXP3* expression may change during the clinical course of allergic disease.

COMMENT: The ability to predict the severity of atopic disease would be helpful to the practicing allergist. This study found the lowest levels of *FOXP3* mRNA expression in patients with asthma and food allergy. There was a negative correlation between *FOXP3* expression and specific IgE levels to mite and pollen. Expression of *FOXP3* was decreased in children with asthma, compared to controls. Oral food challenge increased *FOXP3* expression in children with • • •

asthma, whether or not they had food allergy. *FOXP3* expression may be an indication of the severity of asthma in patients with comorbid food allergy. Further studies investigating the correlation of *FOXP3* expression in a larger cohort of patients with atopic disease would be interesting as a possible marker to predict severity of disease.

V.H.T.

Krogulska A, Polakowska E, Wąsowska-Królikowska K, et al: Decreased *FOXP3* mRNA expression in children with atopic asthma and IgE-mediated food allergy.

Ann Allergy Asthma Immunol. 2015;115:415-421.

Keywords: asthma (child), biomarkers, food allergy

Biomarkers of Sputum Eosinophilia in Differing Asthma Phenotypes

Various biomarkers have been evaluated to assess sputum eosinophilia in asthma. Some studies suggest that their accuracy varies between different asthma phenotypes. Markers of sputum eosinophilia were compared among different groups of adult patients with asthma.

The study included 366 adult asthma patients from three prospective observational studies. Four biomarkers were evaluated: blood and sputum eosinophils, exhaled nitric oxide, and total IgE. Their performance in identifying sputum eosinophilia of 3% or greater was assessed in severe versus mild asthma and in obese versus nonobese, atopic versus nonatopic, and smoking versus nonsmoking patients.

Thirty-five percent of patients had sputum eosinophilia. Overall area under the receiver operating characteristic curve was 0.83 for blood eosinophils, 0.82 for exhaled NO, and 0.69 for total IgE. For total IgE, accuracy in detecting sputum eosinophilia was lower in atopic and obese patients.

As predictors of sputum eosinophilia, blood eosinophils and exhaled NO have similar accuracy across subgroups of adult asthma patients with differing phenotypic characteristics. Preferably in combination, these may become the preferred biomarkers for assessing eosinophilic airway inflammation. Total IgE does not perform as well, at least in some patient subgroups.

COMMENT: As we continue to search for appropriate surrogates for sputum eosinophil counts, these data are helpful in reinforcing the reliability of blood eosinophil counts and exhaled NO. Previous data have suggested that the airway lumen eosinophils are not reflective of sputum eosinophils in obese patients. This study is reassuring that the predictive relationships still hold true. The findings should be confirmed in other cohorts, but the relationships appear to be true.

B.E.C.

Westerhof GA, Korevaar DA, Amelink M, et al: Biomarkers to identify sputum eosinophilia in different adult asthma phenotypes.

Eur Respir J. 2015;46: 688-696.

Keywords: asthma (adult), biomarkers, eosinophils, nitric oxide

Preventing Allergic Rhinitis–Hygiene Hypothesis May Not Apply

Better knowledge of risk and protective factors is needed to help in preventing allergic rhinitis (AR). This very long-term follow-up study evaluated a wide range of early life exposures potentially associated with the risk of developing AR through childhood and adolescence.

The analysis included 1,314 infants born in five German cities in 1990, and evaluated at frequent intervals up to age 20. Forty-one different early-life environmental, lifestyle, and biological factors were evaluated as risk/protective factors for development of AR and aeroallergen sensitization during follow-up. Nonallergic rhinitis and AR plus asthma were evaluated as secondary outcomes.

Allergic rhinitis developed before age 20 in 290 subjects, or 22% of the cohort. Factors associated with increased risk of AR included parental history of AR, adjusted hazard ratio (HR) 2.49; urticaria, HR 1.32; and asthma, HR 1.29. Other independent risk factors included early allergic sensitization, HR 4.53; eczema before age 3, HR 1.83; male sex, HR 1.28; and summer or autumn birthday, HR 1.26. None of the potentially modifiable exposures or behaviors through age 3 had a significant influence on AR risk.

In this large, long-term follow-up study, the main risk factors for developing AR by age 20 are parental AR, early allergic sensitization, and eczema. While there may be a chance for primary prevention of AR in combination with asthma, the study identifies no modifiable factors amenable to early-life strategies to prevent AR.

COMMENT: Parents frequently ask, "What can I do to help keep my child from developing allergies?" These researchers reported data from a 20-year birth cohort from five German cities and analyzed 41 different early-life factors. It shouldn't be surprising that parental history of allergy, early allergic sensitization, and eczema were associated with AR, but none of the modifiable factors were associated with AR alone. Avoiding smoking and thyroxine during pregnancy, avoiding coal/firewood heating after birth, starting daycare between 18 and 36 months, and sleeping on animal fur during infancy did help protect against developing asthma—but not AR. According to this study, we'll have to answer our parents' query, "There's not much we can do to prevent children from developing hay fever, but there is for asthma."

S.M.F.

Grabenhenrich LB, Keil T, Reich A, et al: Prediction and prevention of allergic rhinitis: a birth cohort study of 20 years.

J Allergy Clin Immunol. 2015;136:932-940.

Keywords: allergic rhinitis, asthma (child), hygiene hypothesis, primary prevention

Does Eczema Cause Heart Disease?

Adults with eczema have increased cardiovascular risk factors, including sedentary lifestyle, obesity, and smoking. Associations of adult eczema with cardiovascular and cerebrovascular disease were evaluated, along with contributing clinical and behavioral factors.

The analysis included data on 4,970 subjects from the 2005-06 National Health and Nutrition Examination Survey (NHANES), 27,157 from the 2010 National Health Interview Survey (NHIS), and 34,525 from the 2012 NHIS. Associations between eczema and coronary artery disease (CAD), angina, heart attack, stroke, and peripheral vascular disease were assessed.

The NHANES data showed a 3.1% one-year prevalence of flexural eczema. This finding was associated with significantly increased odds of CAD, controlling for sociodemographic factors, comorbid asthma, and hay fever. Flexural eczema was also associated with increased odds of heart attack and congestive heart failure, but not stroke. After controlling for cardiovascular risk factors, only the association with CAD remained significant: odds ratio 1.96.

There was a 10.2% prevalence of eczema in the 2010 NHIS and a 7.2% prevalence of health care-diagnosed eczema in NHIS 2012. In these samples, eczema was similarly associated with increased odds of CAD, angina, heart attack, other heart disease, stroke, and peripheral vascular disease. Most of these associations remained significant after controlling for cardiovascular risk factors.

This very large analysis suggests that adults with atopic dermatitis may be at increased risk of cardiovascular and cerebrovascular disease. Lifestyle factors likely contribute to these risks. Further studies are needed to confirm the associations and identify effective approaches to prevention.

COMMENT: This study explores the association between atopic dermatitis and cardiovascular disease, by mining the data of the 2005-06 and 2010 NHANES as well as the 2012 NHIS, involving over 66,000 subjects. The researchers found a significant rise in CAD and congestive heart failure in the NHANES cohort as well as higher odds of CAD, angina, heart attack, stroke, and peripheral vascular disease in the NHIS data, among individuals suffering from flexural crease eczema in the past year.

As noted by Dr. Silverberg, the mechanism for this association is unknown; however, it could involve behavioral and/or lifestyle issues (ie, a decrease in exercise if it worsens eczema). He also suggests that the chronic inflammation associated with eczema may contribute to cardiovascular disease, similar to psoriasis. Certainly this association warrants further research.

J.J.O.

Silverberg JI: Association between adult atopic dermatitis, cardiovascular disease, and increased heart attacks in three population-based studies.
Allergy. 2015;70:1300-1308.

Keywords: atopic dermatitis, cardiovascular disease, risk factors

School Endotoxin Exposure: Harmful or Helpful?

Endotoxin exposure at home and at work contributes to asthma. But little is known about the potential contributions of endotoxin exposure at school, where children spend most of their time each day. The relationship between school endotoxin exposure and asthma symptoms was assessed, including atopic versus nonatopic asthma.

The study included 248 asthmatic children from the School Inner-City Asthma Study, enrolled at 38 elementary schools in Baltimore. Asthma-related outcomes during the school year were evaluated for association with dust and air endotoxin levels in classrooms and dust endotoxin levels at home. The main outcome of interest was maximum asthma symptom-days per 2-week period, with separate analyses of children with atopic versus nonatopic asthma.

Dust endotoxin levels were significantly higher at school than at home: 14.3 versus 11.3 endotoxin units/mg, respectively. In 22% of classrooms, airborne endotoxin levels exceeded the occupational exposure limit of 90 endotoxin units/m_3. Classroom dust and air endotoxin levels were not strongly correlated with each other, and varied significantly within schools.

After adjustment for home dust endotoxin levels, asthma symptom-days increased with classroom endotoxin exposure in dose-dependent fashion among children with nonatopic asthma: adjusted incidence ratio 1.16. For these children, the difference between the lowest and average classroom air endotoxin level was associated with a 1.3-day increase in maximum symptom-days per 14-day period. There was no significant association for children with atopic asthma.

High levels of endotoxin exposure in urban school classrooms may contribute to increased asthma burden in inner-city children. Higher endotoxin exposure at school is associated with increased asthma symptoms in children with nonatopic, but not atopic, asthma. Efforts to mitigate school endotoxin exposure might decrease asthma symptoms in this population.

COMMENT: This study found high levels of airborne endotoxin in schools—1 in 5 classrooms had levels exceeding occupational limits for adults! Classroom-specific airborne endotoxin levels were independently associated with asthma symptoms, but only in children with nonatopic asthma. Atopic children had reduced asthma symptoms at very low and very high endotoxin levels. The authors suggest that efforts at mitigating endotoxin in schools could lead to significantly fewer missed school days. However, since most children with asthma are atopic, high endotoxin levels may be beneficial and mitigation could potentially reduce the overall effect. Clearly, an interventional study would be required to determine if reducing school endotoxin is helpful or not.

D.A.K.

Lai PS, Sheehan WJ, Gaffin JM, et al: School endotoxin exposure and asthma morbidity in inner-city children.
Chest. 2015;148:1251-1258.

Keywords: asthma (child), allergic sensitization, endotoxin

Component Testing in ABPA: Another Diagnostic Aid

Because of cross-reactivity between different fungi, it can be challenging to distinguish between patients with allergic bronchopulmonary aspergillosis (ABPA) and asthma patients sensitized to *Aspergillus fumigatus* (Af) but without ABPA. A component-resolved diagnostic strategy was evaluated to differentiate between these two groups.

The Japanese study included 53 patients with ABPA and 253 asthma patients with Af sensitization but without ABPA. Using the ImmunoCAP system, the researchers measured levels of serum IgE and IgG antibodies to allergen components from Af, as well as IgE antibodies to various fungal allergen extracts. Sensitization profile analyses were performed, accounting for the effects of comorbid atopic dermatitis (AD).

Patients with ABPA had higher levels of IgE antibodies to Asp f 1 and Asp f 2 compared to Af-sensitized asthma patients. For diagnosis of ABPA, areas under the receiver operating characteristic curve for IgE antibodies to Asp f 1 and Asp f 2 were 0.75 and 0.78, respectively. Sensitivity was higher in the presence of IgE positivity to either component, with little effect on specificity.

Patients with comorbid AD had higher levels of IgE antibodies to the "ubiquitous pan-allergen" Asp f 6, plus low but positive levels anti-IgE to other Af-components. This complicated the serologic diagnosis of ABPA in the presence of AD. Twenty percent of patients with ABPA tested negative for both Asp f 1 and Asp f 2.

Measurement of IgE antibodies to Asp f 1 or Asp f 2, and especially both, performs well in differentiating ABPA patients from Af-sensitized asthma patients without ABPA. IgE to Asp 5 6 is highly specific for ABPA, but not when comorbid AD is present. IgG antibodies to Asp f 1 also perform well, but no better than IgE antibodies.

COMMENT: Differentiating asthma patients with ABPA from those who are merely sensitized to *Aspergillus* can be a challenge. These authors evaluated Japanese patients with ABPA, asthma with Af sensitization, and atopic dermatitis patients using ImmunoCAP testing to specific components of Af. The combination of IgE to Asp f 1 and Asp f 2 had a sensitivity of 77% and specificity of 85% using a cutoff of 0.7 kUA/L. Asp f 4 was highly specific (96%) at this same level but had low sensitivity (32%). Asp f 6 was also elevated in atopic dermatitis as it shares similarity to *Malassezia*. These tests need to be evaluated in a U.S.-based population.

D.A.K.

Tanimoto H, Fukutomi Y, Yasueda H, et al: Molecular-based allergy diagnosis of allergic bronchopulmonary aspergillosis in *Aspergillus fumigatus*-sensitized Japanese patients. Clin Exp Allergy. 2015;45:1790-1800.

Keywords: Aspergillus, asthma (adult), component-resolved diagnosis

Sex and Age Differences in New-Onset Adult Asthma

From early adulthood to middle age, asthma is more frequent in women than men. Less is known about asthma incidence at older ages. Twenty-year follow-up data were used to assess the incidence of adult asthma in a Swiss population, including the effects of sex, age, and allergic sensitization.

The study included 5,128 subjects, aged 18 to 60, who were free of asthma at baseline in 1991-92. Incidence of self-reported, physician-diagnosed asthma was assessed at follow-up in 2010-11. The age-related probability of incident asthma was assessed, stratified by sex and baseline allergic sensitization and adjusted for potential confounders.

Through 20 years, a new diagnosis of asthma was reported by 5.1% of men and 7.5% of women. On adjusted analysis, odds ratios for asthma were 1.99 in females, 3.21 in nonsensitized subjects and 1.43 in sensitized subjects. The probability of new-onset asthma decreased at older baseline ages in women, but not men. The increased risk of new asthma in sensitized versus nonsensitized men was unrelated to age in men. In contrast, this risk decreased with age in women.

Women have a higher incidence of adult-onset asthma than men, but this difference decreases with age. The increase in asthma incidence among women is stronger in those without allergic sensitization at baseline. More research is needed to explain the pathways of the observed age/sex differences, especially in the 20- to 40-year age range.

COMMENT: This study lends further insight as to the etiology of asthma in adults. Adult asthma incidence is higher in females than males—especially nonsensitized females—and increases with age. The data raise significant questions regarding the pathophysiologic incidence of airway injury in this age range. Confirmatory studies are needed to understand the mechanisms involved in the presentation of asthma. This will hopefully help gain insight into the appropriate treatment modalities.

B.E.C.

Hansen S, Probst-Hensch N, Keidel D, et al: Gender differences in adult-onset asthma: results from the Swiss SAPALDIA cohort study. Eur Respir J. 2015;46:1011-1020.

Keywords: allergic sensitization, asthma (adult), risk factors

Link between Celiac Disease and IgE-Mediated Food Allergy

The association between celiac disease (CD) and allergic disorders remains unclear. Abnormal intestinal permeability in CD might predispose to the development of atopy in the mucosal immune system, and the two conditions might share common genetic factors. The prevalence of CD was assessed in children with severe food allergy.

The study included 319 children, mean age 9 years, ...

receiving specific food oral immunotherapy for allergy to cow's milk, egg, or wheat. All had very severe food allergy, with a history of severe allergic reactions and IgE values of greater than 85 kU/L. Serologic markers of CD (IgA anti-endomysium antibodies and IgA-IgG anti-TG2 antibodies) and genetic susceptibility alleles (HLA DQ2/8) were assessed in the children with severe food allergy versus children with mild food allergy who recovered without oral immunotherapy. The same markers were assessed in a historical cohort of healthy schoolchildren.

Both serologic and genetic markers of CD were present in 5% of the children with severe food allergy and 0.8% of those with mild food allergy, as well as 1% of healthy children. The diagnosis of CD was confirmed by intestinal biopsy in 13 out of 16 patients with severe food allergy, and in the 1 child with mild food allergy.

Celiac disease prevalence may be elevated up to fivefold in children with severe food allergy. The findings raise the possibility that impaired intestinal permeability might promote development of CD in genetically predisposed children. The researchers suggest that children with severe food allergy should undergo routine screening for CD.

COMMENT: Prior studies exploring the association between CD and food allergy have demonstrated mixed results. Pillon and colleagues found a four- to fivefold rise in CD among children with severe food allergy undergoing food oral immunotherapy. The researchers postulate that this may be a manifestation of intestinal permeability or even a consequence of the upregulation of interleukin-15 seen in CD, with downstream effects on the Th2 response. If this is true, it is just one more reason to find an effective therapy for food allergy.

J.J.O.

Pillon R, Ziberna F, Badina L, et al: Prevalence of celiac disease in patients with severe food allergy.
Allergy. 2015;70:1346-1349.

Keywords: autoimmune disease, food allergy, immunotherapy

Protecting Children from Tobacco: Three New Policy Statements

Tobacco is a major health hazard for all age groups, with adverse effects starting in the womb. Tobacco dependence begins in childhood, and leads to illness and premature death in children as well as adults. The Section on Tobacco Control of the American Academy of Pediatrics has issued a Clinical Practice Policy statement guiding efforts to protect children from harms related to tobacco, nicotine, and tobacco smoke.

Evidence shows that most US children are exposed to tobacco. Parent/caregiver smoking is not only an important source of exposure, but also increases children's risk of tobacco use and dependence. Pediatricians should ask about tobacco use and tobacco smoke exposure at routine visits and at visits for diseases potentially caused or exacerbated by tobacco use. Anticipatory guidance for school-aged children or adolescents should include interventions to prevent initiation of tobacco use. The parent or caregiver's tobacco dependence should be addressed as well, including recommendations for and help in accessing counseling and treatment. Strategies to reduce tobacco smoke exposure, such as bans on smoking at home or in the car, should be recommended if the source of smoking cannot be eliminated.

Adolescents who want to stop smoking should also be offered tobacco dependence treatment or referral. This may include pharmacotherapy for moderate or severe tobacco dependence—however, evidence in this age group is limited and the potential for neuropsychiatric symptoms should be considered. Quitline referral should be offered, such as 1-800-QUIT-NOW or SmokefreeTXT. Electronic nicotine delivery systems should not be recommended.

The Clinical Practice Policy statement also includes recommendations for addressing tobacco exposure for health care systems and for medical education. Separate statements address public policy recommendations to protect children from tobacco use and exposure, as well as the harmful effects of electronic nicotine delivery systems.

COMMENT: This important evidence-based Clinical Practice Policy statement outlines recommendations for pediatricians' role in preventing initiation of tobacco use and helping children, parents, and caregivers obtain treatment for tobacco dependence. This is truly a comprehensive and well-laid out document that details helpful strategies and resources. An accompanying public policy report describes recommendations that policymakers at the international, national, state, and local levels should adopt in order to protect children from exposure to tobacco products. The third policy report summarizes the dangers of electronic nicotine delivery systems in youth and states actions that pediatricians and policymakers can take in order to protect this vulnerable population. All in all, these concise yet inclusive documents provide an excellent review of cutting-edge knowledge and delineate useful strategies that clinicians can adopt.

C.D.

Section on Tobacco Control: Clinical practice policy to protect children from tobacco, nicotine, and tobacco smoke. Pediatrics. 2015;136:1008-1017.
Section on Tobacco Control: Public policy to protect children from tobacco, nicotine, and tobacco smoke.
Pediatrics. 2015;136:998-1001.
Section on Tobacco Control: Electronic nicotine delivery systems.
Pediatrics. 2015;136:1018-1026.

Keywords: e-cigarettes, primary prevention, smoking

How Confident Are Parents in Managing Food Allergy?

Managing a child's food allergy places a considerable burden on the family. Parents' confidence in their ability to manage this condition may significantly affect their perceptions of quality of life, anxiety, and worry. This study reports • • •

the development and validation of a questionnaire for evaluating parental self-efficacy in managing food allergies in children.

Developed with input from parent interviews, data from the literature, and expert review, the Food Allergy Self-Efficacy Scale (FASE-P) included items assessing parents' confidence related to managing their child's food allergy. The FASE-P was completed by 443 parents of children with food allergy, along with measures of general self-efficacy, food allergy-specific parental burden and impact, and a general health questionnaire.

The final 21-item scale included five subscales: managing social activities, precaution and prevention, allergic treatment, food allergen identification, and seeking information about food allergy. Internal consistency was excellent to good for the scale overall and for subscales, with good stability over time.

The FASE-P showed low to moderate correlations with most of the other subscales. However, there were strong correlations with the measure of parental quality of life burden—parental confidence was linked to increased general self-efficacy, improved quality of life, and better mental health for parents. Self-efficacy was lower for parents of children with egg and milk allergy, but was unrelated to the severity of food allergy.

The FASE-P provides a valid and reliable tool for assessing parents' confidence in managing their child's food allergy. This scale might be clinically useful in targeting healthcare assessment and advice. Initial evaluation suggests that higher food allergy-specific self-efficacy is related to better parental quality of life.

COMMENT: These UK investigators developed and rigorously evaluated a tool to measure parental confidence in managing their child's food allergy. Interestingly, parents struggled with egg and milk allergy more than peanut and tree nut allergy. In addition, the severity of allergic reactions did not affect the parents' confidence. While more work needs to be done prior to implementing this tool in clinical practice, it may prove useful to identify areas of parental concern in management.

D.A.K.

Knibb RC, Barnes C, Stalker C: Parental confidence in managing food allergy: development and validation of the food allergy self-efficacy scale for parents (FASE-P).

Clin Exp Allergy. 2015;45:1681-1689.

Keywords: food allergy, parents, self-efficacy

Factors Associated with Poor Prognosis in Egg Allergy

Although most children with egg allergy outgrow their allergy by school age, recent studies suggest differing patterns of developing egg tolerance. Factors affecting the risk of persistent egg allergy remain to be clarified. Variables associated with the course of egg allergy were investigated in a longitudinal study of Turkish children.

Six-year follow-up data were available for 203 out of a cohort of 363 children diagnosed with IgE-mediated egg allergy. All children had a clear clinical history or challenge test results, positive skin prick test, and egg-specific IgE level of 0.35 kU/L or greater. Through 6 years, 145 children had "outgrown" their egg allergy while 58 had persistent allergy. The proportion of children who outgrew their egg allergy increased from 45% at age 2 years, to 45% at 4 years, to 71% at 6 years.

Egg allergy was more likely to resolve in children with a baseline egg-specific IgE level of 6.2 kU/L or less, hazard ratio 0.32; and those without a history of anaphylaxis, hazard ratio 0.38. Other baseline factors associated with later resolution included gastrointestinal symptoms in response to egg and concomitant egg and cow's milk allergy. On multivariate analysis, factors independently associated with a higher risk of anaphylactic reactions to egg were the natural algorithm for egg white-specific IgE, odds ratio 1.44; and baseline gastrointestinal symptoms after egg exposure, odds ratio 6.86.

The study identifies several factors associated with more severe egg allergy and a reduced chance of outgrowing egg allergy by age 6. Anaphylaxis risk appears higher for children with gastrointestinal symptoms on egg exposure and those with higher gg-specific IgE levels.

COMMENT: Parents frequently ask whether we can predict when their children will outgrow food allergy. In this cohort of pediatric patients with egg allergy in Turkey, almost half had resolution by age 2 and almost three-fourths by age 6. Patients with baseline egg-specific IgE above 6.2 kU/L, history of anaphylaxis to egg, or accompanying milk allergy were more likely to be older at the time their egg allergy resolved. Baseline gastrointestinal symptoms were also associated with increased risk of anaphylaxis to egg. These results may help us advise our pediatric patients with egg allergy regarding risk of anaphylaxis and likely later resolution of egg allergy.

V.H.-T.

Arik Yilmaz E, Cavkaytar O, Buyuktiryaki B, et al: Factors associated with the course of egg allergy in children.

Ann Allergy Asthma Immunol. 2015;115:434-438.

Keywords: anaphylaxis, egg allergy, food allergy

More Evidence for Testing Ara h 6 in Peanut Allergy

Component-resolved diagnostic testing may offer a useful approach to identifying patients with potentially life-threatening peanut allergy. In northern Europe, where many young adults are sensitized to birch, cross-sensitization to peanut is common. In this setting, the authors sought to optimize the use of component-resolved diagnostics for identifying patients at high risk of severe allergic reactions to peanut.

The study included a Finnish referral population of 102 children and adolescents, age 6 to 18, who were sensitized to peanut or had high suspicion of peanut allergy, ...

including anaphylaxis. Double-blind, placebo-controlled peanut challenge was performed using peanut products tested for allergen activity by IgE microarray inhibition. Sixty-nine patients had positive peanut challenges, including severe reactions in 36%, moderate reactions in 52%, and mild reactions in 12%.

Analysis of component-resolved diagnosis included measurement of specific IgE antibodies to Ara h 1, 2, 3, 6, 8, and 9. The strongest marker of moderate to severe reactions was specific IgE to Ara h 6, with an area under the curve of 0.98. The combination of specific IgE to Ara h 2 and Ara h 6 correctly identified all subjects with severe reactions to low doses of peanut.

In contrast, specific IgE to Ara h 8 had no diagnostic value: area under the curve 0.42. IgE binding to Ara h 1, 2, 3, and 6 was completely inhibited by both roasted and nonroasted peanut. IgE binding to Ara h 8 was 87% inhibited by nonroasted peanut, compared to 30% with roasted peanut. The peanut products used in the study did not have Ara h 9 activity.

Among patients with suspected peanut allergy, co-sensitization to Ara h 2 and Ara h 6 differentiates a group with severe allergy from those with mild symptoms. The results suggest that component-resolved testing could be a useful tool for diagnosis of severe peanut allergy while avoiding the need for food challenges.

COMMENT: As we continue to search for a surrogate marker to identify peanut-allergic patients more likely to suffer from severe reactions, we hope that component-resolved diagnostics will fill the void. In this study of Finnish children, the researchers found that co-sensitization of Ara h 2 and Ara h 6 was associated with severe reactions and distinguished severe from mild disease in children undergoing food challenge. Specifically, sensitization to Ara h 2 (ImmunoCap) or Ara h 6 (ISAC microarray) in 6- to 18-year-olds was 100% sensitive, and co-sensitization to Ara h 1, Ara h 2, and Ara h 3 was 100% specific for moderate/severe peanut allergy. The optimal cutoff point, with 95% sensitivity and 95% specificity, was 0.8 ISU for Ara h 6. Furthermore, specific IgE to Ara h 8 provided no diagnostic value.

J.J.O.

Kukkonen AK, Pelkonen AS, Mäkinen-Kiljunen S, et al: Ara h 2 and Ara 6 are the best predictors of severe peanut allergy: a double-blind placebo-controlled study.
Allergy. 2015;70:1239-1245.

Keywords: biomarkers, component-resolved diagnosis, food allergy, peanut allergy

Does Smoking Reduce the Late-Phase Allergic Asthma Response?

Inhaled corticosteroid (ICS) therapy may be less effective in asthma patients who smoke. Little is known about how smoking affects the ICS-induced attenuation of the early and late asthmatic responses. Allergen-induced airway responses were compared for ICS-treated allergic asthma patients who did and did not smoke.

The randomized, double-blind crossover study included 17 smoking and 18 nonsmoking patients with atopic asthma. All received 7 days of treatment twice-daily fluticasone propionate (FP) 100 μg, FP 500 μg, and placebo. On day 6 of each treatment period, airway responses were assessed by measuring FEV_1 for up to 10 hours after allergen challenge. This was followed on day 7 by assessment of exhaled nitric oxide, induced sputum cell counts, and methacholine responsiveness.

In both smokers and nonsmokers, FP significantly suppressed the late asthmatic response (LAR). In addition, the LAR was significantly attenuated during the placebo periods in smokers compared to nonsmokers. Fluticasone suppressed the early allergic response in smokers, but not nonsmokers.

Nonsmokers had a greater reduction in methacholine responsiveness while on FP, compared to smokers. Smokers had lower allergen-induced increases in exhaled NO and sputum eosinophils compared to nonsmokers; in both groups, these responses were suppressed by FP.

In allergic asthma, smokers and nonsmokers have similar allergen-induced LARs at the end of a week of ICS therapy, compared to placebo. However, attenuation of the LAR in smokers is only partly explained by the effects of ICS. Further study is needed to clarify the significance of the observed reduction of the LAR in smokers during placebo treatment.

COMMENT: This study is the first to evaluate the effects of smoking status on the efficacy of ICS in the allergen-induced asthmatic response. The allergen-induced LAR was similar in amplitude between smokers and nonsmokers. However, smokers also had marked attenuation of the LAR compared to nonsmokers when on placebo. Why this reduction in LAR occurred in the smoking subset is an interesting question. The authors examined several other parameters and found that the smoking group also had lower baseline exhaled NO and sputum eosinophil count. Thus immunologic changes associated with smoking in allergic asthma patients might explain the reduction in LAR. More work is needed in this arena; however, I am not prepared to recommend that asthmatic patients begin smoking.

J.J.O.

Cahn A, Boyce M, Mistry S, et al: Randomized trial of allergen-induced asthmatic response in smokers and non-smokers: effects of inhaled corticosteroids.
Clin Exp Allergy. 2015;45:1531-1541.

Keywords: asthma (adult), inhaled corticosteroids, smoking

Aeroallergen Component Testing Is Useful in Vernal Conjunctivitis

Vernal conjunctivitis is a chronic form of conjunctivitis, mainly affecting young children and usually occurring in the spring and summer months. Conventional allergy tests are insufficient to identify the origin of this disorder. This study evaluated a component-resolved diagnostic • • •

approach to identifying the cause of allergic hypersensitivity in vernal conjunctivitis.

The study included 25 patients with vernal conjunctivitis, 50 patients with grass pollen allergy and seasonal allergic conjunctivitis, and 50 healthy controls. Component-resolved diagnostics was used to assess IgE-mediated hypersensitivity to aeroallergens in tears and serum. Patients in whom the allergens responsible for vernal conjunctivitis were identified received a year of specific immunotherapy.

Component-resolved diagnostics in serum, but not tears, identified several different triggering allergens in patients with vernal conjunctivitis. The implicated allergens were Lol p 1 in 11 patients, n Cyn d 1 in 8 patients, group 4 and 6 grasses in 6 patients, and group 6 grasses in 5 patients. Just 1 patient had positive results on skin-prick testing and specific IgE measurement. Allergen-specific immunotherapy was indicated in 13 patients with vernal conjunctivitis, as well as 37 with seasonal allergic conjunctivitis. All showed significant improvement after 1 year of specific immunotherapy.

Component-resolved diagnostics may be more sensitive than standard allergy tests in identifying the allergens responsible for causing vernal conjunctivitis. Specific immunotherapy, guided by the results of component-resolved testing, leads to significant clinical improvement.

COMMENT: Ocular allergy can be challenging to diagnose. These authors found that component-resolved diagnostics in serum from patients with vernal conjunctivitis was more sensitive than either skin-prick tests or specific IgE. All patients with seasonal allergic conjunctivitis or vernal conjunctivitis clinically improved after immunotherapy, and almost all were free of medications after one year. Perhaps we should consider component-resolved diagnostics in our patients with vernal conjunctivitis.

V.H.T.

Armentia A, Iglesias B, Iglesias D, et al: Component-resolved diagnostics in vernal conjunctivitis.

Ann Allergy Asthma Immunol. 2015;115:446-450.

Keywords: allergic conjunctivitis, component-resolved diagnosis, immunotherapy

REVIEWS OF NOTE

COMMENT: The World Allergy Organization appointed an expert panel to evaluate research and make recommendations for the use of probiotics in their Guideline for Allergic Disease Prevention. This paper reports the meta-analysis of 29 studies, which were selected to help answer the questions: Should supplemental probiotics be used in pregnancy, while breast-feeding, or in infancy to help prevent the development of allergy? Although the strength of the evidence was relatively low, the authors conclude that in these three scenarios probiotics can help prevent eczema, but not other allergic conditions. The quandary for clinicians is that although probiotics are considered safe, the specific type of probiotic used in the various studies is highly variable.

S.M.F.

Cuello-Garcia CA, Brozek JL, Fiocchi A, et al: Probiotics for the prevention of allergy: a systemic review and meta-analysis of randomized controlled trials.

J Allergy Clin Immunol. 2015;136:952-961.

COMMENT: Here is a crisp, succinct, and informative review of eosinophilic esophagitis, ranging from diagnostic criteria to treatment. It will be helpful to learners of all ages.

C.D.

Furuta GT, Katzka DA: Eosinophilic esophagitis.

N Engl J Med. 2015;373:1640-1648.

COMMENT: This is an excellent summary of the current Global Initiative for Asthma guidelines for asthma control.

B.E.C.

Reddel HK, Bateman ED, Becker A, et al: A summary of the new GINA strategy: a roadmap to asthma control.

Eur Respir J. 2015;46:622-639.

COMMENT: These authors present an excellent review of allergen-induced airway responsiveness.

Gauvreau GM, El-Gammal AI, O'Byrne PM, et al: Allergen-induced airway responsiveness.

Eur Respir J. 2015;46:819-831.