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FEATURE ARTICLES

Nasal Epithelial Tight Junctions in Dust Mite Allergy

Recent studies have found disturbances of the tight junctions and their epithelial barrier function in asthma and chronic rhinosinusitis. This study examined the function, expression, and regulation of tight junctions in house dust mite (HDM)-induced allergic rhinitis (AR).

Experiments using air-liquid interface cultures of primary nasal epithelial cells from HDM-sensitized patients with AR found decreased transepithelial resistance, compared to cultures from control subjects. The AR cultures also showed increased permeability to fluorescein isothiocyanate-dextran 4 kDa (FD4) and reduced expression of occludin and zonula occludens-1 (ZO-1)—proteins involved in regulating the tight junction "leak pathway."

The extent of transepithelial resistance in cultures was inversely correlated with AR symptoms in individual patients. In vitro studies showed decreased resistance and increased FD4 permeability in response to interleukin-4 (IL-4), but not interferon-γ. The IL-4 effect on barrier dysfunction was blocked by fluticasone propionate. In an HDM-induced mouse model of allergic airway disease, fluticasone prevented an increase in mucosal permeability induced by allergen challenge.

These experiments show impaired epithelial integrity, increased permeability, and altered expression of occludin and ZO-1 in patients with HDM-induced AR. Epithelial integrity is disrupted by IL-4 in culture, while barrier function is restored by fluticasone in vitro and in an animal model. The authors suggest that the restoration of epithelial barrier integrity by intranasal steroids might involve upregulation of tight junction proteins.

COMMENT: Airway epithelium integrity is at least partially determined by the tight junctions between cells. • • •

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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 Asthma
- 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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These investigators showed that the defective nasal epithelial barrier in patients with HDM-induced allergic rhinitis was linked to reduced expression of the tight junction molecules occludin and ZO-1. Symptom severity correlated with nasal biopsy and ex vivo nasal mucosal barrier dysfunction. Nasal steroids improved barrier dysfunction through upregulation of the occludin and ZO-1 proteins. Interleukin-4 also disrupted barrier dysfunction in vitro, but this could be prevented with intranasal steroid as well. As our understanding of the mechanism of the epithelial barrier in allergic diseases improves, there could be new therapies developed to help our patients.

S.M.F.

Steelant B, et al: Impaired barrier function in patients with house dust mite-induced allergic rhinitis is accompanied by decreased occludin and zonula occludens-1 expression. J Allergy Clin Immunol. 2016;137:1043-1053.

Keywords: allergic rhinitis, house dust mite allergy

Impaired Lung Growth in Kids Predicts Impaired Lung Function in Adulthood

Trajectories of lung function from childhood to early adulthood have a major impact on lung function in later adulthood. There are few longitudinal data on abnormal patterns of FEV_1 growth and decline, particularly in asthma. This study used long-term follow-up data from the Childhood Asthma Management Program (CAMP) cohort to assess trajectories of lung growth and decline associated with persistent childhood asthma.

The analysis included 684 CAMP cohort members who had persistent, mild to moderate asthma as children. Analysis of spirometric studies performed from childhood (age 5 to 12) to the third decade of life identified four patterns of FEV_1 growth and decline. Twenty-five percent of subjects had normal lung function growth without early decline, 26% had reduced growth and early decline, 23% had reduced growth without early decline, and 26% had normal growth and early decline.

Factors associated with reduced lung function growth included lower baseline FEV_1, smaller bronchodilator response, baseline airway hyperresponsiveness, and male sex. At the last follow-up evaluation (mean 26 years), 11% of cohort members met lung function criteria for chronic obstructive pulmonary disease (COPD). A reduced pattern of lung function growth was noted for 18% of these subjects, compared to 3% of those not meeting COPD criteria.

Among children with persistent asthma, impaired childhood lung function and male sex are the main factors associated with abnormal lung function growth and decline. These factors may identify patients at risk of developing fixed airflow obstruction, and possibly COPD, before age 30. Serial monitoring of FEV_1 may identify young patients at risk of abnormal lung function growth who might develop chronic airflow obstruction in adulthood.

COMMENT: As specialists who treat children with asthma, we not only worry about controlling symptoms and asthma exacerbations, but also strive to optimize long-term lung growth. In this follow up study of CAMP study participants who had at least one spirometric measurement at 23 years of age or older, impaired lung function at enrollment and male sex were key predictors of abnormal patterns of • • •

lung-function growth and decline. A pattern of reduced growth was evident early in childhood in over half of the patients with mild to moderate, persistent asthma. The study adds justification to early and ongoing serial FEV_1 monitoring to identify these at-risk children. However, interventions that can alter the impairment in lung growth remain to be determined.

C.D.

McGeachie MJ, Yates KP, Zhou X, et al: Patterns of growth and decline in lung function in persistent childhood asthma.
N Engl J Med. 2016;374:1842-1852.

Keywords: asthma (childhood), COPD, lung growth

Sinusitis Has Endotypes Too!

Chronic rhinosinusitis (CRS) is typically phenotyped as CRS with or without nasal polyps. However, this clinical classification may not represent the full range of underlying immunologic profiles. Inflammatory endotypes of CRS were analyzed by biomarker cluster analysis.

The study by the GA²LEN Sinusitis Cohort study group included 173 case patients undergoing sinus surgery for CRS matched to 89 controls undergoing septal surgery. A wide range of inflammatory biomarkers were measured in tissue samples, and biomarker cluster analysis was performed in a phenotype-free approach. These endotypes were subsequently matched to clinical phenotypes and selected clinical parameters.

Ten clusters were identified, including four with low or undetectable levels of interleukin-5 (IL-5), eosinophilic cationic protein, IgE, and albumin; and six with high concentrations of these same biomarkers. Three of the four IL-5-negative clusters were associated with a clinical phenotype of CRS without nasal polyps, with no increased prevalence of asthma. The remaining IL-5-negative cluster was associated with a Th17 profile and mixed CRS with and without nasal polyps.

Of the IL-5-positive clusters, one group had moderate IL-5 concentrations, mixed CRS with and without nasal polyps, and increased prevalence of asthma. The other group had high IL-5 levels, CRS with nasal polyps almost exclusively, and a strongly increased asthma prevalence. Two of these clusters were associated with the highest IgE concentrations and the greatest increase in asthma prevalence, with all specimens testing positive for *Staphylococcus aureus* enterotoxin-specific IgE.

The findings illustrate the wide range of inflammatory endotypes in CRS. These inflammatory profiles are largely correlated with, and help to differentiate, the clinical phenotypes. The inflammatory mechanisms of CRS appear more diverse than previously thought.

COMMENT: These European researchers analyzed postsurgical tissue from patients with CRS to identify inflammatory endotypes based on cluster analysis of biomarkers. Of the clusters with higher IL-5, there were three with a moderate level of cytokines resulting in mixed-type phenotypes. Identifying inflammatory endotypes might help us with therapy decisions, particularly with newer biologics targeting specific biomarkers.

S.M.F.

Tomassen P, Vandeplas G, Van Zele T, et al: Inflammatory endotypes of chronic rhinosinusitis (CRS) based on cluster analysis of biomarkers.
J Allergy Clin Immunol. 2016;137:1449-1456.

Keywords: biomarkers, chronic rhinosinusitis, endotypes

Living near a Freeway May Stunt Lung Volume Growth in Children

Long-term exposure to air pollution is associated with adverse effects on childhood lung function. Studies performed since the implementation of air quality standards have suggested that children's lung function is improving as pollution decreases. This follow-up study analyzed the effects of lifetime exposure to ambient pollution on children's lung function.

The prospective cohort study included 614 mother-child pairs in the Boston area, enrolled between 1999 and 2002. Follow-up when the children were a median of 7.7 years included spirometry and bronchodilator response testing. The subjects' addresses were geocoded and analyzed for proximity to the nearest major roadway. Exposure to particulate matter smaller than 2.5 μm and to black carbon were estimated at different time points, and associations with mid-childhood lung function were assessed.

Living close to a major roadway, prior-year exposure to $PM_{2.5}$ and black carbon, and lifetime exposure to the same pollutants were significantly associated with lower forced vital capacity (FVC). Similar negative associations were observed for FEV_1. Ambient pollutant exposure was not significantly related to FEV_1/FVC ratio or bronchodilator response.

Children who lived within 100 m of a major roadway had a -98.6 mL decrement in FCV, compared to those living at least 400 m away. For each 2 $\mu g/m^3$ increase in prior-year $PM_{2.5}$, there was a -21.8 mL decrease in FVC and a 1.41-fold increase in the odds of FEV_1 less than 80% predicted. For each 0.2 $\mu g/m^3$ increase in prior-year BC, there was a 38.9 mL decrease in FVC.

Using data collected since recent improvements in air quality, this study finds that lifetime exposure to ambient air pollution is associated with reduced childhood lung function, but not with airflow obstruction. More recent exposures have greater effects on lung function; the associations are of similar magnitude for FEV_1 and FVC. Even within current air quality standards, exposure to fine particulates is associated with impaired lung function in children.

COMMENT: The body of evidence regarding early-life exposure to pollution continues to grow. Exposure to particulate matter and $PM_{2.5}$ irritants has significant effects on both lung growth (FVC) and obstruction (FEV_1). These data support findings from the USC group and reinforce the • • •

recent article in *JAMA* (2016;315:1491-1501). It is important to note that the expected growth in FVC of 200 mL/y in 7- to 10-year-olds is decreased by 50% in children living within 100 meters of a major roadway. This effect is obviated in children living more than 400 meters from a major roadway. The data are very important as they relate to public health regulations and our understanding of the effects of air pollution on the growing lung. (See the accompanying editorial: Am J Respir Crit Care Med. 2016;193:819-820.)

B.E.C.

Rice MB, Rifas-Shiman SL, Litonjua AA, et al: Lifetime exposure to ambient pollution and lung function in children.

Am J Respir Crit Care Med. 2016;193:881-888.

Keywords: air pollution, lung growth

FOCUS ON FOOD ALLERGY

Persistent Cow's Milk Allergy Lowers Bone Mineral Density

In children with cow's milk allergy (CMA), strict elimination diets may lead to limited calcium intake at a time of skeletal growth. This study compared bone mineral density (BMD), vitamin D status, and dietary calcium and vitamin D intake for children with persistent CMA versus other types of food allergy.

The study included 52 children with persistent CMA, mean 6.9 years, and 29 children of similar age with other food allergies. Both groups underwent measurement of BMD and plasma 25-dehydroxyvitamin D. Dietary calcium and vitamin D intake and compliance with recommended supplements were assessed as well.

Children with CMA had significantly reduced lumbar spine BMD *z* scores. Six percent of the CMA group had low BMD (*z* scores at least two standard deviations less than normal), compared to none of the controls. More than 60 percent of children with CMA had low calcium intake, although vitamin D status was similar between groups. Less than half of children in the CMA group were taking calcium and vitamin D supplements; among those who were taking supplements, compliance was good.

Prepubertal children with CMA may have low BMD, probably reflecting low calcium intake. The results support the importance of nutritional counseling and monitoring in this group of patients. Further studies are needed to determine the consequences of decreased BMD in children with CMA.

COMMENT: This study of children with persistent CMA confirms one of our fears—that restricting this important source of dietary calcium may adversely affect BMD. The prepubertal children in the study indeed had reduced lumbar spine BMD and calcium intake, despite similar vitamin D status and intake, compared to children of similar age with other food allergies. The clinical significance and long-term impact of this finding need to be further elucidated. However, with the increasing tendency of the general public (including those without true milk allergy) to avoid "dairy" products, providers may need to be proactively watchful for this issue.

C.D.

Mailhot G, Perrone V, Alos N, et al: Cow's milk allergy and bone mineral density in prepubertal children.

Pediatrics. 2016;137:e20151742.

Keywords: bone density, cow's milk allergy, food allergy

Socioeconomic Disparities in Food Allergy Care

Food allergies affect about 8 percent of US children, with high direct and indirect costs. Families may bear significant costs for prevention and treatment, such as for epinephrine autoinjectors and allergen-free foods. This study examined socioeconomic disparities in direct and out-of-pocket costs associated with childhood food allergies.

Caregivers of children with food allergies were surveyed regarding direct medical costs, out-of-pocket costs, and opportunity costs associated with their child's condition. The study included 629 families from a previous study of food allergy prevalence and 1,014 from a food allergy advocacy organization. The effects of household income and race/ethnicity on each category of costs were estimated.

Adjusted mean emergency department (ED) and hospitalization costs were $1,021 for children at the lowest income level, compared to $416 for higher-income families. In contrast, the lowest-income group had lower costs for specialist visits, approximately $228 versus $311; and lower out-of-pocket medication costs, $117 versus $366. African-American families had the lowest adjusted direct medical costs and out-of-pocket costs: $493 and $395, respectively.

Lower-income children with food allergies incur higher costs for ED and inpatient care, but lower costs for specialty care and medications. These disparities suggest that lower-income families may be at higher risk of adverse outcomes due to reduced access to essential care. African American-children may have a unique pattern of costs that is not completely explained by lower income.

COMMENT: It is critical for food-allergic children to have access to allergen-free foods to prevent allergic reactions, as well as to medications to treat reactions. It is therefore important to identify barriers to care. This survey identified multiple socioeconomic, racial and ethnic disparities in the economic impact of food allergy. Children in the lowest income stratum incurred 2.5 times higher costs for ED visits and hospitalizations than higher-income children. They also incurred lower costs for specialist visits and spent less on out-of-pocket costs for key preventive measures. Clinicians and policymakers need to ensure these children have access to specialty care, allergen-free foods, and emergency medica-

tions such as epinephrine autoinjectors.

C.D.

Bilaver LA, Kester KM, Smith BM, Gupta RS: Socioeconomic disparities in the economic impact of childhood food allergy.

Pediatrics. 2016;137:e2 0153678.

Keywords: costs, food allergies, socioeconomic disparities

How Do Families Adapt to Food Allergy?

Having a child with food allergy (FA) can have a major impact on families' anxiety level and quality of life. If excessive, anxiety can lead to high burden and family maladjustment. This study sought to identify patterns of adaptation among families affected by FA, including groups who could benefit from intervention.

The study included 57 children with FA, aged 6 to 12 years, and their mothers. Families were evaluated on the Food Allergy Management and Adaptation Scale and on measures of quality of life, anxiety, FA management, and psychosocial impairment. Hierarchical cluster analysis was performed to identify patterns of adaptation in terms of adequacy of family FA management, anxiety level, and balanced psychosocial functioning.

The analysis identified three hypothesized groups: balanced responders, accounting for 41% of families; high responders, 45%; and low responders, 5%. The high responders were highly competent in FA management, but had high anxiety with a potential impact on normal child and family functioning. The low responders had moderate anxiety, but shortfalls in food avoidance and knowledge about responding to reactions.

The remaining 9% of families fell into a fourth group, anxious high responders. This group was characterized by extremely high maternal anxiety and low scores for balanced integration of FA management and psychosocial functioning. The four clusters showed significant variations in illness characteristics and psychosocial outcomes.

The identified patterns help in understanding patterns of disease management, anxiety, and life balance for families affected by FA. Allergists can use this framework to guide discussions and advice regarding FA management, anxiety regulation, and life adjustments. Behavioral health referral may be helpful for families with very high anxiety or activity limitations.

COMMENT: Adaptation patterns among families of food-allergic children can be characterized along dimensions of FA management adequacy, optimal anxiety levels, and overall balance in family life. This approach allows identification of subsets of families in need of intervention. The authors encourage allergists to use clinical encounters to query and guide children and parents regarding strategies for FA management, anxiety regulation, and adjustments in daily life. Families reporting debilitating anxiety or excessive activity restriction may merit referral to behavioral health clinicians. Allergists and behavioral health clinicians can aid families in understanding that living with FA does not need not be an unbearable burden with negative family impacts, but rather an opportunity for proactive coping.

J.J.O.

Fedele DA, McQuaid EL, Faino A, et al: Patterns of adaptation to children's food allergies.

Allergy. 2016;71:505-513.

Keywords: anxiety, coping, food allergy

Nuts! Advice Doesn't Increase Non-Allergic Nuts in the Diet

A growing body of evidence suggests that avoidance of all nuts may not be beneficial for children with nut allergy. However, families may have difficulty introducing nuts to which the child isn't allergic into the diet. This study evaluated a dietary advice strategy to increase ingestion of "non-allergic" nuts.

The randomized, double-blind trial included 75 children and adolescents with confirmed or suspected nut allergy who had been advised to introduce one or more nuts into the diet after oral food challenge. One group received dietary advice in the form of a booklet, titled "Go Nuts!" providing information on nuts to be included in the diet, serving sizes, etc. Parents also received monthly text message reminders.

Controls received no additional advice. At six months' follow-up, both groups completed a survey on nut ingestion.

Overall, just 14% of children ingested non-allergic nuts as recommended (one or more nuts at one serving per week): 19% in the advice group and 9% in the control group. More than three-fourths introduced any kind of nut, with no difference between groups. Inclusion of nuts was more likely for children who underwent a nut challenge in the hospital (compared to home challenge), and less likely for those concerned about having a reaction. There was no significant change in quality of life scores; skin prick test results were unaffected by whether or not nuts were introduced.

Even with the dietary advice intervention, very few families of nut-allergic children introduced nonallergenic nuts into the diet. Children undergoing in-hospital challenge are more likely to follow advice on nut ingestion. The short-term study finds no effects on quality of life or tolerance acquisition.

COMMENT: Avoiding foods is an added burden to children and families affected by food allergy, impairing quality of life. This randomized study from Australia looked at the value of the "Go Nuts!" booklet about reintroducing nuts into the diet in children who passed a nut challenge. About 75% of children added nuts back into the diet, but having the booklet and getting text messages about eating nuts made

no difference. Children who passed a hospital-based as opposed to a home nut challenge were much more likely to have nuts in their diet (81% versus 38%). This emphasizes the importance of a controlled challenge to reassure patients and families.

D.A.K.

Norman M, South C, Quinn P, et al: Does providing written dietary advice improve the ingestion of non-allergic nuts in children with existing nut allergies?—a randomized controlled trial.
Clin Exp Allergy. 2016;46:741-748.

Keywords: allergen avoidance, education, food allergy, nut allergy

Should We Routinely Test AD Patients For Food Allergy?

Many children with atopic dermatitis (AD) also have food allergy. The risk is reportedly higher in patients with more severe AD; testing for food allergy is usually not recommended in children with mild AD. This study further examined the relationship between food allergy and AD, including the association between food allergens and AD exacerbations.

The researchers analyzed the results of 1,186 double-blind, placebo-controlled food challenges (DBPCFCs) in children with AD or other symptoms suggestive of food allergy. The tests were performed as part of regular care at a tertiary allergy clinic between 2001 and 2011. Assessment included telephone calls to identify late reactions 48 hours after challenge. The relationship between specific IgE results and food challenge outcomes was assessed in children with or without AD.

Children with a previous history of AD were more likely to be sensitized to foods: 75.8%, compared to 55.6% for those without a history of AD. This association was significant for children with previous or recurrent AD, but was stronger for those without current AD. Food challenges were positive in 53.3% of children with mild AD, 51.7% with moderate AD, and 100% with severe AD. Children whose only symptom was AD and a history of worsening AD were just as likely to react to placebo as to the challenge food. Exacerbations of AD in response to food challenge usually occurred together with other symptoms; delayed reactions (6 to 48 hours) were rare.

Children seen at an allergy clinic for a current history of AD are more likely to have asymptomatic sensitization to food allergens, compared to children without AD. The results suggest that food challenge should be considered in children with suspected food allergy, regardless of AD severity. Children who have AD exacerbations without a history of other symptoms are unlikely to have food allergy.

COMMENT: Studies have shown varying degrees of food allergy among patients with AD. These authors recommend that children with a history suggesting possible food allergy be tested regardless of AD severity. More than half of children with mild AD and suspected food allergy had positive double-blind, placebo-controlled food challenge. Interestingly, the AD patients in this study rarely had eczematous reactions during food challenge. The authors remind us that AD without other symptoms is not likely due to food allergy, which helps the practicing allergist in speaking with parents regarding this disease.

V.H.-T.

Roerdink EM, Flokstra-de Blok B, Blok JL, et al: Association of food allergy and atopic dermatitis exacerbations.
Ann Allergy Asthma Immunol. 2016;116:334-338.

Keywords: atopic dermatitis, food allergy, food challenge

Symptomatic Smokers with Normal Lung Function Can Be COPD-Like

Some patients who smoke have symptoms suggestive of chronic obstructive pulmonary disease (COPD)—cough, sputum production, and shortness of breath—without meeting lung function criteria for airway obstruction. This study examined the clinical significance of respiratory symptoms in smokers with preserved pulmonary function.

The COPD Assessment Test was used to measure respiratory symptoms in 2,736 current or former smokers and a nonsmoking control group. Subjects with a CAT score of 10 or higher were considered to have respiratory symptoms. On spirometry, those with a FEV_1/FVC ratio of 70 or greater and a postbronchodilator FVC above the lower limit of normal were considered to have preserved pulmonary function.

One-half of current or former smokers with preserved pulmonary function met the study definition of respiratory symptoms. For this group, the rate of respiratory exacerbations was 0.27 events per year, compared to 0.08 per year for asymptomatic smokers and 0.003 per year for nonsmoking controls. The symptomatic smokers also had more activity limitations; slightly decreased FEV_1, FVC, and inspiratory capacity; and increased airway wall thickening without emphysema, compared to asymptomatic smokers. Bronchodilator use was reported by 42% of symptomatic smokers, while 23% were using inhaled glucocorticoids.

Many current or former smokers with preserved pulmonary function have respiratory symptoms, associated with an increased risk of exacerbations, activity limitations, and other evidence of airway disease. Some of these patients are receiving respiratory medications in the absence of evidence-based criteria.

COMMENT: Smokers with symptoms and normal lung functions are a challenge to the practicing provider since they do not meet the criteria that help to classify their disease severity. This large observational study included current or former smokers with preserved pulmonary function, who thus did not meet the criteria for COPD. Symptomatic individuals were found to have significant numbers of exacerbations, activity limitation, and evidence of airway disease • • •

compared to nonsmoking controls. These patients were also using a variety of respiratory medications without any evidence base. Spirometry therefore does not appear to be the best method of picking up such individuals. Clearly further study of this patient subgroup is needed to ensure they get the appropriate treatment.

C.D.

Woodruff PG, Barr RG, Bleecker E, et al: Clinical significance of symptoms in smokers with preserved pulmonary function.
N Engl J Med. 2016;374:1811-1121.

Keywords: COPD, smoking

Anaphylaxis in Children: The Latest

The diagnosis of anaphylaxis can be challenging to make, highlighting the need for reliable biomarkers. Mast cell mediators such as tryptase may be useful in this regard. This study assessed the value of tryptase levels before and after anaphylactic episodes in children.

The study included 965 children with anaphylaxis seen at a Canadian children's hospital from 2011 to 2015. In 203 children, tryptase levels were measured within 2 hours after the reaction. Tryptase levels before and after anaphylaxis were analyzed, including factors associated with an elevated reaction tryptase level. Post-reaction tryptase levels (1 to 10 months later) were measured in 68 children.

An elevated tryptase level of 11.4 μg/L or greater was found in 19.2% of children. Elevated tryptase levels were found in 50% of children with severe anaphylaxis, compared to 16.2% of those with moderate or mild reactions. Factors associated with increased tryptase during the reaction were severe reactions, beta-adjusted odds ratio (OR) 7.5; and reactions to milk, OR 4.0. Tryptase reaction levels greater than the threshold of 2 ng/mL + 1.2 × (postreaction tryptase level) identified most cases of anaphylaxis, especially if the post-reaction level was measured within 2 months after the episode.

Tryptase is not a sensitive biomarker of anaphylaxis in children. However, it may be of diagnostic value in children with severe reactions, particularly to milk. Comparing tryptase levels during and after the reaction may improve sensitivity.

Pediatric anaphylaxis is a potentially life-threatening but clinically variable condition. It may differ in children and adolescents versus adults, highlighting the need for specific research and targeted guidelines. This report summarizes data on pediatric patients from the European Anaphylaxis Registry, focusing on severe reactions.

The data included 1,970 pediatric patients with anaphylaxis referred to 90 European allergy centers, with oversampling of the most severe reactions. Forty-six percent of reactions occurred in private homes while 19% occurred outdoors. One-third of patients had previous anaphylactic reactions. Triggering allergens were foods in 66% of cases and insect venom in 19%. Reactions to cow's milk and hen's egg were common in children up to age 2, hazelnut and cashew in preschool-aged children, and peanut in all age groups. Reactions to insect venom and drugs increased, while reactions to food decreased, up to 10 years.

Vomiting and cough were common symptoms in children up to age 10, with subjective symptoms such as nausea, throat tightness, and dizziness becoming more common thereafter. Non-healthcare personnel treated 30% of reactions, including epinephrine autoinjector use in 10% of cases. In professional settings, the use of intramuscular epinephrine increased from 12% in 2011 to 25% in 2014. The diagnostic workup was similar across age groups, with most patients undergoing skin testing and specific IgE measurement. Life-threatening or fatal reactions occurred in 1.3% of patients. These severe reactions occurred in all age groups and had eliciting factors similar to those among the most severe reactions.

These registry data provide a population-based update on pediatric anaphylaxis. The findings highlight the importance of anaphylactic reactions to foods in younger children, and to insect venom in older children and adolescents. Life-threatening or fatal anaphylaxis occurs in about 1 out of 100 severe reactions.

COMMENT: These two studies focus on anaphylaxis in children. The first analyzed tryptase levels obtained during anaphylaxis treated at a pediatric hospital. Although tryptase was elevated in only 19% of cases (when available), it was elevated in 50% of severe anaphylaxis cases versus 16% of mild or moderate reactions. There was some benefit in comparing these elevated levels to post-episode tryptase levels about 8 months later. The authors do recommend measuring tryptase, despite its limited diagnostic utility. They suggest it may be helpful to check tryptase again 8 months after the episode.

The second report includes data from an 8-year surveillance of European tertiary allergy centers identifying 1,970 children and adolescents with anaphylaxis. Not surprisingly food was the major elicitor—particularly milk and egg in younger children, and tree nuts in preschoolers. Interestingly, 30% of reactions were initially treated by a layperson. Epinephrine was used in 10% of preschoolers and 19% of adolescents; in 37% of the adolescents, epinephrine was self-administered. The fact that epinephrine use increased from 12% in 2011 to 25% in 2014 is reassuring that our educational efforts may be helping improve treatment in these patients.

S.M.F.

De Schryver S, Halbrich M, Clarke A, et al: Tryptase levels in children presenting with anaphylaxis: temporal trends and associated factors.J Allergy Clin Immunol. 2016;137:1138-1142.
Grabenhenrich LB, Dölle L, Moneret-Vautrin A, et al: Anaphylaxis in children and adolescents: the European Anaphylaxis Registry.
J Allergy Clin Immunol. 1016;137:1128-1137.

Keywords: anaphylaxis, food allergy, venom allergy

Obese Adults More Likely To Have Non-Allergic Rhinitis

There is a strong association between asthma and obesity in both children and adults. However, studies of the relationship between obesity and rhinitis have been inconsistent. Nationally representative US data were used to examine the association between obesity and rhinitis.

The analysis used data on 8,165 children and adults from the 2005-06 National Health and Nutrition Examination Survey (NHANES). The study definition of allergic rhinitis (AR) was physician-diagnosed hay fever or allergy, symptoms in the past year, and one or more positive allergen-specific IgE level. For non-allergic rhinitis, the definition was physician diagnosis and symptoms without positive specific IgE. Associations of obesity with both types of rhinitis were evaluated by multivariate regression analysis.

Nonallergic rhinitis was more likely to be present in adults who were either overweight or obese: adjusted odds ratio (OR) 1.43. Nonallergic rhinitis was also associated with central obesity: OR 1.61. On sex-stratified analysis, the associations were significant only in men. Obesity and overweight were not associated with an increased risk of AR in adults.

Children with central obesity were less likely to have AR: adjusted OR 0.35. This association was significant for both boys and girls. Obesity measures were unrelated to nonallergic rhinitis in children.

Obese adults, especially men, are more likely to have nonallergic rhinitis. In children, central obesity is inversely associated with allergic rhinitis. The temporal associations between obesity and rhinitis remain unclear. The authors suggest that allergy testing may be indicated in obese adults with symptoms of rhinitis.

COMMENT: The link between asthma and obesity is well-established, particularly for nonatopic asthma. Using NHANES data from 2005-06, these authors investigated the link between obesity and rhinitis. In adults who are overweight or obese, as well as those with central obesity, there was an increased risk of nonallergic rhinitis, but not AR. This association was not found in children, although children with central obesity did have a 65% reduction in odds of developing AR. The authors suggest that the Th1 predominant phenotype with chronic inflammatory changes found in obese patients may contribute to this association.

S.M.F.

Han Y-Y, Forno E, Gogna M, Celedón JC: Obesity and rhinitis in a nationwide study of children and adults in the United States.
J Allergy Clin Immunol. 2016;137:1460-1465.

Keywords: allergic rhinitis, nonallergic rhinitis, obesity, risk factors

More on the Hygiene Hypothesis...

Growing up on a farm has protective effects against childhood asthma and early wheezing. A genetic polymorphism at 17q21 is associated with increased asthma risk for infants who develop virus-associated wheezing. Environmental risk factors for infections and wheezing during infancy were assessed, including the possible modifying effect of 17q21.

The study used data on a cohort of children in rural areas of Europe, followed up from birth to age 6. Genotyping for single nucleotide polymorphisms at 17q21 (SNP rs8076131 in *ORMDL3* and SNPs rs2290400 and rs7326389 in *GSCMB*) was performed in cord blood. Information on wheezing, rhinitis, fever, and environmental factors up to age 1 was assessed from weekly diaries. Asthma was assessed by physician diagnosis at age 6.

For infants with known asthma risk alleles at 17q21, having older siblings was associated with wheezing during the first year of life: adjusted odds ratio (OR) 1.53. Wheezing was less likely for children exposed to animal sheds: OR 0.44. Both the presence of siblings and exposure to animal sheds affected transient wheezing up to age 3 in children who did not go on to develop asthma.

The SNPs at chromosome 17q21 appear to be related to both transient wheezing and asthma. The results show that the effects of these alleles are affected by environmental factors. If the genetic risk factor is amenable to environmental modification, it may have implications for preventive strategies.

COMMENT: This study expands our understanding of the hygiene hypothesis. When patients with asthma risk genotype 17q21 (rs8076131 AA/GA) are exposed to farm animals early in life, there is a significant protective effect. However, when the same subjects contract a viral infection early in life, asthma is more likely to occur. This finding in patients with this asthma risk genotype is extremely important in our quest to understand the determinants for inception and persistence of wheezing and may lead us to more targeted precision medicine in the future. (See the accompanying editorial: Am J Respir Crit Care Med. 2016;193:821-822.)

B.E.C.

Loss GJ, Depner M, Hose AJ, et al: The early development of wheeze: environmental determinants and genetic susceptibility at 17q21.
Am J Respir Crit Care Med. 2016;193:889-897.

Keywords: asthma, farm environment, hygiene hypothesis, risk factors

Ads Affect e-Cigarette Use by Teens

Use of electronic cigarettes among US students has increased dramatically in recent years, and marketing and advertising have likely contributed to this trend. Data from the National Youth Tobacco Survey were used to assess the relationship of e-cigarette advertising and use among US middle and high school students.

The data included survey responses from about 22,000 students in grades 6 through 12. Exposure to e-cigarette ads on the Internet, in newspapers and magazines, in stores, and on movies and TV was assessed. Associations with e-cigarette use were estimated, with adjustment for sex, race/ethnicity, grade, and tobacco use.

Students who said they were exposed to e-cigarette ads most of the time/always were more likely to use e-cigarettes, compared to those exposed never/rarely: adjusted odds ratio 1.44 for middle schoolers and 1.49 for high schoolers. For those exposed sometimes, the odds ratios were 2.91 and 2.02, respectively. Advertising on the Internet and in stores was associated with e-cigarette use in middle schoolers. All four kinds of advertising were significant for high schoolers.

Exposure to e-cigarette advertising is associated with increased use of e-cigarettes by adolescents. Reducing exposure to advertising should be part of efforts to prevent all tobacco use among youth.

COMMENT: We are well aware that there has been an alarming uptick in the use of e-cigarettes in US children and youth. Advertising targeted to young people—using themes such as rebellion, freedom, independence, and glamour—is being used to promote the sale of e-cigarettes. These 2014 survey data affirm the suspicion that greater exposure to e-cigarette advertisements in multiple venues is associated with higher odds of current e-cigarette use by US middle and high school students. This study certainly adds weight to the recent FDA regulation banning the sale of e-cigarettes to children.

C.D.

Singh T, Agaku IT, Arrazola RA, et al: Exposure to advertisements and electronic cigarette use among US middle and high school students.
Pediatrics. 2016;137:e20154155.

Keywords: e-cigarettes, prevention, smoking

Study Shows Mast Cell Subtypes in Asthma

Mast cells are thought to play an important role in asthma, and particularly in severe, uncontrolled disease. However, their contributions to the biology of different asthma inflammatory phenotypes are unclear. This study examined relationships among airway mast cells, inflammatory phenotypes, and response to treatment in asthma.

Induced sputum samples from 55 patients with stable asthma were analyzed, including inflammatory cell counts and gene expression microarrays. Molecular phenotyping of mast cells was performed, based on mRNA expression of genes for tryptase *(TPSAB1),* chymase *(CMA1),* and carboxypeptidase A3 *(CPA3).* The results identified a MC_T subtype in 18 patients and an $MC_{T/CPA3}$ subtype—with expression of *TPSAB1* and *CPA3*—in 29 patients. The remaining 8 patients had no mast cell gene expression.

Patients with the $MC_{T/CPA3}$ subtype had worse asthma control, increased bronchial sensitivity and reactivity, higher exhaled nitric oxide, and increased sputum eosinophil count. They also showed upregulation of 13 genes. On multivariable analysis, $_{CPA3}$ was associated with eosinophilic asthma (odds ratio 1.21), while $_{TBSAB1}$ was not. Patients in the $MC_{T/CPA3}$ group had a better clinical response and reduced signature gene expression in response to corticosteroids.

This study identifies different mast cell subtypes in patients with stable asthma. The $MC_{T/CPA3}$ subtype is most common, and is associated with increased bronchial sensitivity and reactivity, airway eosinophilia, and increased corticosteroid responsiveness.

COMMENT: T-helper 2-high asthma is associated with increased numbers of airway mast cells. Mast cells that have expression of both tryptase and carboxypeptidase A3 genes are associated with increased markers of eosinophilic airway injury and more significant bronchial hyperreactivity. This raises the possibility that a more feasible blood-based biomarker might help to determine response to therapy in patients treated with inhaled corticosteroids. (See the accompanying editorial:Eur Respir J. 2016;47:1040-1042.)

B.E.C.

Wang G, Baines KJ, Fu J, et al: Sputum mast cell subtypes relate to eosinophilia and corticosteroid response in asthma.
Eur Respir J. 2016;47:1123-1133.

Keywords: asthma (adult), mast cells, phenotypes

Bronchial Remodeling in Some Patients with Nonsevere Asthma

Severe asthma is thought to involve increased bronchial smooth muscle mass (BSM), with proliferation of BSM cells occurring via a mitochondria-dependent pathway. Few studies have looked at these processes in nonsevere asthma. This study examined the role of increased BSM mass and mitochondrial biogenesis in nonsevere asthma.

The "Mitasthme" study included 34 never-smokers with nonsevere asthma from one French medical center, along with 56 subjects with nonsevere asthma and 19 with severe asthma from a cohort study. Asthma phenotypes were assessed by questionnaires, pulmonary function and atopy testing, exhaled nitric oxide measurement, and blood sampling. Bronchial biopsy specimens were analyzed for BSM remodeling and mitochondrial biogenesis.

Some patients with nonsevere asthma had evidence of remodeling, with BSM area greater than the median value of 26.6%, together with increased mitochondrial number within the BSM. There was a significant positive correlation between the number of BSM mitochondria and the BSM area. At 12 months' follow-up, high BSM was associated with poorer asthma control and a higher exacerbation rate.

The presence of BSM remodeling in nonsevere asthma is associated with an increased mitochondrial number, as well as an increased exacerbation rate and other adverse clinical outcomes. Noninvasive approaches to measuring bronchial remodeling are needed, particularly in patients with nonsevere asthma.

COMMENT: Dr. Andy Bush's group first described air-

way smooth muscle remodeling in preschool children as a predictor of persistent asthma at school age (J Allergy Clin Immunol. 2013;131:1024-1032). Smooth muscle bulk may be a new way to endotype asthma and predict which patients are at risk for asthma attacks. It should be noted that BSM remodeling is not clearly associated with concomitant eosinophilia or longstanding disease. These data are important to help expand our understanding of the vast majority of asthmatics who have less severe disease. (See the accompanying editorial: Am J Respir Crit Care Med. 2016;193:596-598.)

B.E.C.

Girodet P-O, Allard B, Thumerel M, et al: Bronchial smooth muscle remodeling in nonsevere asthma.

Am J Respir Crit Care Med 2016;193:627-633.

Keywords: airway remodeling, asthma (adult), asthma (severe)

Exhaled NO Has Poor Utility in Asthmatic Smokers

Exhaled nitric oxide and blood eosinophil count are commonly used markers of airway inflammation in asthma. This study examined the relationship between these biomarkers and asthma in smokers versus nonsmokers.

The cross-sectional study included data on exhaled NO and blood eosinophils from a general population sample of middle-aged adults. Allergic asthma was present in 5.1% of the study population and nonallergic asthma in 2%. Only about 16% of asthmatic subjects were using inhaled corticosteroids, suggesting that most had mild asthma. Relationships of exhaled NO and blood eosinophils with atopy and asthma were assessed, with stratification for smoking status.

In multivariate models explaining exhaled NO and blood eosinophils, there was a positive interaction between smoking status and allergic asthma. Exhaled NO and blood eosinophil count were both about 63% higher in subjects with allergic asthma—but only in never and former smokers, not in current smokers. On receiver-operating characteristic curve analysis, both markers were able to distinguish allergic asthma only in nonsmokers.

The results suggest that exhaled NO and blood eosinophil count are associated with mild allergic asthma only in nonsmoking patients. The findings question the value of these two inflammatory biomarkers in asthmatic patients who smoke.

COMMENT: Exhaled NO and blood eosinophil count are useful noninvasive measures in asthma, but have not been as well studied in asthmatics who smoke. This study examined the relationship between both exhaled NO and blood eosinophils in atopic and nonatopic asthmatics, stratified by smoking status. Both markers were associated with the presence of mild allergic asthma only in nonsmokers—not in current smokers. The findings raise questions about the clinical value of exhaled NO and blood eosinophils in smoking asthmatics. Sadly, this represents just one more impediment in our quest to find the perfect single measure of inflammation in asthma.

J.J.O.

Giovannelli J, Chérot-Kornobis N, Hulo S, et al: Both exhaled nitric oxide and blood eosinophil count were associated with mild allergic asthma only in smokers.

Clin Exp Allergy. 2016;46:543-554.

Keywords: asthma (adult), biomarkers, smoking

Ranitidine Anaphylaxis–Really!

The H_2 receptor antagonist ranitidine is widely used for treatment of gastroesophageal reflux disease, chronic urticaria, and other conditions. This drug is regarded as safe, although there have been few studies of adverse drug reactions. A series of 99 patients with ranitidine-induced anaphylaxis is presented.

Using a Korean drug safety database, the researchers identified 584 patients with adverse reactions to ranitidine from 2007 to 2014. Cutaneous symptoms were the most common type of adverse reaction, accounting for nearly 40% of events. The 99 cases of anaphylaxis represented 14.3% of events, making it the third most common category. Forty-one cases of ranitidine anaphylaxis were only recognized retrospectively.

On evaluation of 23 patients, 91.7% had positive ranitidine skin-prick tests. More than 80% of patients were exposed again because ranitidine was overlooked as the cause of anaphylaxis. Six of six patients had acute reactions to oral ranitidine challenge. Cimetidine and proton pump inhibitors did not cross-react with ranitidine.

This pharmacovigilance study suggests a 0.003% incidence of ranitidine-induced anaphylaxis. Skin-prick testing for this rare cause of anaphylaxis is sensitive and specific.

COMMENT: Ranitidine is a commonly used H_2 receptor antagonist that is generally thought to be safe. This study from Korea found 99 cases of anaphylaxis over an 8-year period. Ranitidine skin prick tests were surprisingly sensitive at 91%. Cimetidine appeared to be well tolerated in a limited number of patients. The vast majority of anaphylactic patients were given ranitidine again as it was overlooked as a cause. While the incidence of anaphylaxis to ranitidine is low (0.0003%), it should not be dismissed as a potential culprit in patients with anaphylaxis.

D.A.K.

Park KH, Song D-G, Sim DW, et al: Ranitidine-induced anaphylaxis: clinical features, cross-reactivity, and skin testing.

Clin Exp Allergy. 2016;46:631-639.

Keywords: anaphylaxis, drug allergy

FOCUS ON BIOMARKERS

Surfactant-D: A New Biomarker in Severe Asthma?

Surfactant protein-D (SP-D) is an essential part of the innate immune system in the distal airway, and also plays roles in regulating allergic inflammation and removing apoptotic cells. This study looked for evidence of SP-D dysregulation in severe, treatment-resistant asthma.

The study included 28 patients with severe asthma, 22 with mild asthma, and 10 healthy controls. Bronchoalveolar lavage (BAL) showed lower SP-D levels in samples from patients with severe asthma, compared to the mild asthma or control groups. In severe asthma, SP-D levels in BAL fluid were inversely correlated with BAL eosinophil cationic protein concentrations.

Patients with severe asthma also had increased serum SP-D levels and lower BAL/serum ratios. The high serum and low BAL SP-D levels in severe asthma represented degraded fragments of SP-D in serum and increased neutrophil counts and lipopolysaccharide levels in BAL.

The results suggest reduced airway SP-D concentrations in patients with severe asthma, which may increase the effect of airway eosinophilic inflammation. Serum SP-D levels are elevated, providing a potential biomarker of treatment-resistant asthma. With further study, airway replacement of SP-D might offer a new approach to treatment for severe asthma.

COMMENT: Surfactant-D is an important component of innate immunity in the airway. This study compared SP-D levels in BAL and serum in patients with severe asthma versus mild asthma and controls. Surfactant-D levels were increased in serum but lower and fragmented in the airway of severe asthma patients. Further research is still needed to confirm the findings, but this work suggests that SP-D may be a potential biomarker—and replacement could be a potential therapeutic option—in refractory severe asthma.

D.A.K.

Mackay R-MA, Grainge CL, Lau LC, et al: Airway surfactant protein D deficiency in adults with severe asthma.
Chest. 2016;149:1165-1172.

Keywords: asthma (severe), biomarkers

EPX–The Next Asthma Marker?

There is a need for less-invasive, accurate biomarkers of airway eosinophilia to guide changes in asthma therapy. Eosinophil peroxidase (EPX) is a secondary granule unique to eosinophils that correlates closely with sputum eosinophil count. Nasal and pharyngeal EPX levels were compared with sputum eosinophil percentage in patients with asthma.

An enzyme-linked immunosorbent assay was used to measure EPX (normalized for g of protein) in nasal and pharyngeal specimens from 10 adults with poorly controlled asthma and 10 healthy controls. Induced sputum samples were obtained for measurement of EPX (normalized for mL-g of protein) and sputum eosinophil percentage.

Levels of EPX were significantly different between asthma patients and controls in all three samples compared. Nasal and pharyngeal EPX levels were strongly correlated with induced sputum eosinophil percentage, with Spearman correlation coefficients of 0.81 and 0.78, respectively.

Nasal and pharyngeal EPX measurements reflect the induced sputum eosinophil percentage in patients with poorly controlled asthma. Minimally invasive measurement of EPX may provide a simple and clinically relevant point of care test for asthma management.

COMMENT: Measurement of induced sputum eosinophils is considered the gold standard metric of inflammation in asthma for adjusting asthma therapy. However, it has limited use in clinical medicine in light of the fact that it requires technical expertise and is labor intensive. This study demonstrates that the use of a nasal and pharyngeal swab assayed for EPX levels may represent a clinically useful and easy to use diagnostic measure of inflammation in the management of asthmatic patients. The authors suggest that this may be of greatest utility in the management of pediatric patients, where the diagnostic tools available to clinicians are more limited.

J.J.O.

Rank MA, Ochkur SI, Lewis JC, et al: Nasal and pharyngeal eosinophil peroxidase levels in adults with poorly controlled asthma correlate with sputum eosinophilia.
Allergy. 2016;71:567-570.

Keywords: asthma (adult), biomarkers

FOCUS ON COPD

ACOS: Clinical Differences from COPD

Patients with asthma-COPD overlap syndrome (ACOS) have symptoms of both disorders, but the characteristics of ACOS seen in routine clinical care are unclear. This study assessed the prevalence of ACOS in a "real world" population, including patterns of comorbid conditions and hospitalization rates.

The retrospective analysis included 5,093 patients with physician-diagnosed ACOS and 22,778 with COPD, identified from the Majorca Real-Life Investigation in COPD and Asthma cohort. Population prevalence was 5.55 per 1,000 inhabitants for ACOS and 30.40 per 1,000 for COPD.

Women accounted for 53.4% of ACOS patients versus 30.8% of those with COPD. The ACOS group was younger, 64.0 versus 65.8 years, and had a higher rate of non-

smoking status, 41.4% versus 22.1%. Comorbid conditions that were more common in ACOS were allergic rhinitis, odds ratio (OR) 1.81; anxiety, OR 1.18; gastroesophageal reflux disease (GERD), OR 1.18; and osteoporosis, OR 1.14. The ACOS patients were less likely to have chronic kidney disease or ischemic heart disease: OR 0.79 and 0.88, respectively. Cardiovascular disease had a strong effect on hospitalization risk in the ACOS group.

These population-based data suggest that ACOS is a relatively common condition that affects more women, younger patients, and patients with lower exposure to smoking, compared to COPD. A diverse range of comorbid conditions are more common among patients with ACOS. Important causes of hospitalization in this group include cor pulmonale, heart failure, ischemic heart disease, atrial fibrillation, and lung cancer.

COMMENT: Asthma-COPD overlap syndrome is an evolving syndrome with variable definitions. This study of a large population from the Balearic islands in Spain evaluated ACOS patients (diagnosed with both COPD and asthma) and compared them to COPD patients. Patients with ACOS accounted for 18% of all COPD patients. The ACOS patients were younger, more often female, had lower smoking histories and had higher rates of allergic rhinitis, GERD, and anxiety. Not surprisingly, chronic kidney disease and heart disease were more common in COPD. Subgroup analysis using a more stringent definition of ACOS led to similar findings. Although optimal therapy for ACOS is unclear, simply identifying those COPD patients with a prior diagnosis of asthma may be adequate to make a diagnosis of ACOS.

D.A.K.

van Boven JFM, Roman-Rodriguez M, Palmer JF, et al: Comorbidome, pattern, and impact of asthma-COPD overlap syndrome in real life.
Chest. 2016;149:1011-1020.

Keywords: asthma-COPD overlap syndrome, COPD

Blood Eosinophils Affect Response to Inhaled Steroids in COPD

Some evidence suggests that chronic obstructive pulmonary disease (COPD) patients with higher blood eosinophil counts are more likely to have exacerbations if they stop inhaled corticosteroid (ICS) therapy. This question was tested using data from a randomized trial of ICS withdrawal in COPD.

The study included 2,296 patients with severe COPD from the "Withdrawal of Inhaled Steroids During Optimised bronchodilator Management" (WISDOM) trial who were randomly assigned to ICS withdrawal or continuation. Exacerbation rates were compared for patients with differing blood eosinophil levels.

The increase in moderate to severe exacerbation risk after ICS withdrawal was greater in patients with higher blood eosinophil counts. Rate ratios for exacerbation were 1.22 for patients at an eosinophil percentage of 2% or greater, 1.63 at 4% or greater, and 1.82 at 5% or greater. The treatment by subgroup interaction was significant only in the 4% and 5% eosinophil groups. Similar increases in exacerbations were noted above eosinophil counts of 300 and 400 cells/μL.

In patients with severe COPD, the baseline blood eosinophil count may predict the risk of exacerbations after ICS withdrawal. Moderate to severe exacerbations are more likely to occur after stopping ICS in patients at or above blood eosinophil thresholds of 4% or 300 cells/μL.

COMMENT: Just as in the case of asthma, those caring for patients with COPD continue to strive to determine measures to help better stratify response to therapy. Several recent studies have demonstrated that subjects with COPD with elevated peripheral eosinophil counts are more likely to benefit from the addition of ICS. This study offers further proof, demonstrating that patients with eosinophil counts of 4% or greater, or 300 cells/μL or more, are more likely to suffer a moderate to severe exacerbation with ICS withdrawal.

J.J.O.

Watz H, Tetzlaff K, Wouters EFM, et al: Blood eosinophil count and exacerbations in severe chronic obstructive pulmonary disease after withdrawal of inhaled corticosteroids: a post-hoc analysis of the WISDOM trial.
Lancet Respir Med. 2016;4:390-398.

Keywords: COPD, eosinophils, exacerbations

REVIEW OF NOTE

COMMENT: The increasing incidence of pediatric obesity-related asthma, particularly in ethnic minorities, makes it important for us to learn about appropriate prevention and treatment for these young patients. This excellent review helps us understand the genetic and epigenetic factors that may underlie susceptibility to metabolic dysregulation and concomitant pulmonary morbidity. The authors suggest a simple clinical screening test: evaluation of truncal adiposity by measuring waist circumference in children who are overweight/obese, and then flagging them for evaluation for metabolic of dysregulation and pulmonary function.

C.D.

Vijayakanthi N, Greally JM, Rastogi D, et al: Pediatric obesity-related asthma: the role of metabolic dysregulation.
Pediatrics. 2016;137:e20150812.