NOT FOR CREDIT

allergywatch®

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

American College of Allergy, Asthma & Immunology

A PUBLICATION OF THE AMERICAN COLLEGE OF ALLERGY, ASTHMA & IMMUNOLOGY

Volume 19, Number 3 • May-June 2017

FEATURE ARTICLES

Treating Obese Asthmatics –Weight Loss Plus Exercise Works!

For obese patients with asthma, weight loss may help to improve clinical control. There are few data on the potential benefits of exercise for obese asthma patients. This randomized trial evaluated an exercise training program for obese patients with asthma, focusing on asthma control and quality of life.

The study included 55 patients with a moderate/severe asthma and a body mass index between 35 and 40 kg/m^2. All received a weight loss intervention consisting of nutritional counseling and behavioral therapies. In addition, one group received an exercise training program including both aerobic and resistance muscle training: two sessions per week for 3 months. A sham control intervention consisted of breathing and stretching exercises,

At 3 months, patients assigned to weight loss plus exercise lost a mean 6.8% of body weight, compared to 3.1% in the control group. The exercise group also had greater improvement in aerobic capacity: 3.0 versus 0.9 mL/kg/min. Asthma Control Questionnaire score improved from 2.0 to 1.1 in the exercise training group, compared to no significant change for controls. Rates of clinically significant improvement in asthma control were 69% and 36%, respectively.

The exercise group also had greater improvement in asthma-specific quality of life scores. Improvements in asthma control were associated with reductions in fat mass and inflammatory biomarkers and increases in lung function, lean mass, aerobic fitness, anti-inflammatory biomarkers, and adiponectin.

Added to a weight loss intervention, an exercise training program can improve disease control in obese patients with asthma. The mechanism of this benefit appears to involve improvements in lung function along with anti-inflammatory effects. • • •

2017 Editor-in-Chief Disclosure:
Stephen A. Tilles, MD, Editor-in-Chief, Research Grants: Amgen, Astellas, Astrazeneca, Boehringer Ingelheim, Circassia, DBV Technologies, Genentech, Immune Tolerance Network (NIH), Merck, Mylan, Novartis, Pulmagen, Stanford Univ., Gilead, Teva, Aimmune, Biota (Full editorial board disclosures can be found at college.acaai.org/aw-editors)

AstraZeneca

TEVA Respiratory

This activity has been supported through independent educational grants from AstraZeneca and Teva Pharmaceuticals.

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

"AllergyWatch®" is an official publication and a registered trademark of The American College of Allergy, Asthma & Immunology and is published six times per year in one volume. Subscription rates: U.S., Individual $120.00 Outside the U.S.: $150.00, Residents, Fellows, Students within the U.S.: $85.00, outside the U.S., add $30.00, bulk subscription pricing available upon request of the publisher. Send subscription inquiries to AllergyWatch®, 85 West Algonquin Road, Suite 550, Arlington Heights, IL, 60005. Address editorial enquiries to: AllergyWatch®, c/o Stephen A. Tilles, MD., Editor, The Northwest Asthma and Allergy Center,, 9725 Third Ave. NE, Suite 500, Seattle, WA 98115. Telephone (206) 527-1200 ISSN 1521-2440.

COMMENT: Weight loss has been shown to be a very important non-pharmacologic intervention to improve quality of life and physiology in asthma. Body weight reduction of approximately 3.5% (5% to 10% body weight loss) may relate to significant improvement not in only airflow limitation and quality of life but also in exercise tolerance, as exemplified by increased oxygen consumption. These data suggest that reduction in systemic airway inflammation related to obesity may be appropriately addressed without requiring pharmacologic intervention. (See the accompanying editorial by Wood: Am J Respir Crit Care Med. 2017;195:4-5.)

B.E.C.

Freitas PD, Ferreira PG, Silva AG, et al: The role of exercise in a weight-loss program on clinical control in obese adults with asthma: a randomized controlled trial.
Am J Respir Crit Care Med. 2017;195:32-42.

Keywords: asthma (adult), obesity, weight loss

Prenatal Fish Oil to Prevent Asthma–More Evidence

Prenatal supplementation with long-chain n-3 polyunsaturated fatty acids (n-3 PUFAs) may affect function of the fetal immune system via anti-inflammatory pathways. A previous randomized trial linked fish oil supplementation in pregnancy to fewer asthma discharge diagnoses in offspring. Very-long-term follow-up data were analyzed to more fully assess the impact on allergic respiratory disease risk.

The study included 24-year follow-up data from the Aarhus Trial, in which 533 women were assigned to receive fish oil (2.7 g of long-chain n-3 PUFAs), olive oil, or no supplement during the third trimester of pregnancy. Danish national prescription data were analyzed to assess the offsprings, receipt of medications used to treat asthma and allergic rhinitis. At age 18 to 19 years, 382 of the offspring completed a questionnaire and 243 attended a clinical examination.

On intention-to-treat analysis, offspring whose mothers took fish oil were about half as likely to receive asthma medications: hazard ratio (HR) 0.54, compared to both control groups. Consistent with the previous analysis, the fish oil group also had a lower probability of asthma discharge diagnosis: HR 0.31. There was a trend toward reduced prescriptions for allergic rhinitis medications, although the HR was not statistically significant.

Self-reported outcomes at age 18 to 19 showed a similar pattern: odds ratio 0.34 for current asthma medication use in the fish oil group. There were no significant associations with lung function outcomes or allergic sensitization, and no differences between males and females.

Fish oil supplementation during pregnancy may reduce asthma medication use and asthma discharge diagnoses in offspring into young adulthood. The findings add to previous studies suggesting that prenatal long-chain n-3 PUFAs may prevent the development of asthma. They also highlight the importance of the intrauterine environment for asthma risk, throughout childhood and beyond.

COMMENT: Previous studies have demonstrated the anti-inflammatory properties and beneficial effects of fish oil supplementation during pregnancy. This unique study analyzed data from offspring

of women who participated in a randomized trial of fish oil supplementation 24 years prior. Although there was statistical benefit of fish oil protecting against the development of asthma, there was only a trend toward benefit for allergic rhinitis. One potential cofounder was that even mothers receiving placebo may have increased their intake of fish oil, although probably not as high as the study dose. These data further support the use of long-chain n-3 PUFAs in pregnancy to help reduce the risk for asthma in infants.

S.M.F.

Hansen S, Storm M, Maslova E, et al: Fish oil supplementation during pregnancy and allergic respiratory disease in offspring.
J Allergy Clin Immunol. 2017;139:104-111.

Keywords: asthma (child), fish oil, primary prevention

Have Guidelines Improved Appropriate Asthma Medication Use?

Extensive evidence has shown that a low ratio of asthma controller to reliever medications is associated with adverse outcomes. This population-based study examined whether these research findings are reflected in real-world use of asthma medications.

The researchers analyzed British Columbia health data on 356,112 adults meeting a case definition of asthma between 2002 and 2013, for a total of 2.6 million patient years. Rates of inappropriate or excessive use of short-acting beta-agonists were analyzed, along with the balance between asthma controllers and relievers.

Overall, SABAs were prescribed inappropriately in 7.3% of patient-years, decreasing by a relative rate of 5.3% per year. Evidence of inappropriate SABA use was present in 6.3% of patients in the year asthma was diagnosed. This rate declined for the next 3 years, but then rose back to 6.0% by year 12. Excessive SABA prescription increased by age, with a change of 5.1% per year. The ratio of asthma controllers to relievers fell below the recommended threshold in more than half of patient-years.

Although there is some positive change, many asthma patients continue to receive inappropriate SABA prescriptions. Excessive SABA prescribing might contribute to the elevated asthma mortality in older adults. Although inappropriate prescriptions decreased during the period studied, they increased during the time course of asthma.

COMMENT: This study analyzed asthma medication use in British Columbia using a large database involving more than 126,000 patients with at least 5 years of data. Inappropriate use of SABAs declined from 8.7% in 2002 to 4.6% in 2013. Very excessive SABA use (12 or more canisters per year) occurred in 1.1% of patients in 2002 and only 0.4% in 2013. Despite these encouraging data, excessive SABA use increased with age and over the course of asthma. While the findings suggest improvement in appropriate asthma medication use in recent years, the problem clearly has not been solved.

D.A.K.

Sadatsafavi M, Tavakoli H, Lynd L, FitzGerald JM: Has asthma medication use caught up with the evidence? A 12-year population-based study of trends.
Chest. 2017;151:612-618.

Keywords: asthma (adult), guidelines, SABAs

FOCUS ON ASTHMA BIOMARKERS

Transcriptomics: The Key to Phenotyping Asthma?

Defining asthma phenotypes based on clinical characteristics, including inflammatory biomarkers, is of limited value for personalized asthma therapy. The authors used gene set variation analysis (GSVA) to analyze transcriptome data from bronchial biopsy specimens to assess molecular phenotypes in patients with severe asthma.

The study included transcriptomic data from bronchial biopsy specimens from 107 UBIOPRED cohort members with moderate to severe asthma. The GSVA included 42 sets associated with asthma and immune/inflammatory pathways; associations between GSVA signatures and clinicopathologic characteristics were assessed. In a further analysis, epithelial brush specimens were used to assess the transcriptomic signatures to distinguish Th2-high eosinophilic versus non-Th2 asthma.

In both types of specimens, nine GVSA signatures identified two asthma subtypes associated with high Th2 expression and nonresponse to corticosteroids. Group 1 was associated with high submucosal eosinophils and exhaled nitric oxide and group 3 with high sputum eosinophils and body mass index. Compared with these Th2-high groups, patients in groups 2 and 4 were 86% and 64% likely to have noneosinophilic inflammation. An inference tree framework based on sputum eosinophilia, exhaled NO, and oral corticosteroid use performed well in predicting gene expression subtypes.

Transcriptomic analysis of specimens from patients with moderate to severe asthma reflects variable mechanisms in terms of Th2 expression and steroid insensitivity, and thus defines differing asthma phenotypes. With further research, this approach could aid in predicting which asthma patients will benefit most from treatments targeting Th2-mediated inflammation and corticosteroid nonresponse.

COMMENT: The ability to understand who is an appropriate candidate for Th2 biologics by using bioinformatic clustering techniques is a major advancement. These data allow for identification of patients who may be candidates for • • •

therapy, and also those who are not likely to respond to these expensive biologic agents. We must be careful about over-analysis and over-optimism from the results of gene expression studies. However, these findings may be of great significance when reconfirmed. Also see the accompanying editorial (Am J Respir Crit Care Med 2017;195:411-412).

D.A.K.

Scott Kuo CH, Pavlidis S, Loza M, et al: A transcriptome-driven analysis of epithelial brushings and bronchial biopsies to define asthma phenotypes in U-BIOPRED.

Am J Respir Crit Care Med. 2017;195:443-455.

Keywords: asthma (severe), biologics, phenotypes, transcriptome analysis

Could Blood Eosinophil Count Become the Asthma 'Glucometer'?

The small percentage of patients with severe uncontrolled asthma (SUA) have a high burden of disease, including a high risk of exacerbations. A subgroup of SUA patients have high blood eosinophil counts; the association of this eosinophilic phenotype with disease burden is unclear. The present study assessed the relationship between blood eosinophil count and exacerbations and other outcomes in patients with SUA.

The prospective study enrolled patients aged 12 or older with SUA, based on history of exacerbations, medium- to high-dose inhaled corticosteroid (ICS) use, and non-ICS controller use. Of 514 invited patients, 261 had blood tests to measure eosinophil count and other biomarkers. Blood eosinophil cutoffs were analyzed for association with measures of clinical and economic disease burden 1 year after testing.

Seventy-seven patients had a blood eosinophil count of 400/mm^3 or higher. On adjusted analysis, this group was more likely to have two or more asthma exacerbations, risk ratio (RR) 1.55; and at least one emergency department visit or hospitalization, RR 2.29. Eosinophil count was unrelated to direct costs.

In patients with SUA, a blood eosinophil cutoff of 400/mm^3 is an independent risk factor for multiple exacerbations, asthma emergency department visits, or hospital admission. High blood eosinophils may identify severe asthma patients in need of more intensive anti-inflammatory therapy. Further research is needed to identify blood eosinophil levels associated with a response to treatment, in the context of other clinical features and biomarkers.

COMMENT: This very interesting study demonstrated that a high blood eosinophil count was a risk factor for future frequent and more severe asthma exacerbations in patients with SUA. As the authors note, future studies are needed to determine what features of asthma or specific biomarkers may aid in optimizing the clinical management of asthma. In the meantime, a high blood eosinophil count may help to identify patients who may need more intensive anti-inflammatory therapy.

J.J.O.

Zeiger RS, Schatz M, Dalal AA, et al: Blood eosinophil count and outcomes in severe uncontrolled asthma: a prospective study.

J Allergy Clin Immunol Pract. 2017;5:144-153.

Keywords: asthma (severe), biomarkers, eosinophils, exacerbations

More on Exhaled Nitric Oxide

Exhaled nitric oxide measurement has become a practical and affordable test, but its role in clinical management of asthma is still unclear. The authors present a systematic review of the evidence on exhaled NO, focusing on key issues regarding its use in asthma diagnosis.

A comprehensive, systematic review of the literature identified 27 studies evaluating exhaled nitric oxide for asthma diagnosis in adult patients. Studies were considered in several categories, reflecting specific clinical situations in which exhaled NO testing might be used.

Meta-analysis could not be performed due to study heterogeneity; the results were variable even within study subgroups. Cutoff values for the best combination of sensitivity and specificity varied substantially, from 12 to 55 ppb. Accuracy values were not high. However, some studies reported sensitivity or specificity of 100%, suggesting that exhaled NO might be a useful part of rule-in or rule-out strategies.

The available evidence shows continued uncertainty regarding the use of exhaled nitric oxide measurement for asthma diagnosis. Estimates of diagnostic accuracy and cutoff values vary widely, likely reflecting heterogeneity in study and patient characteristics. The authors make recommendations for future research on diagnostic uses of exhaled NO.

COMMENT: We have long been searching for a diagnostic tool regarding airway inflammation. It was hoped that exhaled nitric oxide would be that tool; however, its use has not been as easily implemented as was first hoped. This systematic review examined the diagnostic accuracy of exhaled NO. Currently, there is no consensus as to the cutoff between normal and abnormal levels, or whether exhaled NO should be used as a rule-in test, a rule-out test, or both. In clinical practice, choosing different cutoff levels will alter sensitivity, specificity, and positive and negative predictive values. These authors were clearly unable to draw conclusions regarding optimal cutoff points, whether accuracy varies according to patient populations and reference standards, and where exhaled NO should be placed within a diagnostic pathway.

J.J.O.

Harnan SE, Essat M, Gomersall T, et al: Exhaled nitric oxide in the diagnosis of asthma in adults: a systematic review.

Clin Exp Allergy. 2017;410:410-429.

Keywords: asthma (adult), biomarkers, exhaled NO

Conquering the Itch: Anti-IL-31 Shows Promise for AD

Interleukin (IL)-31 is involved in the pathogenesis of AD, specifically including the symptom of pruritus. The humanized monoclonal antibody nemolizumab inhibits IL-31 signaling via binding to interleukin-31 receptor A. This phase 2 randomized trial evaluated the safety and efficacy of nemolizumab in patients with AD.

The 12-week study included 264 patients with moderate-to-severe AD that did not respond to topical agents. Patients were assigned to receive subcutaneous nemolizumab 0.1, 0.5, or 2.0 mg/kg or placebo every 4 weeks. (An exploratory group received nemolizumab 2.0 mg/kg every 8 weeks.) There were 216 study completers.

Percentage change on a pruritus visual analog scale in the 4-week treatment groups was -43.7% with the 0.1 mg/kg dose of nemolizumab, -59.8% with the 0.5 mg/kg dose, and -63.1% with the 2.0 mg/kg dose, compared to -20.9% with placebo. Changes on the Eczema Area and Severity Index were -23.0%, -42.3%, -40.9% in the three nemolizumab dose groups compared to -26.6% with placebo. Changes in body surface area affected were -7.5%, -20.0%, -19.4%, and -15.7%, respectively. Treatment discontinuation rate was 13% in the nemolizumab 20 mg/kg dose group and 17% in all other groups.

At all monthly doses studied, nemolizumab reduced pruritus scores in patients with moderate to severe AD. The study supports an approach targeting IL-31 receptor A in patients with AD. Within its limitations, the study suggests that a nemolizumab dose of 0.5 mg/kg every 4 weeks provides the best risk-benefit profile.

COMMENT: The finding that neurons have receptors for thymic stromal lymphopoietin and IL-31 may help explain why type 2 responses trigger pruritus. The nearly 30% reduction in pruritus score in the first week of treatment with the anti-IL-31 receptor A antibody nemolizumab in adults with AD shows that this is clinically relevant. The use of targeted biologics (including recent encouraging results with dupilumab) to conquer the itch and improve the lives of individuals with AD is definitely a step in the right direction. (Also see the editorial by Schneider: N Engl J Med. 2017; 376:878-879.)

C.D.

Ruzicka T, Hanifin JM, Furue M, et al: Anti-interleukin-31 receptor A antibody for atopic dermatitis.
N Engl J Med. 2017;376:826-835.

Keywords: atopic dermatitis, biologics, pruritus

Which Comes First, the Staph or the AD?

Atopic dermatitis (AD) is associated with colonization and increased risk of infections with *Staphylococcus aureus*. However, it's unclear how the skin microbiome during infancy affects the incidence of AD. This prospective study evaluated the effects of skin microbiome on the risk of developing AD during the first year of life.

The study included 50 randomly selected infants from an Irish birth cohort study. Skin swabs from four sites relevant to AD were collected at 2 days and 2 and 6 months of age, with bacterial 16S rRNA gene sequencing and analysis performed directly from clinical samples. Patterns and changes in bacterial skin colonization were analyzed for association with the incidence of AD at 1 year.

The types and diversity of bacteria in the skin microbiome changed significantly between sampling periods. In contrast to patients with established AD, occurrence of infantile AD was not associated with skin dysbiosis or colonization with *S. aureus.* Development of AD during the first year of life was associated with significant differences in bacterial communities detected in swabs from the antecubital fossa at 2 months. In particular, commensal staphylococci were significantly less abundant in infants who went on to develop AD. The skin microbiome was unrelated to mode of delivery or feeding method.

Skin colonization with *S. aureus* does not appear to occur before the development of AD in infants. Early colonization with commensal staphylococci may have a protective effect against infantile AD. The authors emphasize the need for further research to understand the pathophysiology and mechanisms by which the skin microbiome affects the development of skin immunity and AD.

COMMENT: This birth cohort study analyzed data from skin samples at age 2 days, 2 months, and 6 months, with gene sequencing to determine microbiome changes. Children were then followed up for the clinical development of AD. Interestingly the presence of *S. aureus* did not precede the development of AD—in fact, several commensal Staph species present at 2 months were associated with a reduced incidence of AD. This suggests that the relationship between the microbiome and skin inflammation is complicated, and that some commensal bacteria may even have a protective effect against eczema in infants.

S.M.F.

Kennedy EA, Connolly J, Hourihane JO, et al: Skin microbiome before development of atopic dermatitis: early colonization with commensal staphylococci at 2 months is associated with a lower risk of atopic dermatitis at 1 year.
J Allergy Clin Immunol. 2017;139:166-172.

Keywords: atopic dermatitis, hygiene hypothesis, microbiome

Conquering HAE: Kallikrein Inhibitor Shows Promise

In hereditary angioedema (HAE) with C1 inhibitor deficiency, episodes of angioedema and pain are caused by uncontrolled plasma kallikrein generation, with pro-

teolysis of high-molecular-weight kininogen leading to excessive bradykinin production. This phase 1b trial evaluated lanadelumab, a new kallikrein inhibitor, for long-term prevention of attacks in patients with HAE.

The study included 37 adults with type I or II HAE with C1 inhibitor deficiency. In a 2:1 ratio, they were randomly assigned to lanadelumab or placebo, with two treatments given 14 days apart. Lanadelumab was given in ascending doses, with a total dose of 300 mg in 5 patients and 400 mg in 11 patients. The main efficacy outcome was the rate of angioedema attacks from day 8 to day 50 in patients receiving lanadelumab 300 or 400 mg, compared to placebo.

Lanadelumab had a mean elimination half-life of about 2 weeks. At both dose levels, patients receiving lanadelumab reduced cleavage of high-molecular-weight kininogen to levels seen in subjects without HAE. All patients in the 300 mg group and 82% of those in the 400 mg group were free of attacks from day 8 to 50, compared to 27% in the placebo group. In the combined 300 and 400 mg groups, the attack rate was reduced by 91%.

There were no lanadelumab discontinuations due to adverse events, and no important treatment-related safety issues. Adverse events occurring in at least 5 patients were injection-site pain, headache, and angioedema attacks.

This initial trial shows encouraging results with a plasma kallikrein inhibitor for prophylactic treatment of HAE with C1 inhibitor deficiency. Lanadelumab reduces cleavage of high-molecular-weight kininogen and reduces the frequency of angioedema attacks. A phase 3 trial evaluating lanadelumab with a 6-month treatment period is underway.

COMMENT: This preliminary study by Banerji and Busse et al is an exciting "first to" for a few reasons. It shows that lanadelumab allows sustained inhibition of kallikrein and subsequent downstream tempering effects on bradykinin release. The findings suggest an unprecedented high level of protection against angioedema. Administration by subcutaneous injection every 2 weeks can enhance convenience and accessibility. Further studies using this biologic prophylactic agent in mitigating the burden of hereditary angioedema are eagerly awaited. (Also see the editorial by Longhurst: N Engl J Med. 2017;376:788-789.)

C.D.

Banerji A, Busse P, Shennak M, et al: Inhibiting plasma kallikrein for hereditary angioedema prophylaxis.
N Engl J Med. 2017;376:717-728.

Keywords: biologics, HAE, kallikrein

Anaphylaxis Can Activate Neutrophils Too

Questions remain as to what factors lead to amplification of mast cell responses during anaphylaxis. In mouse models of anaphylaxis, neutrophils play an important role. The authors measured neutrophil activation during episodes of acute anaphylaxis in humans.

Serial blood samples were collected from 72 emergency department (ED) patients with anaphylaxis. In addition to histamine and mast cell tryptase, the investigators measured plasma myeloperoxidase (MPO) and serum soluble CD62L as indicators of neutrophil activation.

Fifty-one percent of patients had severe anaphylaxis, mainly caused by adverse reactions to drugs. At sampling times up to 5 hours, plasma histamine concentrations were positive in 60% of patients and serum mast cell tryptase in 70%.

In baseline samples, plasma MPO concentration was 2.9 times higher in patients with moderate anaphylaxis and 5 times higher in those with severe anaphylaxis, compared to healthy controls. Soluble CD62L levels were 29% and 31% lower, respectively. Both neutrophil activation markers remained stable over 5 hours; they were unrelated to each other and to the traditional anaphylaxis biomarkers.

Neutrophils seem to play an important role in human anaphylaxis. Neutrophil activation occurs early during anaphylaxis, is sustained during ED management, and is accompanied by mast cell activation. While further study is needed, the results suggest that "neutrophils are actively involved during IgE-mediated anaphylaxis, perhaps in the amplification of the immune response."

COMMENT: Anaphylaxis is typically thought of as a disorder of mast cell activation. Based on data from murine models, these investigators evaluated neutrophil activation, as assessed by MPO, in 72 ED patients with anaphylaxis. Myeloperoxidase levels were higher in anaphylaxis patients than controls and were higher in more severe cases. However, there was no correlation with serum tryptase. Whether neutrophil activation is important in the pathophysiology of human anaphylaxis, as in mice, is not yet clear.

D.A.K.

Francis A, Bosio E, Stone SF, et al: Neutrophil activation during acute human anaphylaxis: analysis of MPO and sCD62L.
Clin Exp Allergy. 2017;47:361-370.

Keywords: anaphylaxis, biomarkers, neutrophils

'VCD' in Asthmatic Adults: A New Perspective

Vocal cord dysfunction (VCD) can cause symptoms similar to asthma. The authors previously reported that paradoxical vocal cord movement (PVCM) during inspiration was present in up to 40% of patients with severe asthma. This study assessed PVCM in asthma patients with and without airflow limitation.

The study included 155 patients with asthma symptoms, drawn from general practice and severe asthma clinics. Evaluation included pulmonary function testing and assessment of asthma control and dysfunctional breathing • • •

(Nijmegen score). Patients were evaluated for PVCM using dynamic 320-slice computed tomography (CT) of the larynx.

About one-fourth of patients (27.1%) had PVCM during inspiration. This percentage increased to 36.8% for patients with FEV_1 less than 80% predicted, compared to 19.5% of those with normal spirometry. Older age was associated with PVCM, but sex and body mass index were not. Odds ratio for PVCM was 6.5 for patients with a Nijmegen score over 20, and 9.30 for those with an FEV_1 less than 80% predicted plus Nijmegen score over 20.

Paradoxical vocal cord movement is common in patients with asthma, especially those with airflow limitation. Further study of PVCM in asthma is needed, including whether treatment for intermittent middle airway obstruction can help to reduce airway symptoms and improve apparent asthma control.

COMMENT: This fascinating study demonstrates that CT-diagnosed PVCM is more common in asthmatic patients with airway obstruction than in those without airway obstruction, suggesting that this abnormality may be interrelated with asthma itself. The authors note that more research is needed to determine the extent to which this extrathoracic airway obstruction contributes to the symptoms of asthma. They suggest that effective treatment of this "middle airway obstruction" may reduce symptoms of poorly controlled asthma.

J.J.O.

Low K, Ruane L, Uddin N, et al: Abnormal vocal cord movement in patients with and without airway obstruction and asthma symptoms.
Clin Exp Allergy. 2017;47:200-207.

Keywords: asthma (adult), VCD

Asthma Diagnosis in Teens–Gender Matters

The authors previously reported an increased prevalence of asthma, apparently related to the duration and intensity of training, in "elite-aspiring" swimmers. Here they examined sex differences in asthma-related outcomes in adolescent swimmers, tennis players, and controls.

The study included elite-level adolescent athletes—101 swimmers and 86 tennis players—and a reference group of 1,628 adolescents. Respiratory and allergic symptoms, lifestyle factors, psychosomatic symptoms, and well-being were assessed by questionnaires. The two groups of athletes underwent mannitol provocation testing and sport-specific exercise challenge.

Females reported more asthma symptoms: 56.4% versus 40.2% among athletes and 29.1% versus 22.3% in the reference group. Mannitol provocation was positive in 48.7% of female versus 35.8% of male athletes, and 15.1% versus 7.7% in female versus male swimmers. Female swimmers had a higher rate of positive exercise challenge. Across groups, rates of physician-diagnosed asthma and inhaled corticosteroid prescriptions were similar between the sexes.

In all groups, psychosomatic symptoms were more commonly reported by females than males. In the reference group, males reported higher self-esteem and well-being.

Among athletes and nonathletes, female adolescents report more asthma symptoms than males. Mannitol provocation testing appears more frequently positive in elite-level female adolescent athletes than in males. The study raises concerns about inadequate diagnosis in female athletes.

COMMENT: This Swedish study explored sex-related differences in adolescent athletes who were swimmers or tennis players versus a matched reference group. Females who were athletes or in the reference group had higher rates of asthma symptoms but also had higher rates of psychosomatic symptoms (eg, nervousness, dizziness, sleep disorders). Mannitol challenge was more frequently positive in female athletes. The high rate of respiratory symptoms and other findings highlight the importance of objective confirmation of asthma in adolescent athletes.

D.M.L.

Romberg K, Tufvesson E, Bjermer L: Sex differences in asthma in swimmers and tennis players.
Ann Allergy Asthma Immunol. 2017;118:311-317.

Keywords: asthma (adult), athletes

Combining ICS and LABA: Fixed-Dose vs Separate Inhalers

Current guidelines for children with asthma call for the use of a fixed-dose combination (FDC) inhaler when step-up therapy is needed, rather than separate inhaled corticosteroid (ICS) and long-acting β-agonist (LABA) inhalers. However, there is unclear evidence showing the advantages of FDC inhalers. This study compared outcomes in a large population of asthmatic children receiving FDC versus separate ICS plus LABA inhalers.

Using UK primary care databases, the researchers identified matched cohorts of children receiving initial step-up therapy for asthma: one group receiving an FDC inhaler and the other receiving separate ICS and LABA inhalers. Both cohorts included 1,330 children; the mean age was 9 years and 59% of children were boys. Over 2 years' follow-up, the groups were compared for overall asthma control, defined as no asthma-related hospital admissions or emergency room visits, no oral corticosteroid or antibiotic prescriptions, and no more than 2 puffs per day of short-acting β-agonist.

Initial asthma severity and control were similar between cohorts. During follow-up, overall asthma control was achieved in 35% of children receiving separate ICS and LABA inhalers versus 37% in the FDC cohort. The adjusted odds ratio for asthma control in the group with separate inhalers was 0.77. Children with separate ICS plus LABA inhalers also had more acute respiratory events and more severe exacerbations: adjusted rate ratio 1.21 and 1.31, respectively.

The results suggest a small but significant improvement in overall asthma control for asthmatic children receiving step-up therapy with an FDC inhaler, compared to separate ICS and LABA inhalers. These real-world data support current recommendations favoring FDC inhalers for children with uncontrolled asthma.

COMMENT: In this matched cohort study, LABA add-on treatment to ICS as a separate inhaler was associated with poorer asthma control, compared to an FDC inhaler. Surprisingly, the authors found no evidence for improved ICS adherence between cohorts, in terms of refill prescription rates. However, an increased number of children were treated for thrush in the FDC group compared to the separate ICS plus LABA cohort. The authors note that this may suggest increased adherence with ICS in the FDC cohort. In any event, these data provide evidence that LABA treatment in children should be administered as an FDC and not as a separate inhaler.

J.J.O.

Turner S, Richardson K, Murray C, et al: Long-acting β-agonist in combination or separate inhaler as step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids.
J Allergy Clin Immunol Pract. 2017;5:99-106.

Keywords: asthma (child), ICS, LABAs, step-up therapy

Omalizumab May Help Nonatopic Asthma

Previous studies have suggested that IgE plays a role in asthma, whether or not it is atopic. This study explored omalizumab's effects on airway inflammation and clinical outcomes in nonatopic asthma.

Eighteen patients with uncontrolled nonatopic asthma were randomly assigned to 20 weeks of omalizumab or placebo, added to previous treatment. Biopsy specimens were obtained at 12 to 14 weeks for measurement of bronchial mucosal IgE+ cells. Regular asthma therapy was then reduced to assess the effects on lung function, asthma symptom scores, and quality of life.

Median total IgE+ cells were significantly reduced (by 5.44/mm^2) with omalizumab but not placebo. Other airway inflammatory markers were unchanged, including mast cells and eosinophils. The omalizumab group had improved lung function, including an 11% increase in FEV_1 predicted, while the placebo group had significant deterioration. Omalizumab was also associated with clinically meaningful improvement in asthma control.

This initial study provides evidence of benefits with omalizumab in patients with symptomatic, nonatopic asthma. Pending further study, anti-IgE therapy has the potential to reduce airway inflammation and improve asthma control in this group of patients.

COMMENT: This small proof-of-concept study supports the expanded application of omalizumab. In patients with nonatopic asthma, omalizumab was associated with improvement in lung function and quality of life compared to placebo. There was also a very significant reduction in nominal ICS dose, from 2,000 to 200 μg beclomethasone equivalent). These data, albeit in a small series of patients, give insight into the 40% to 50% of patients who do not have a rich eosinophilic or allergic phenotype.

B.E.C.

Pillai P, Chan Y-C, Wu S-Y, et al: Omalizumab reduces bronchial mucosal IgE and improves lung function in nonatopic asthma.
Eur Respir J. 2016;48:1593-1601.

Keywords: asthma (nonatopic), biologics, omalizumab

Traffic-Related Air Pollution – Bad for Allergic Adults Too!

Previous studies have shown reduced lung function and an increased risk of allergic respiratory diseases in children with higher exposure to traffic-related air pollution (TRAP). Less is known about the effects of TRAP in adults. This study examined the association between TRAP exposure, asthma, and other respiratory outcomes in middle-aged adults in a low-pollution area.

The analysis included subjects from the Tasmanian Longitudinal Health Study, enrolled as children in 1968. In their forties, 1,405 adults participated in a laboratory study including skin prick and lung function testing. Each subject's mean annual residential nitrogen oxide exposure was calculated based on their current residential address. Exposure to TRAP was evaluated for associated with allergic sensitization, lung function. current wheezing, and asthma.

Higher NO_2 exposure was associated with an increased risk of atopy, adjusted odds ratio (OR) 1.14 per 1 interquartile range increase; and current wheezing, OR 1.14. Subjects who lived within 200 m of a major road had higher rates of atopy and current wheezing: OR 1.26 and 1.38, respectively. Living near a major road was also associated with decreased lung function, including pre- and postbronchodilator FEV_1 and prebronchodilator FEF 25-75% of forced vital capacity.

Living near a major road also interacted with the gluthathione S-transferase gene to affect the risk of asthma and allergic disease outcomes. Carriers of the *GSTT1* null genotype were at higher risk of atopy, asthma, and atopic asthma with higher TRAP exposure.

Even at relatively low levels, TRAP exposure is associated with atopy, asthma, and reduced lung function in middle-aged adults. These risks appear particularly high in individuals with the *GSTT1* null genotype. This finding may have important public health implications for a genetically susceptible population.

COMMENT: Air pollution, particularly TRAP, causes • • •

oxidative damage to airways and inflammation and enhances allergic reactions. Although this association is well-documented in children, this unique study shows that it is also present in adults. The researchers not only measured allergy skin tests, lung function, and symptoms but also analyzed GST genes, which play an important role in modulating inflammation. Even though nitrogen dioxide exposures in Australia were lower than in North America and Europe, there was still a significant increase in allergy among adults living less than 200 m from a major road—especially for carriers of the GSTT1 null genotype.

S.M.F.

Bowatte G, Lodge CJ, Knibbs LD, et al: Traffic-related air pollution exposure is associated with allergic sensitization, asthma, and poor lung function in middle age.

J Allergy Clin Imunol. 2017;139:122-129.

Keywords: air pollution, asthma (adult), genetics

Does Travel in Early Life Lead to Later Atopy?

The shift to a "westernized lifestyle" has been linked to the increased prevalence of allergic disease, such as occurred in the former East Germany after reunification. One possible contributor is early-life travel, with exposure to new and different allergens. The relationship between early-life travel and later risk of allergic disease was tested using data from two German birth cohort studies.

The study included prospectively collected data on 5,674 children enrolled in the ongoing GINIplus and LISAplus birth cohorts. Detailed information on the frequency and distance of travel, within and outside Germany, was collected during the first 2 years of life. Early-life travel history was analyzed for association with allergic disease outcomes up to age 15 years.

Nearly two-thirds of children traveled outside of Germany during the first 2 years of life. Neither travel frequency nor distance traveled was related to any of the atopic outcomes studied, including physician-diagnosed asthma or allergic rhinitis or sensitization to indoor, outdoor, or food allergens. There was no evidence of age-varying effects.

History of travel during early childhood does not appear to affect the risk of allergic disease outcomes by adolescence. Further studies including more detailed information on travel history would be needed to confirm or refute the findings.

COMMENT: Surprisingly, there has been a paucity of data regarding the impact of travel early in life and the development of atopy. In this study, travel during the first 2 years of life was not shown to increase the risk of atopy up to age 15.

J.J.O.

Markevych I, Baumbach C, Standl M, et al: Early life traveling does not increase the risk of atopic outcomes until 15 years: results from GINIplus and LISAplus.

Clin Exp Allergy. 2017;47:395-400.

Keywords: atopy, risk factors

Depression Symptoms and Lost Productivity in Chronic Rhinosinusitis

In addition to direct healthcare costs, chronic rhinosinusitis (CRS) has been linked to high indirect costs from lost productivity, resulting from missed school or work days. This prospective study evaluated the symptoms primarily responsible for reduced productivity in CRS patients.

The cross-sectional study included 107 patients with CRS: 54% women, mean age 52 years. Scores for sleep, nasal, otologic or facial pain, and emotional functioning were determined from the 22-item Sinonasal Outcomes Test (SNOT-22). Additional questionnaires were used to assess depression risk and nasal obstruction. Productivity was assessed in terms of number of missed work or school days in the last 3 months.

The patients reported a mean of 3 missed work or school days over the past 3 months, with a standard deviation of 13 days. Productivity loss was associated with the total SNOT-22 score and with emotional function. There was also a significant association for depression risk.

Other SNOT-22 domains were not significantly related to productivity loss, although nasal symptoms became significant on multivariable analysis. Nasal obstruction was also nonsignificant.

Depression symptoms seem to be the most important contributor to lost productivity due to CRS. Further study is needed to determine whether treatments targeting emotional function and depression-associated symptoms might help to reduce productivity losses in patients with CRS.

COMMENT: Chronic rhinosinusitis is associated with impairment in quality of life comparable to or worse than asthma or cardiac disease. These authors found that symptoms of depression—depressed affect and anhedonia—are most closely associated with lost productivity (missed work and/or school). The findings are consistent with previous reports of high rates of comorbid depression in patients with CRS. These data raise the possibility that treatment for depressed mood might improve productivity in CRS patients.

D.M.L.

Campbell AP, Phillips KM, Hoehle LP, et al: Depression symptoms and lost productivity in chronic rhinosinusitis.

Ann Allergy Asthma Immunol. 2017;118: 286-289.

Keywords: chronic rhinosinusitis, depression, productivity

Chronic Sinusitis: To Cut May Not Be to Cure

Many patients with chronic rhinosinusitis (CRS) continue to have symptoms despite medical and surgical treat- • • •

ment, including functional endoscopic sinus surgery (FESS). This study evaluated disease control in CRS patients 3 to 5 years after FESS.

The study included 560 adults with CRS who had undergone bilateral FESS between 2008 and 2010. Outcomes were assessed in 2013-14, based on the recently proposed European Position Paper on Sinusitis criteria for disease control, considering major sinonasal symptoms, sleep disturbance/fatigue, nasal endoscopy, and need for oral medications.

At follow-up, CRS was considered well-controlled in 19.5% of patients, partly controlled in 36.8%, and uncontrolled in 43.7%. Assessments of disease control corresponded well to other outcome measures, including total visual analog scale, 22-item Sinonasal Outcomes Test, and Short Form-36.

Women, patients with aspirin intolerance, and those with secondary FESS were more likely to have uncontrolled CRS. Disease control was unaffected by the presence of allergy, asthma, or smoking. Nasal endoscopy, performed in 81 patients, led to a change in CRS control status in only 4.9%. In some cases, patient self-report suggested better CRS control than suggested by disease control criteria.

Three to five years after FESS, more than 40% of patients still have uncontrolled CRS. Pending further research, the study "highlights the need for better treatment strategies in CRS, as the majority of patients may continue to experience symptoms despite surgery."

COMMENT: Sadly, the message from this study is that more than 40% of CRS patients who have undergone FESS have uncontrolled disease 3 to 5 years after intervention. As the authors note, the findings reinforce the need for "better treatment strategies" for this illness.

J.J.O.

van der Veen J, Seys SF, Timmermans M, et al: Real-life study showing uncontrolled rhinosinusitis after sinus surgery in a tertiary referral centre. Allergy. 2017;72:282-290.

Keywords: chronic rhinosinusitis, sinus surgery

Following AIT Guidelines: Are We as Good as We Think?

Adherence to guidelines for labeling of allergen immunotherapy (AIT) is important for promoting safety and effectiveness. The authors previously found that less than one-fourth of independent providers in their university-affiliated health care system adhered to labeling guidelines. The researchers performed a follow-up study to assess AIT labeling adherence in other healthcare systems.

Online surveys were sent to AIT administrators, clinic managers, and allergists at "Big Ten" university healthcare systems. Of 21 responding administrators, about 90% believed that AIT labels meeting all recommended guidelines would reduce errors. Seventy-six percent said that having standardized labels, buildup, and missed dose schedules would improve efficacy, while 90% believed that standardized protocols for systemic reactions would increase safety and efficiency. However, less than 30% of AIT extract labels met all practice parameter guidelines.

Of 762 physicians surveyed, more than 90% were familiar with the guidelines but only 64% actually had guideline-compliant AIT extract labels. Physicians in group practices were more likely to comply with recommendations. The most commonly reported reason for nonadherence, 55%, was having a personalized labeling system. Other reasons included unfamiliarity (14%) and disagreement (9%) with the labeling guidelines.

The results confirm the low rate of compliance with AIT extract labeling guidelines in university healthcare systems. Many physicians do not follow the recommendations even though they are aware of them. The authors conclude, "It is imperative that allergists comply with the highest recommended standards to provide the best clinical outcomes and ensure excellent and efficient care in both allergy and non-allergy offices."

COMMENT: Despite clear guidelines and practice parameters for AIT administration, this study reveals that implementation of the recommendations for patients cared for at ten university clinics was not optimal. Only 64% clinics formally tracked reactions. I find it worrisome that 90% did not monitor whether patients were staying for the recommended waiting period following vaccine administration. Although more than 90% of allergists surveyed were familiar with the practice parameters, less than two-thirds completely followed the recommendations. Further studies are needed to investigate whether improved adherence leads to fewer adverse reactions.

V.H.-T.

Karam M, Holland C, Yang Z, et al: Allergen immunotherapy at university health services and allergist's reasons for guidelines nonadherence. Allergy Asthma Proc. 2017;38:115-120.

Keywords: allergen immunotherapy, guidelines

Alternative Agents for Chronic Hypersensitivity Pneumonitis

Alternatives to systemic corticosteroids are needed for patients with chronic hypersensitivity pneumonitis (cHP). This study reviewed the outcomes of treatment with the cell-cycle inhibitors azathioprine and mycophenolate mofetil for cHP.

The retrospective analysis included 70 patients with cHP treated at four interstitial lung disease centers. Treatment included mycophenolate mofetil in 51 patients and azathioprine in 19. Before these treatments, the patients had a mean monthly decline of 0.12% in forced vital capacity • • •

(FVC) and 0.11% in diffusion capacity for the lung for carbon monoxide (Dlco) % predicted. Median follow-up was 11 months.

There was no improvement in FVC at one year, but there was a significant 4.2% improvement in Dlco. This pattern was similar for patients receiving the two medications, both of which were well tolerated.

This experience suggests improved gas transfer in cHP patients treated with mycophenolate mofetil or azathioprine. The authors conclude that prospective trials of these possible long-term treatment options for cHP are "desperately needed."

COMMENT: While antigen removal is recommended for all patients with cHP, many are treated with systemic corticosteroids, despite well-known adverse effects and a lack of documented efficacy. This retrospective study from four sites analyzed data on 70 patients with cHP treated with either mycophenolate or azathioprine. Both agents showed improvement in Dlco but not FVC. Both medications were well-tolerated, with gastrointestinal adverse effects being most common.

D.A.K.

Morisset J, Johannson KA, Vittinghof E, et al: Use of mycophenolate mofetil or azathioprine for the management of chronic hypersensitivity pneumonitis. Chest. 2017;151:619-625.

Keywords: azathioprine, hypersensitivity pneumonitis, mycophenolate mofetil

SLIT for Peach May Reduce Peanut Allergy

Peach allergy is common in the Mediterranean region, with the non-specific lipid transfer protein Pru p 3 being the primary sensitizer. Many patients with peach allergy are also allergic to other plant-derived foods, including peanut. This study assessed the effects of sublingual immunotherapy (SLIT) to Pru p 3 on both peach and peanut allergy.

The study included 48 patients with peach allergy at one Spanish center: 36 treated with Pru p 3 SLIT and 12 untreated. All had a history of systemic allergic reactions, not just oral allergy syndrome. Twelve of the treated patients were also allergic to peanut.

At 12 months, patients receiving Pru p 3 SLIT showed a significant reduction in skin prick test response and tolerance to oral challenge with peach. Those allergic to peanut also had similar improvements in responses to peanut: 58% ingested the maximum amount of peanut tested without reacting. Immunologic changes in the SLIT group included decreased specific IgE and increases in specific IgG4, sIgG4/sIgE ratio, and basophil reactivity for Ara h 9 as well as Pru p 3.

In Spanish patients with peach allergy and a history of systemic reactions, Pru p 3 SLIT leads to desensitization for peach but also for other food allergens, including peanut. The authors note that treatment was highly effective and safe, despite a high rate of adverse symptoms mainly during the buildup phase.

COMMENT: Well-described in Europe but rare in the United States, systemic reactions to peach are usually related to lipid transfer proteins. This study evaluated 36 patients with confirmed systemic reactions to peach who underwent peach SLIT, of whom 12 also had clinical peanut allergy. After 1 year of SLIT, 91% tolerated the maximum dose of peach during double-blind placebo-controlled food challenge. Fifty-eight percent of the co-sensitized peanut group tolerated oral challenge with peanut. The lack of a placebo group is a significant limitation of this study.

D.A.K.

Gomez F, Bogas G, Gonzalez M, et al: The clinical and immunological effects of Pru p 3 sublingual immunotherapy on peach and peanut allergy in patients with systemic reactions. Clin Exp Allergy. 2017;47:339-350.

Keywords: food allergy, peanut allergy, SLIT

Symptomatic Smokers with Normal Spirometry: What To Do?

Previous reports have described a group of smokers with chronic respiratory symptoms, who have normal findings on spirometry but are at high risk of poor outcomes. The authors present an updated review of knowledge on these "symptomatic but unobstructed" patients.

The initial Global Initiative for Chronic Obstructive Lung Disease (GOLD) report classified patients with chronic respiratory symptoms and a postbronchodilator FEV_1/FVC at stage 0 or "at risk" for chronic obstructive pulmonary disease (COPD). Although the GOLD 0 classification was omitted from revised reports, subsequent studies suggested that a substantial number of patients have these findings, with increased risks of COPD and death.

In five recent cohort studies, these patients were shown to have CT findings consistent with large-airway abnormalities, associated with substantial morbidity and high healthcare utilization. Greater symptoms appear to be a risk factor for rapid lung function decline, suggesting that this clinical entity may be a form of early COPD. Yet "GOLD 0" is not the only pathway to airflow limitation; many patients with this pattern do not progress to COPD.

The authors identify key research questions for understanding the short- and long-term clinical significance of chronic respiratory symptoms in smokers with normal results on spirometry, including preventive and therapeutic strategies. Future studies of this "likely distinct condition" may lend new insights into the natural history of COPD.

COMMENT: This important "Pulmonary Perspective" article provides further understanding of the landmark article published by Woodruff et al (N Engl J Med. 2016;374:1811-1821), showing that patients with normal spirometry

who are smokers may have a significant burden of disease.

B.E.C.

Rodriguez-Roisin R, Han MK, Vestbo J, et al: Chronic respiratory symptoms with normal spirometry: a reliable clinical entity?

Am J Respir Crit Care Med. 2017;195:17-22.

Keywords: COPD, diagnosis, smoking

Genetic Causes of Kidney Defects in 22q11 Deletions

Patients with DiGeorge syndrome, caused by chromosome 22q11.2 deletions, have features including heart malformations, velopharyngeal deficiency, and thymic aplasia with immune deficiency, among others. About 30% of affected patients have congenital kidney and urinary tract abnormalities. The authors report the identification of the genetic driver of the kidney defects in DiGeorge syndrome.

A genomewide search identified heterozygous deletions of 22q11.2 in 1.1% of 2,080 patients with congenital kidney defects, compared to 0.01% of population controls: odds ratio 81.5. The critical region for the phenotype associated with congenital kidney and urinary tract abnormalities was localized to a 370 kb region containing nine genes. Functional modeling in zebrafish linked renal defects to loss of function in three genes: *snap29, aifm3,* and *crkl,* the latter being sufficient on its own to cause defects.

Of 586 study patients with congenital urinary anomalies, 5 had novel heterozygous protein-altering variants, including a premature termination codon of *CRKL* In a mouse model, *Ckrl* inactivation caused a pattern of urinary anomalies similar to that observed in humans

These experiments implicate a recurrent 370 kb deletion on chromosome 22q11.2 as the genetic driver of sporadic kidney and urinary tract defects in DiGeorge syndrome. Haploinsufficiency of *CRKL* appears to be the main genetic driver, although other genes may be involved as well. The authors note that *CRKL* encodes an adapter protein that regulates intracellular signaling transduction from fibroblast growth factors, among others.

COMMENT: Chromosome 22q11.2 deletions (including DiGeorge syndrome and velocardiofacial syndrome) are the most common microdeletion disorder in humans, occurring in about 1 in 2,000 to 4,000 live births. Up to one-third of affected patients have congenital kidney and urinary tract anomalies. Identifying the genetic drivers of the pathogenesis of this phenotype is the first step in generating potential targets for therapeutic manipulation.

C.D.

Lopez-Rivera E, Liu M, Verbitsky M, et al: Genetic drivers of kidney defects in the DiGeorge syndrome.

N Engl J Med. 2017;376:742-754.

Keywords: genetics, immune deficiency

REVIEWS OF NOTE

COMMENT: An update from the American Academy of Pediatrics helps clinicians identify patients at risk of anaphylaxis and provides information about epinephrine dosing. Key points include validated clinical criteria to facilitate prompt diagnosis of anaphylaxis and suggested doses for epinephrine use in infants and young children. A sister clinical report provides a comprehensive written plan that can be universally used, with guidance on individualizing instructions to suit specific patient circumstances.

C.D.

Sicherer SH, Simons ER: Epinephrine for first-aid management of anaphylaxis. Pediatrics. 2017;139:e20164006.

Wang J, Sicherer SH: Guidance on completing a written allergy and anaphylaxis emergency plan.

Pediatrics. 2017;139:e20164005.

COMMENT: Based on previous studies, we have abbreviated our aspirin desensitization protocols to omit in-office challenge to the 650 mg aspirin dose. In this review of 104 aspirin desensitization procedures, patients with aspirin-exacerbated respiratory disease who exhibited initial respiratory reaction to a challenge dose less than 162 mg—and in whom the reaction was subsequently extinguished with repeat dosing—were extremely unlikely to experience respiratory reaction when challenged with 325 mg of aspirin. These data support at-home administration of the 325 mg dose for such patients. For patients undergoing desensitization who do not react at 162 mg, in-office challenge with 325 mg is still warranted.

D.M.L.

Schuler CF, Baldwin JL, Baptist AP: Frequency and severity of reactions to a 325 mg aspirin dose during desensitization.

Ann Allergy Asthma Immunol. 2017;118: 333-338.

COMMENT: This review reminds us of the different effects that living with chronic disease, such as food allergy, has on families. Due to lack of treatment options, avoidance can lead to malnutrition. Bullying is also a problem for patients with food allergy. Families may not feel comfortable volunteering their concerns. We as allergists need to ask families about quality-of-life concerns. Through proper education, helping improve access to medications, using both resources and multidisciplinary approaches with the aid of nutritionists, psychologists and social workers, families may be better prepared to deal with the challenges of living with food allergy.

V.H.-T.

Patel N, Herbert L, Green TG: The emotional, social, and financial burden of food allergies on children and their families. Allergy Asthma Proc. 2017;38:88-91.