

FEATURE ARTICLES

Oral immunotherapy to peanut shows promise under age 3

For children with peanut allergy, oral immunotherapy (OIT) may provide a margin of safety against accidental exposure, but its use is limited by a high rate of interrupted treatment. Recent reports have suggested that starting OIT in newly diagnosed children at a young age might interrupt the process of allergic priming. The authors report a randomized, double-blind trial of this early intervention OIT approach in preschool children.

The study included 40 children, aged 9 to 36 months, with suspected or known peanut allergy. All received peanut OIT, with a target maintenance dose of 300 or 3,000 mg/d. Treatment continued until the children met four specified criteria, or until they completed 3 years of maintenance therapy. Double-blind, placebo-controlled food challenge was performed to assess sustained unresponsiveness at 4 weeks

after stopping OIT (4-SU). Outcomes were compared to those in a retrospective group of 154 matched children receiving standard care.

Thirty-seven children qualified for the OIT protocol. On intention-to-treat analysis, median follow-up 29 months, 4-SU was achieved in 85% of the 300 mg target group and 71% of the 3,000 mg group. On per-protocol analysis, 91% of children met the primary outcome. Allergic side effects of OIT were common but mild to moderate.

Early intervention OIT led to a significant reduction in peanut-specific IgE, compared to a significant increase in the comparison group. Successful peanut introduction was 19 times more likely to be achieved in children receiving OIT. Treatment failure was more likely for children with higher peanut-specific IgE levels.

The results support the safety and effectiveness of an early intervention OIT approach for preschool-aged children recently diagnosed with peanut allergy. Both low- ● ● ●

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and high-dose OIT are associated with high rates of sustained responsiveness and modulation of allergic immune responses. With further study, early OIT "has the potential to further transform the standard of care in the post-LEAP era," the authors conclude.

COMMENT: We have seen a surge in the prevalence of peanut allergy, for which the lack of management options other than strict avoidance poses an unmet need. This study, focusing on children less than 3 years old, assessed the efficacy of peanut OIT in a randomized, blinded fashion. There was no placebo group; the 40 children enrolled were compared with 154 matched controls who received standard care. Almost all patients had adverse events, but they were generally mild and the rate of systemic reactions requiring epinephrine injections was much lower than published OIT studies in older children. Unfortunately, 1 of the 37 subjects developed persistent EoE. Stay tuned for more on this promising therapy but **DO NOT TRY THIS AT HOME!**

D.M.L.

Vickery BP, et al: Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. *J Allergy Clin Immunol.* 2017;139:173-181. ●

Keywords: food allergy, peanut allergy, oral immunotherapy

Dupilumab for AD: Phase III Data Do Not Disappoint

Patients with atopic dermatitis need safe and effective long-term treatments. Previous studies have suggested benefits with dupilumab: a human monoclonal antibody against interleukin (IL)-4 receptor alpha that inhibits signaling of the type 2 cytokines IL-4 and IL-13. Two randomized, placebo-controlled trials of dupilumab for AD are reported.

The SOLO 1 and 2 trials included 671 and 708 patients, respectively, with moderate to severe AD that was inadequately controlled by topical medications. Patients were assigned to 16 weeks of treatment with dupilumab, 300 mg given weekly or alternating with placebo every other week; or placebo given weekly. The primary outcome was a score of 0 or 1 on the Investigator's Global Assessment, indicating clear or almost clear of AD; plus at least a 2-point reduction in the same score from baseline to 16 weeks.

The primary outcome was achieved in 37% of patients receiving weekly dupilumab and 38% with dupilumab every other week, compared to 10% with weekly placebo. Results were similar across the two trials. The dupilumab groups were also more likely to achieve at least 75% improvement in the Eczema Area and Severity Index. Other key outcomes were also improved with dupilumab, including pruritus, anxiety and depression symptoms, and quality of life. The main adverse effects of dupilumab were injection site reactions and conjunctivitis.

The SOLO 1 and 2 results show significant improvement in AD signs and symptoms with dupilumab over 16 weeks. The benefits appear similar with treatment given weekly or every other week, compared to placebo. Further studies are needed to establish dupilumab's long-term safety and effectiveness.

COMMENT: This is certainly exciting: a therapeutic option that helps attenuate the signs and symptoms of AD, including pruritus and sleep effects; causes clinically meaningful reductions in patient- ● ● ●

reported anxiety and depression; improves health-related quality of life; and can be administered subcutaneously weekly or every 2 weeks. In two independent 4-month randomized trials of identical design (to provide replication of results), injection-site reactions and conjunctivitis were the most frequent adverse effects. The etiology of the conjunctivitis was not clear; this finding was not seen in studies of dupilumab in asthma and sinusitis and polyposis. While trials of longer duration are needed to assess efficacy and other safety issues, a once every 2 weeks subcutaneous shot may be a tolerable option to these long-suffering patients.

C.D.

Simpson EL, et al: Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375:2335-2348. ●

Keywords: atopic dermatitis, biologics, dupilumab

hibition of Th2 mediators including IL-13, eotaxin-2, and eotaxin-3 by PPIs. These effects occurred partially by blocking nongastric H,K-ATPase, which is encoded by the gene *ATP12A*. Although there was no reported clinical correlation with patient responses to PPI, this study is of interest since we are seeing increased use of PPIs in our patients with CRS, particularly those with GERD. The authors suggest that inhibiting these mechanisms using medications such as PPIs may be helpful for our patients with CRS.

S.M.F.

Min J-Y, Ocampo CJ, Stevens WW, et al: Proton pump inhibitors decrease eotaxin-3/CCL26 expression in patients with chronic rhinosinusitis with nasal polyps: Possible role of the nongastric H,K-ATPase.

J Allergy Clin Immunol 2017;139:130-141. ●

Keywords: chronic rhinosinusitis, eosinophils, PPIs

Are PPIs Beneficial for Nasal Polyps?

In patients with chronic rhinosinusitis with nasal polyps (CRSwNP), type 2 inflammation and tissue eosinophilia suggest a poor prognosis, including increased postoperative recurrence risk. Recent studies have found that proton pump inhibitors (PPIs) can suppress production of the eosinophil chemoattractant eotaxin-3. The authors assessed the role of Th2 mediators in CRSwNP, along with the effects of eotaxin-3 inhibition using PPIs.

Tests of nasal tissues and secretions from CRSwNP patients showed elevated levels of interleukin-13 (IL-13), eotaxin-2, and eotaxin-3. These Th2 mediators were associated with tissue eosinophil cationic protein levels and radiographic severity in CRS patients. In cultured human sinonasal epithelial cells (HNECs) and BEAS-2B cells, eotaxin-3 expression was induced by IL-13 stimulation and inhibited by PPIs. In CRS patients, PPI treatment was associated with lower eotaxin-3 levels.

In studies using intracellular pH imaging with alteration of extracellular K⁺, H⁺,K⁺-exchange was enhanced by IL-13 and blocked by PPIs, as well as by SCH=28080, an H,K-ATPase inhibitor. Gene knockdown of *ATP12A*, which encodes the nongastric H,K-ATPase, reduced IL-13-induced eotaxin-3 expression in cultured HNECs. There was also evidence of accelerated IL-13-induced eotaxin-3 mRNA decay in the presence of PPIs.

The study provides in vitro and in vivo evidence that IL-13-induced eotaxin-3 expression by airway epithelial cells is reduced by PPIs. The mechanism of IL-13-mediated epithelial responses appears to involve nongastric H,K-ATPase, which is inhibited by PPIs. Further studies are needed to evaluate the clinical benefits of reducing epithelial eotaxin-3 production using PPIs in patients with CRSwNP.

COMMENT: Patients with CRSwNP have increased eosinophils and Th2 mediators. Using cell cultures of surgical specimens and nasal lavage specimens from CRSwNP patients, these researchers reported impressive in vitro inhi-

Coseasonal Immunotherapy—Is It Safe?

There is concern that coseasonal immunotherapy—starting allergen immunotherapy during pollen season—might be associated with an elevated risk of systemic allergic reactions. Guidelines vary in their recommendations regarding coseasonal immunotherapy, or present recommendations without evidence. The authors performed a systematic review of evidence on the safety of coseasonal initiation of immunotherapy.

A comprehensive literature review identified 19 studies reporting on coseasonal immunotherapy. There were eight studies of subcutaneous immunotherapy (SCIT) including 947 patients and eleven studies of sublingual immunotherapy (SLIT) including 2,668 patients. The analysis included 340 and 565 patients, respectively, enrolled in randomized, double-blind, placebo-controlled trials.

The studies varied in design and reporting of safety outcomes. The highest reported discontinuation rates with coseasonal immunotherapy initiation were 6% in SCIT studies and 10% in SLIT studies. Rates of systemic allergic reactions in SCIT studies were 0% to 7% with coseasonal initiation "up to peak season," 0% to 6% "after peak season" (or with out-of-season initiation), and 0% to 6% with placebo. Rates of serious treatment-related adverse events with coseasonal initiation ranged from 0% to 2%. There were few severe adverse events.

In SLIT studies, rates of systemic allergic reactions were 0% to 4% with coseasonal initiation, 0% with out-of-season initiation, and 0% to 2% with placebo.

There were 2 serious treatment-related adverse events. Rates of severe adverse events were 0% to 8% with coseasonal initiation, 0% to 12% with out-of-season initiation, and 0% to 8% with placebo.

Within the limitations of the available data, coseasonal initiation of allergen immunotherapy, either SCIT or SLIT, appears to be well tolerated. There is no apparent increase in safety risks with coseasonal initiation, compared to ●●●

out-of-season initiation or placebo. However, the authors emphasize the need for better-controlled studies of coseasonal initiation.

COMMENT: Survey and case reports regarding coseasonal initiation of SCIT indicate an increase in morbidity and even mortality, while a prospective evaluation demonstrated no such increase. Recent guidelines suggest not increasing and in some cases reducing the dose of allergy immunotherapy during a patient's allergy season, especially in those with poor symptom control. Creticos and colleagues attempt to bring closure to this question through a systematic review. Thankfully, they find no increase morbidity with either SCIT or SLIT when used coseasonally. However, the authors acknowledge the heterogeneity of safety reporting in these studies. That makes it difficult to evaluate safety outcomes between the studies, reinforcing the need for standardizing reporting in future trials.

J.J.O.

Creticos PS, Bernstein DI, Casale TB, et al: Coseasonal initiation of allergen immunotherapy: a systematic review.

J Allergy Clin Immunol Pract. 2017;2016;1194-1204. ●

Keywords: allergen immunotherapy, coseasonal, SCIT, SLIT

SCIT in the Morning May Be Safer!

Adverse reactions to subcutaneous immunotherapy (SCIT) injections are common and potentially problematic. Diurnal variations in cortisol level and cutaneous hypersensitivity might be relevant to patterns of immunotherapy reactions. The authors evaluated the effects of the timing of SCIT injections on the risk of adverse reactions.

The retrospective analysis included 289 adults receiving outpatient SCIT injections at a single center between 2004 and 2014. Associations between the time of SCIT administration and the occurrence of reactions were assessed, with adjustment for other factors.

In a total of 17,457 injections, 574 reactions occurred. Reactions were more likely after afternoon or evening injections, compared to morning injections: 3.8% versus 2.8%. This diurnal variation did not apply to systemic reactions (World Allergy Organization grade 1 or higher), which occurred at a rate of 0.67% for afternoon/evening and 0.64% for morning injections.

In the fully adjusted model, reactions were 43% more likely to occur after afternoon/evening injections, compared to morning injections. The difference was even greater for injections given between 3:00 and 5:30 pm—a 55% increase.

The results suggest diurnal variation in cutaneous reaction rates to SCIT, with reactions being more likely to occur with afternoon/evening injections compared to morning injections. The results suggest that morning injections might be advantageous for patients who have troublesome local reactions to SCIT. The authors highlight the need for further studies, including possible diurnal variations in reactions to sublingual immunotherapy.

COMMENT: While SCIT is generally well tolerated, this study brings an interesting observation for the practicing allergist. Since cortisol peaks in the early morning, it may be an option for patients with local reactions to SCIT to receive their injections in the morning. Prospective studies are needed to evaluate administration time in larger groups, along with information regarding antihistamine pretreatment.

V.H.-T.

Bavishi AA, Grammer LC, Pongracic J, et al: Diurnal variations in subcutaneous allergen immunotherapy reactions.

Ann Allergy Asthma Immunol. 2017;118:103-107. ●

Keywords: allergen immunotherapy, local reactions, SCIT

Mast Cells Are Important in Severe Asthma Too

Mast cells are known to play a role in the pathogenesis of adult asthma, but their contribution to childhood asthma remains unclear. This study evaluated mast cells in the airways of children with severe asthma, and their association of mast cells with the clinical presentation.

The researchers performed airway smooth muscle biopsies in 36 children, aged 5 to 18 years, with severe asthma. Twenty-four children had frequent severe asthma, daily symptoms, or both; the other 12 had persistent obstruction but few symptoms. Nine healthy children were studied as controls.

Among the children with severe asthma, submucosal mast cell numbers were higher in the symptomatic group, and were correlated with the frequency of severe exacerbations. Submucosal mast cells were also correlated with submucosal eosinophilic infiltration. Mast cell numbers were unrelated to measures of lung function or airway remodeling.

The cross-sectional study finds that mast cells are located in the airway smooth muscle of children with severe asthma, and are correlated with severe exacerbations and submucosal eosinophils. The results add evidence that mast cells are involved in asthma exacerbations as well as chronic airway inflammation. Treatments targeting mast cells might have benefits for highly symptomatic children with eosinophilic severe asthma.

COMMENT: Mast cells appear to be associated with severe exacerbations in addition to eosinophilic inflammation in patients with severe asthma. These patients have higher potential for exacerbations, while increased numbers of mast cells are an independent risk for asthma exacerbations. These insights could lead to treatments that extend beyond the relatively weak effects of cromolyn. (Also see the editorial by Fleming et al: Eur Respir J. 2016;48:1261-1264.)

B.E.C.

Lezmi G, Galmiche-Rolland L, Rioux S, et al: Mast cells are associated with exacerbations and eosinophilia in children with severe asthma.

Eur Respir J. 2016; 48:1320-1328. ●

Keywords: asthma (child), asthma (severe), exacerbations, mast cells

Intermittent Asthma: Did the Guidelines Get It Wrong?

Current guidelines reserve inhaled corticosteroid (ICS) therapy for patients with asthma symptoms at least 2 days per week, although the evidence for this recommendation is limited. This study assessed the effects of budesonide versus placebo in patients with mild asthma at differing levels of baseline symptom frequency.

The study was a post-hoc analysis of the multicenter Steroid Treatment As Regular Therapy (START) study. In that trial, children and adults diagnosed with mild asthma within the past two years were randomly assigned to once-daily inhaled budesonide (200 µg in children 400 µg in adolescents and adults) or placebo. Main outcomes of interest were time to first severe asthma-related event (SARE) and post-bronchodilator change in lung function.

Of 7,138 patients in the study, 31% initially had symptoms no more than 1 day per week, 27% had symptoms 2 days per week, and 43% had symptoms more than 2 days per week. In all three frequency subgroups, budesonide was associated with a longer time to first SARE, compared to placebo: hazard ratio 0.54, 0.60, and 0.57, respectively. At 3 years' follow-up, budesonide-treated patients also had a lesser decline in postbronchodilator lung function.

Budesonide was also associated with a reduced risk of severe exacerbations requiring corticosteroids: rate ratio 0.48 in patients with 0 to 1 symptom days per week, 0.56 with 2 days, and 0.66 with more than 2 days. There were also significant differences in prebronchodilator lung function and symptom-free days, with no interaction by symptom frequency. The effects of budesonide were also similar when patients were classified as having "persistent" or "intermittent" asthma.

The results confirm the benefits of once-daily, low-dose budesonide for patients with recently diagnosed mild asthma, regardless of baseline symptom frequency. The findings question the recommendation to limit ICS to patients with symptoms 2 or more days per week.

COMMENT: These findings challenge the longstanding doctrine that asthma should be treated with short-acting beta-agonists alone in patients who have symptoms two or fewer times per week. In a post-hoc analysis of the START study, the authors demonstrate that in patients with recently diagnosed mild asthma, low-dose ICS therapy halved the risk of serious asthma-related events, diminished the decline in lung function, and improved daily symptom control compared to placebo. This improvement was seen not only in patients with mild persistent asthma, but also in those with intermittent disease. The authors opine that guidelines should "take into account the potential to reduce the population-level risk of serious asthma-related events, even if day to day symptoms are not burdensome."

J.J.O.

Reddel HK, Busse WW, Pedersen S, et al: Should recommendations about start-

ing inhaled corticosteroid treatment for mild asthma be based on symptom frequency: a post-hoc efficacy analysis of the START study. *Lancet*. 2017;389:157-166. ●

Keywords: asthma (adult), asthma (mild), ICS

Should We Re-Think Who Provides Care for Asthmatic Patients?

There are questions regarding the diagnosis and course of asthma in the community. These include the rate of spontaneous remission and whether treatment is appropriately stepped down once disease control is achieved. This study evaluated the diagnostic and treatment status of adults in the community with a recent diagnosis of asthma.

The study included a random sample of 701 adults with a physician diagnosis of asthma within the past 5 years. The mean age was 51 years; two-thirds of patients were women. Information from the diagnosing physician was obtained to determine how the diagnosis was made. Patients underwent home peak flow and symptom monitoring, spirometry, and bronchial challenge testing. In those taking daily asthma medications, treatment was tapered in a series of office visits.

In 613 patients who completed the study, the diagnosis of current asthma was excluded in 201. In 2% of patients, study evaluation led to diagnosis of serious cardiorespiratory conditions that had been misdiagnosed as asthma. After 1 year of follow-up, 29.5% of patients still had no clinical or laboratory evidence of asthma. Patients in whom asthma was ruled out were less likely to undergo airflow limitation testing at the time asthma was diagnosed in the community: 43.8%, compared to 55.6% of those in whom asthma was confirmed. Factors associated with confirmed of current asthma included lower FEV₁ predicted, daily asthma medication use, airflow limitation testing, and history of wheezing.

On specialist evaluation, asthma is excluded in one-third of adults with a recent diagnosis of asthma in the community. In most of these patients, asthma medications can be safely stopped during subsequent clinical follow-up. The authors discuss the role of spontaneous remission and initial misdiagnosis in patients with community-diagnosed asthma.

COMMENT: Prior research has demonstrated that care through asthma specialists complies more closely with guideline recommendations and is associated with better outcomes. In this study, patients with a diagnosis of asthma were randomly recruited from the community. A whopping 33.1% of these patients had no evidence of current asthma when they were prospectively evaluated while not using asthma medications. More than 90% of participants in whom asthma was ruled out had asthma medications safely stopped for an additional 1-year period. Those incorrectly diagnosed with asthma ultimately had diagnoses including rhinitis, gastroesophageal reflux disease, ischemic heart disease, pulmonary hypertension, and sarcoidosis, to ●●●

name just a few. This study reinforces the importance of specialty care and raises the question as to whether we should consider paradigm changes in the caregivers of asthmatic patients. This article is a must-read for all asthma specialists. J.J.O.

Aaron SD, Vandemheen KL, FitzGerald JM, et al: Re-evaluation of diagnosis in adults with physician-diagnosed asthma. *JAMA*. 2017;317:269-279. ●

Keywords: asthma (adult), diagnosis, specialty care

Risk Factors for ED Failures in Asthma

There are conflicting results regarding management of acute asthma exacerbations in preschool-aged children—only some studies have supported the effectiveness of guideline-recommended treatment including bronchodilators and oral corticosteroids. This study sought to identify risk factors associated with failure of emergency department (ED) therapy for moderate to severe asthma exacerbations in children.

The prospective cohort study included 1,012 children with moderate or severe asthma seen at five Canadian pediatric EDs. Patients received guideline-recommended management including oral corticosteroids and inhaled bronchodilators. The study definition of ED failure included hospital admission, ED stay of 8 hours or longer, or relapse within 72 hours after ED discharge. Potential determinants of response included viral infection, assessed by polymerase chain reaction of nasopharyngeal specimens; and secondhand smoke exposure, assessed by salivary cotinine measurement.

On analysis of 965 children, 17% met the study definition of ED management failure. The ED failure rate was 19% in children with viral detection versus 13% of those without a viral cause: odds ratio (OR) 1.57. Other significant factors were fever, OR 1.96; baseline Pediatric Respiratory Assessment Measure score, OR 1.38 per 1-point increment; oxygen saturation less than 92%, OR 3.94; and presence of symptoms between exacerbations, OR 1.13. Age, secondhand smoke, and oral corticosteroid dose were not significant factors.

Preschool-aged children were more likely to have viral detection and fever, compared to older children. Children with a viral cause also had slower recovery over 10 days postdischarge.

Viral infection appears to be an important risk factor for failure of ED management in children with moderate to severe asthma exacerbations. The association is independent of baseline severity, fever, and chronic asthma symptoms; age is not a significant factor. Further study is needed to evaluate the possible association with secondhand smoke exposure.

COMMENT: Prior research has attempted to uncover determinants of failure in emergency care of asthma exacerbation, with mixed results. This well-controlled prospective multicenter pediatric cohort provides great insight into this question. The authors found several unexpected risk factors for ED fail-

ure, including viral detection, fever, greater exacerbation severity, and symptom chronicity. Elevated salivary cotinine was associated with 2-fold increase in ED failure—although this finding did not reach statistical significance, likely because the study was underpowered to assess this potential trigger. As noted in the accompanying editorial by Arnold (*Lancet Respir Med*. 2016;4:930-932), this paper provides great direction for future development of prognostic tools to help risk stratify patients seeking care for an exacerbation of asthma.

J.J.O.

Durcharme FM, Zemek R, Chauhan BF, et al: Factors associated with failure of emergency department management in children with acute moderate or severe asthma: a prospective, multicenter, cohort study.

Lancet Respir Med. 2016;4:990-998. ●

Keywords: asthma (child), emergency department, risk factors

Asthma Severity Linked to Animal Dander-Specific IgE

Sensitization to indoor allergens plays a major role in asthma, although the association between these allergens and asthma symptoms remains unclear. This study assessed the relationship between sensitization to dog and cat allergen and asthma symptoms, in a northern area with low exposure to other indoor allergens.

The study included participants from an ongoing population-based cohort study in northern Sweden—an area where the climate discourages indoor allergens such as cockroach, dust mite, and fungi. Specific IgE to cat and dog allergens were measured in serum samples from 963 participants at age 19 years. Associations of cat and dog sensitization with the presence, severity, and persistence of asthma were assessed.

Titers of specific IgE for cat and dog allergens were strongly associated with asthma prevalence and severity. Out of 103 patients with asthma at 19 years, 50 had asthma before 12 years. In this group, the odds ratio for asthma associated with any animal dander-specific IgE was 9.2. The association was even stronger, odds ratio 13, for high-titer IgE antibodies of 17.5 IU/mL or higher. Specific IgE to Fel d 1 and Can f 5 were both associated with prevalent asthma.

These data from northern Sweden suggest that high titers of animal dander-specific IgE antibodies are strongly associated with the presence and severity of asthma in young adults. For those diagnosed with asthma before age 12, specific IgE to pets is strongly related to asthma. Having a cat or dog at home was not a significant predictor of sensitization or asthma, highlighting the presence of pet allergens throughout the community.

COMMENT: "Should we get rid of our pet because our child has asthma?" How many times have we heard parents ask this question? These researchers used a unique cohort ● ● ●

of children living above the Arctic Circle—with no exposure to dust mites or cockroaches—to examine the association of cat or dog exposure and sensitization with persistence of asthma. The presence of specific IgE to cat or dog was related to both the prevalence and severity of asthma. Interestingly, a high percentage of children without pets had elevated specific IgE to cat and/or dog, indicating that pet dander exposure outside the home is clinically relevant. Our answer to our patients may not be so easy, but having additional data is helpful.

S.M.F.

Perzanowski MS, Ronmark E, James HR, et al: Relevance of specific IgE antibody titer to the prevalence, severity, and persistence of asthma among 19-year-olds in northern Sweden.

J Allergy Clin Immunol. 2016;138:1582-1590. ●

Keywords: asthma (child), pet allergies, specific IgE

Sex-Specific Risk Factors and Longitudinal Phenotypes for Childhood Wheeze

Boys and girls differ in wheezing and asthma prevalence, but relatively little is known about sex-specific risk factors for childhood wheeze, or about the longitudinal trajectory of wheezing. These issues were addressed using data from a large prebirth cohort study.

The analysis included 1,623 children enrolled in Project Viva, which was designed to assess prenatal and perinatal factors affecting maternal and child health. Atopy risk was not a selection factor. Mothers made annual reports of childhood wheezing symptoms. Sex-specific risk factors for wheezing from birth to mid-childhood were analyzed, along with longitudinal wheeze phenotypes and associated sex-specific risk factors.

Paternal asthma was a risk factor for wheezing in both sexes, but was stronger in boys: odds ratio 2.15, compared to 1.53 in girls. Several other factors were stronger in girls than boys, including black or Hispanic race/ethnicity, birth weight for gestational age z score, and duration of breastfeeding.

On phenotype analysis, 74.1% of children had no or infrequent wheeze, 12.7% had early transient wheeze, and 13.1% had persistent wheeze. In both sexes, risk factors for persistent wheeze included maternal asthma, bronchiolitis in infancy, and atopic dermatitis. Paternal asthma was a significant risk factor in boys only, OR 4.27; while black or Hispanic race/ethnicity was specific to girls: OR 3.23 and 3.60, respectively.

Some sex-specific risk factors for childhood wheeze and a persistent wheezing phenotype are identified. Paternal asthma appears to be a significant risk factor for boys, while race/ethnicity may increase risk among girls. The authors discuss the implications for individual prognosis and treatment for childhood wheezing and asthma.

COMMENT: Knowledge of sex-specific risk factors for childhood asthma may have prognostic and clinical implications in the management of children with wheezing. This well-designed study using data from a large prospective birth cohort followed children until 9 years of age. Paternal asthma was an important predictor of persistent wheeze in boys, whereas being black or Hispanic was a stronger risk factor in girls. Three wheezing phenotypes were identified; the risk factors associated with each frequently depended on the sex of the child. The finding that paternal asthma was a predictor for persistent wheeze in boys was novel.

S.M.F.

Tse SM, Rifas-Shiman SL, Coull BA, et al: Sex-specific risk factors for childhood wheeze and longitudinal phenotypes of wheeze.

J Allergy Clin Immunol. 2016;138:1561-1568. ●

Keywords: wheeze (child), risk factors

Rhinovirus-Specific Antibody Responses: A Marker Of Severity In Preschool Wheezing?

Rhinovirus (RV)-associated wheezing in children is associated with an increased risk of later asthma. It is unclear whether wheezing is caused by more virulent RV strains or by host immune responses. This study assessed RV species present in preschool-aged children with wheezing and their association with species-specific IgG₁ and symptoms at follow-up.

The researchers obtained nasopharyngeal and blood specimens from 120 children, under age 4, with acute wheezing. Follow-up samples were obtained at a follow-up visit a median of 11 weeks later. Specific RV strains were identified by nested polymerase chain reaction. Enzyme-linked immunosorbent assays were used to measure serum levels of IgG₁ against purified recombinant VP1 proteins from the RV-A, RV-B, and RV-C species.

Seventy-four percent of children had RV detected at their visit for acute wheezing; of those with rhinovirus, 74% had RV-C. Sixty-one percent of children had increased RV-specific IgG₁ at their follow-up visit. In 86%, the increase was in IgG₁ against RV-A, independent of the strain detected at the acute visit. Increases in IgG₁ against RV-A, alone or with IgG₁ against RV-C, were associated with increased respiratory symptoms. Time with respiratory symptoms was more associated with the respiratory response than with the initially detected RV species.

In preschool-aged children with acute wheezing, IgG₁ antibody responses against RV VP1 proteins are significantly associated with the duration of respiratory symptoms. In particular, children with increased IgG₁ against RV-A and RV-C have a longer time with reported symptoms. Although further studies are needed, this could be a group at high risk of developing later asthma.

COMMENT: The authors detected RV in approximately ● ● ●

74% of children with acute visits for wheeze, and RV-C was the most frequent species. Surprisingly, an increase in RV-specific IgG1 against RV-A or RV-A and C was significantly associated with more respiratory symptoms. The authors propose this finding may be the result of a less effective early innate immune response or a more symptomatic infection with resultant higher antibody response. They raise the question of whether children with this higher IgG1 response to RV may be a "vulnerable" group at greater risk of developing asthma.

J.J.O.

Stenberg-Hammar K, Niespodziana K, Soderhall C, et al: Rhinovirus-specific antibody responses in preschool children with acute wheeze reflect severity of respiratory symptoms. *Allergy*. 2016;71:1728-1735. ●

Keywords: asthma (child), rhinovirus, wheeze (child)

Do Fish Oil Supplements During Pregnancy Prevent Asthma?

Low intake of n-3 long-chain polyunsaturated fatty acids (LCPUFAs) during pregnancy may be associated with an increased risk of childhood wheezing and asthma. Most previous trials of this issue have been underpowered, with inconclusive results. This randomized controlled trial with long-term follow-up evaluated the effects of n-3 LCPUFA supplementation during pregnancy on the risk of wheeze and asthma in offspring.

At 24 weeks' gestation, 736 pregnant women were assigned to supplementation with fish oil, containing 2.4 g of n-3 LCPUFA, or olive oil. Both parents and investigators were unaware of the children's group assignments for the first 3 years of follow-up, and the investigators for an additional two years. Rates of persistent wheeze or asthma were compared between groups.

Of 695 children enrolled in the trial, 95.5% completed 3 years of follow-up. Persistent wheeze or asthma developed in 16.9% of children assigned to n-3 LCPUFA supplementation, compared to 23.7% with olive oil: hazard ratio (HR) 0.69. The effect was even larger in a prespecified subgroup of children whose mothers had low baseline levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA): HR 0.46.

The n-3 LCPUFA supplementation group also had a lower rate of lower respiratory tract infections: 31.7% versus 39.1%, HR 0.75. Other secondary outcomes were similar between groups, including allergic sensitization, eczema, and asthma exacerbations.

Taking supplemental fish oil during the third trimester of pregnancy may reduce the risk of persistent wheeze or asthma in offspring. The intervention effect is stable from age 2 through 5 years, with the largest benefit among women in the lowest one-third of baseline n-3 LCPUFA levels.

COMMENT: High-dose third trimester supplementation of n-3 LCPUFAs, derived from fish oil, significantly reduced the

absolute risk of persistent wheeze or asthma during the first 5 years of a child's life. The effect was most pronounced in children of mothers with low baseline blood levels of EPA and DHA. As pointed out by Ramsden in an accompanying editorial (*N Engl J Med*. 2016;375:2596-2598), it is important to note that the dose of EPA plus DHA provided in this trial (2.4 g per day) was approximately 15 to 20 times the average US normal dietary intake. Further safety studies of this high dose are needed.

C.D.

Bisgaard H, Stokholm J, Chawes BL, et al: Fish oil-derived fatty acids in pregnancy and wheeze and asthma in offspring. *N Engl J Med*. 2016;375:2530-2539. ●

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

Do Genes Determine Lung Function Decline in Childhood Asthma?

Previous studies have linked reduced lung function growth and early decline to future risk of chronic airway obstruction. Similar patterns may be associated with asthma-chronic obstructive pulmonary disease overlap syndrome. This study evaluated the genetic basis of lung function patterns in asthmatic children.

The genomewide association study included 581 non-Hispanic white asthmatic subjects drawn from the Childhood Asthma Management Program (CAMP) cohort, enrolled at age 5 to 12 and followed up to age 18. In previous studies, the subjects were categorized into differing patterns of lung function growth and decline: normal growth, normal growth with early decline, reduced growth, and reduced growth with early decline. Single-nucleotide polymorphisms (SNPs) associated with these longitudinal lung function growth patterns were identified. A generalization analysis of the strongest signal was performed in two further cohorts: a small cohort of asthma patients and a large meta-analysis cohort of patients with chronic obstructive pulmonary disease.

A SNP on chromosome 8, rs4445257, was strongly associated with the pattern of normal lung function growth with early decline: odds ratio 2.8, compared to all other patterns. In the additional cohorts, this variant showed opposite effects in the normal growth with early decline pattern versus the reduced growth with early decline pattern. In chromosome conformation capture experiments to explore biologic mechanisms, the rs4445257 polymorphism showed a physical reaction with the *CSMD3* promoter and was associated with *CSMD3* gene expression.

The analysis of children with asthma identifies a chromosome SNP associated with a longitudinal lung function pattern of normal growth followed by early decline. The same gene variant may have a protective effect against early decline in children with reduced lung function growth.

COMMENT: The effect of the described minor allele on chromosome 8 for early decline following normal growth ● ● ●

of lung function may provide significant insight for development of therapies. Currently, there are no known intervention strategies that will prevent lung function decline in childhood asthma. This finding in the CAMP population gives new hope that the genetic basis of asthma may lead to identification of patients at risk for lung function decline and to more effective treatment strategies.

B.E.C.

McGeachie MJ, Yates KP, Zhou X, et al: Genetics and genomics of longitudinal lung function patterns in individuals with asthma.

Am J Respir Crit Care Med. 2016;194:1465-1474. ●

Keywords: asthma (child), genetics, lung function growth

FOCUS ON COPD

Asthma-like Features In COPD: New Phenotype With Better Prognosis

A subgroup of patients with chronic obstructive pulmonary disease (COPD) have characteristics similar to asthma, despite not having a clinical diagnosis of asthma. The clinical significance of these asthma-like features was evaluated in a long-term follow-up study of patients with COPD.

The analysis included data on 268 patients with COPD from a Japanese cohort study, none of whom were considered to have asthma on respiratory specialist evaluation. Of these, 133 patients had at least one of three asthma-like features: bronchodilator reversibility, 21%; blood eosinophilia, 19%; and atopy, 25%. The patients were prospectively followed up for 10 years, during which they received appropriate treatment. Associations of asthma-like features with the clinical course and outcomes of COPD were analyzed.

The COPD patients with blood eosinophilia had a significantly slower rate of decline in postbronchodilator FEV₁, which was unaffected by the presence of bronchodilator reversibility or atopy. None of the three asthma-like features was associated with development of COPD exacerbations. Patients with at least two asthma-like features had annual postbronchodilator FEV₁ declines and COPD exacerbations similar to those of patients with zero or one feature. Patients with multiple asthma-like features had lower 10-year all-cause mortality.

Among patients with COPD receiving adequate treatment, the presence of asthma-like features is associated with a more favorable clinical course. The authors discuss possible reasons for this finding, including a unique phenotype of COPD or better response to treatment.

COMMENT: Patients with COPD but no previous history of asthma may have features associated with classic asthma. When these features are present, especially eosinophilia, there is a significant protective effect for all-cause mortality and decline in postbronchodilator FEV₁. This has previously

been reported in the CHAIN Study (Cosio BG, et al: Chest 2016;149:45-52). All of the positive effects cannot be solely ascribed to inhaled corticosteroid treatment.

B.E.C.

Suzuki M, Makita H, Konno S, et al: Asthma-like features and clinical course of chronic obstructive pulmonary disease: an analysis from the Hokkaido COPD Cohort Study. Am J Respir Crit Care Med. 2016;194:1358-1365. ●

Keywords: asthma, COPD, phenotypes, prognosis

What's New in ACOS?

Patients with asthma-COPD overlap syndrome (ACOS) have characteristics typically associated with both diseases. It remains unclear whether the clinical course of ACOS differs from that of more typical COPD. This cohort study compared the clinical characteristics and outcomes of patients with ACOS versus "pure" COPD in a real-world cohort.

The study used data from a French cohort study including 998 patients with COPD. The frequency of ACOS was 13%, based on a physician diagnosis of asthma before 40 years of age. Over 3 years' follow-up, mortality was 16.3% for patients with ACOS versus 20.7% for those with pure COPD. However, mortality and disease severity were not significantly different between groups.

On multivariate analysis, ACOS was negatively associated with smoking: odds ratio (OR) 0.992 per pack-year smoked. Several factors were positively associated with ACOS, including obesity, OR 1.97; and history of atopic disease, including hay fever, OR 5.50; atopic dermatitis, OR 3.76. Treatments associated with ACOS included long-acting beta-agonists plus inhaled corticosteroids, OR 1.86; antileukotrienes, OR 4.83; theophylline, OR 2.46; and oral corticosteroids, OR 2.99.

The results suggest some significant differences in the characteristics of patients with ACOS compared to those with "pure" COPD. The ACOS patients have less cumulative smoking, increased obesity and atopic disease, and more use of asthma medications. Outcomes and clinical course appear similar between the two groups.

COMMENT: As we continue to learn more about ACOS, the French COPD cohort "INITIATIVES Broncho Pneu-mopathie Chronique Obstructive" provides further understanding regarding the disparity between these two illnesses. The authors found that compared to "pure" COPD patients, those with ACOS exhibit lower cumulative smoking, suffer more from obesity as well as atopic diseases, and use more asthma therapy. The researchers also found that disease severity (dyspnea, quality of life, and exacerbations) and prognosis (mortality) of patients with ACOS are no different from those with "pure" COPD.

J.J.O.

Caillaud D, Chanez P, Escamilla R, et al: Asthma-COPD overlap syndrome (ACOS) vs 'pure' COPD: a distinct phenotype? Allergy. 2017;137-145. ●

Keywords: ACOS, COPD, phenotypes

What's Riskier in COPD: Tiotropium or LABA?

Recommendations for maintenance therapy in patients with chronic obstructive pulmonary disease (COPD) include long-acting β_2 -agonists (LABAs) and the long-acting muscarinic antagonist (LAMA) tiotropium. There are potential cardiovascular and pulmonary complications with both of these agents, but little information on their comparative risks. This study compared adverse cardiopulmonary outcomes in COPD patients during the first year after starting LABAs or tiotropium.

Using the UK Clinical Practice Research Datalink, the authors identified COPD patients aged 55 or older who were initiating long-acting bronchodilator therapy for the first time. Groups of patients starting LABAs or tiotropium, 26,442 in each group, were matched according to high-dimensional propensity scores and previous inhaled corticosteroid therapy. One-year follow-up data were used to compare rates of acute myocardial infarction, stroke, heart failure, arrhythmia, and pneumonia between groups.

Rates of acute myocardial infarction and stroke were non-significantly higher with tiotropium compared to LABAs, while rates of arrhythmias and heart failure were non-significantly lower with tiotropium. The tiotropium group did have a significantly lower risk of heart failure: hazard ratio 0.81. Similar patterns were observed in sensitivity analyses.

For COPD patients starting long-acting bronchodilator maintenance therapy, cardiovascular risks during the first year are similar with LABAs compared to the LAMA tiotropium. The increase in pneumonia risk with LABAs likely reflects the high use of single-inhaler combined ICS treatment in this real-world COPD cohort.

COMMENT: LABAs and LAMAs are considered first-line therapy for COPD; however, cardiovascular concerns exist for both agents. This study analyzed data from a very large UK database involving more than 88,000 LABA new users (most with ICS) and more than 26,000 tiotropium new users. The results showed similar rates of myocardial infarction, stroke, and arrhythmia between groups. Risk of pneumonia was lower in the tiotropium group, which the authors attributed to the ICS component of treatment for the majority of patients on LABA therapy. The authors defined COPD based on age and medication; therefore some of the patients likely had asthma.

D.A.K.

Suissa S, Dell'Aniello S, Ernst P: Long-acting bronchodilator initiation in COPD and the risk of adverse cardiopulmonary events: a population-based comparative safety study. *Chest*. 2017;151:60-67. ●

Keywords: Cardiovascular risks, COPD, LABAs, tiotropium

Is Omalizumab Helpful in ACOS?

Patients with so-called asthma-COPD overlap syndrome (ACOS) have greater health impairment and more frequent and severe exacerbations than those with either diagnosis alone. Anti-IgE therapy with omalizumab is beneficial for patients with severe persistent asthma, but its role in the ACOS population is unclear. Data from an Australian omalizumab registry were used to assess the response to this medication in ACOS patients.

The analysis included 177 patients prescribed omalizumab: 17 with and 160 without a physician diagnosis of COPD. Outcomes were compared between groups, including subgroups based on postbronchodilator FEV₁ and smoking history.

For patients with severe-allergic asthma and physician-diagnosed COPD, omalizumab was associated with significant improvements in quality of life and asthma control—the ACQ-5 score decreased from 3.68 to 1.69. These benefits extended to all subgroups, regardless of smoking history. At 6 months' follow-up, lung function measures improved significantly among patients with a baseline FEV₁ of less than 80%, but not in those with an FEV₁ greater than 80%. Although small, the study suggests improvements in asthma control and quality of life with omalizumab in patients with severe allergic asthma and associated COPD. The study offers real-world evidence that omalizumab may be helpful in patients with ACOS.

COMMENT: This study from Australia adds a bit more to the scant data available on ACOS patients. Improvements in asthma control and quality of life were observed in the few patients with physician-diagnosed COPD and those with smoking histories and FEV₁ less than 80%. Not surprisingly, lung function did not improve in these groups. Unfortunately, the small size of the more clearly defined ACOS group and the retrospective nature of the data are clear limitations.

D.A.K.

Maltby S, Gibson PG, Powell H, McDonald VM: Omalizumab treatment response in a population with severe allergic asthma and overlapping COPD. *Chest*. 2017;151:78-89. ●

Keywords: ACOS, asthma (allergic), omalizumab

Alcohol Hyperresponsiveness: A New Predictor of Recurrent Nasal Polyps

Some patients with chronic airway inflammatory diseases report that their symptoms get worse after they drink alcohol. Few studies have examined the characteristics and impact of alcohol hyperresponsiveness (HR) in patients with chronic rhinosinusitis with nasal polyps (CRSwNP). A large group of CRSwNP patients were surveyed to assess characteristic and inflammatory markers associated with alcohol HR.

The study included 534 patients with CRSwNP and, as controls, 198 patients with CRS without nasal polyps, ● ● ●

369 patients with allergic rhinitis, and 180 healthy volunteers. The study questionnaire assessed upper and lower airway HR to alcohol and sensitivity to environmental or occupational irritants. Inflammatory markers were measured in nasal tissue specimens obtained at surgery from 138 CRSwNP patients.

The CRSwNP patients were more likely to report asthma and NSAID hypersensitivity; nearly one-fourth of CRSwNP patients with aspirin-exacerbated respiratory disease (AERD) said they did not consume alcohol. All three chronic airway disease groups reported higher rates of alcohol HR, compared to healthy controls, with the highest rate among those with AERD.

Within the CRSwNP group, the prevalence of nasal alcohol HR was higher in patients with recurrent nasal polyps, those with uncontrolled symptoms, and those requiring oral steroids and antibiotics. Nasal symptoms were not limited to any specific type of beverage; symptoms commonly developed within 1 hour and lasted more than 1 hour but less than 1 day. Nasal tissue specimens from CRSwNP patients with nasal alcohol HR showed increased levels of eosinophil cationic protein.

Among patients with CRSwNP, the presence of alcohol HR is associated with greater disease severity and recurrent nasal polyps. The association with polyp recurrence may have important implications for clinical management; these patients might achieve better symptom control by avoiding alcohol.

COMMENT: Recent studies have highlighted the frequency of alcohol-induced upper and lower respiratory symptoms in patients with AERD. This large European study used a survey to compare subtypes of CRS patients with allergic rhinitis and controls. Symptoms of alcohol HR were highest for those with nasal polyps, regardless of AERD. Recurrence of nasal polyps, severity of disease, and higher tissue eosinophil cationic protein levels were found in patients who noted alcohol HR. Inquiring about alcohol-induced nasal and chest symptoms may be a useful clinical tool.

D.A.K.

De Schryver E, Derycke L, Campo P, et al: Alcohol hyper-responsiveness in chronic rhinosinusitis with nasal polyps.

Clin Exp Allergy. 2017;47:245-253. ●

Keywords: AERD, CRSwNP, risk factors

Epinephrine Prescriptions in the Real World

Trends in epinephrine autoinjector prescribing can provide an indication of the prevalence of anaphylaxis occurrence or risk. Data from a population-based records linkage system were used to assess trends in outcome epinephrine prescriptions.

The researchers analyzed trends in epinephrine autoinjector prescribing in Olmsted County, Minn., from 2004 through

2010. There were a total of 7,991 prescriptions in 3,801 patients, with an overall incidence rate of 757 per 100,000 person-years. Over the 7-year study period, the prescription rates increased by about 8% per year, although first-time prescriptions per patient remained relatively stable. The highest prescription rate was noted in boys aged 0 to 9, followed by boys aged 10 to 19. At older ages, the incidence was higher in women than men.

The study lends insights into recent trends in epinephrine autoinjector prescribing in a defined population. The overall number of prescriptions increased, with little change in first-time prescriptions per patient. Factors underlying these trends may include an increased burden of allergic disease, particularly food allergy in children and adolescents.

COMMENT: Surprisingly, little is known on the US population level regarding prescribing patterns of epinephrine over time. This population study, using the Rochester Epidemiology Project database, provides a great deal of insight. Although outpatient prescriptions for epinephrine autoinjectors increased in all ages from 2004 through 2010, first-time prescriptions per patient remained relatively stable. The highest rates of prescription overall were in women; however, the highest rates were in 0-to-9 age group, most commonly boys. The authors suggest that this increase may be a manifestation of several potential issues, including: increased burden of allergic disease (especially for food allergy in young patients), increased public awareness, or increased recognition and diagnosis by health care providers. J.J.O.

Lee S, Hess EP, Lohse C, et al: Epinephrine autoinjector prescribing trends: an outpatient population-based study in Olmsted County, Minnesota.

J Allergy Clin Immunol Pract. 2016;4:1182-1186. ●

Keywords: anaphylaxis, epinephrine autoinjector

Recurrent Anaphylaxis: Population Rates and Risk Factors

Recurrent anaphylaxis is a serious and frequent problem, particularly among patients with multiple triggers. This population-based study examined the incidence of and risk factors for recurrent anaphylaxis.

Using data from the Rochester Epidemiology Project, the researchers analyzed cases of recurrent anaphylaxis occurring in Olmsted County, Minn., from 2001 through 2010. Out of 611 identified patients with anaphylaxis, 60 had recurrent anaphylaxis during the 10-year follow-up period: a rate of 2.6 per 100 person-years. Foods, most commonly peanut or tree nut, were the most frequent inciting trigger; followed by medications and insect venom.

Independent risk factors for recurrence included history of atopic dermatitis, hazard ratio (HR) 5.6; presenting symptom of cough, HR 4.7; oral pruritis, HR 9.9; and treatment with corticosteroids, HR 5.2. Patients experiencing chest ● ● ●

pain were at lower risk of recurrent anaphylaxis: HR 0.24. Nearly three-fourths of patients had epinephrine available at the time of recurrent anaphylaxis.

The data show an 8% risk of recurrent anaphylaxis over 10 years' follow-up in a Minnesota population. Patients with atopic dermatitis and mucocutaneous or oral symptoms appear to be at high risk. Allergy/immunology referral and early access to self-injectable anaphylaxis are key to the management of recurrent anaphylaxis risk.

COMMENT: Few studies have investigated incidence and risk factors for recurrent anaphylaxis. These authors found that 8% of their 611 cases (2.6 per 100 person-years) experienced a recurrence of anaphylaxis. This rate was lower than previously reported, likely reflecting the population-based nature of the study. The median for recurrent anaphylaxis was about 7 months after the index event. The proportion of recurrent cases with access to epinephrine was 73% compared with 18% for the initial episode, and only 1 in 4 of the recurrent anaphylaxis cases were seen by an allergist. These findings underscore the as yet unrealized potential for improved outcomes associated with prompt referral of patients with anaphylaxis to Board-certified allergists.

D.M.L.

Lee S, Bashore C, Lohse CM, et al: Rate of recurrent anaphylaxis and associated risk factors among Olmsted County, Minnesota, residents: A population-based study. *Ann Allergy Asthma Immunol* 2016;117:655-660. ●

Keywords: anaphylaxis, epinephrine autoinjectors, risk factors

Patch Testing in Children: 10-Year Experience

Allergic contact dermatitis (ACD) is a common condition in children, and may become a recurrent and chronic problem. Patch testing is the standard for diagnosis of ACD. The authors review their center's 10-year experience with pediatric patch testing.

From 2005 to 2015, 157 children and adolescents underwent patch testing at the authors' dermatology department. Test procedures followed North American Contact Dermatitis Group standards.

The median patient age was 13 years; 58.6% were female. Symptoms were present for 6 months to 2 years in about one-third of patients, and longer than 2 years in nearly half. Mean number of allergens tested was 59.2; at least one positive reaction occurred in 73.25% of patients. Nickel and cobalt were the most frequently positive allergens.

Rates of allergen sensitivity were similar across age groups; males were more likely than females to react to fragrance mix 1. Reactions to cobalt and chromium were more frequent among patients with a history of atopy. Of 60 patients with available follow-up, 60.7% reported improvement. Most of these patients (88.5%) were treated with topical corticosteroids.

The experience illustrates the use of patch testing for diagnosis and management of ACD in children and adolescents. The authors highlight the need to educate primary care practitioners regarding the importance of prompt referral for patch testing in children with atopic dermatitis.

COMMENT: Allergic contact dermatitis commonly affects children and adolescents. These patients frequently present to allergists for evaluation and management. The prevalence of ACD has increased in recent years in association with exposures to sensitizers via cosmetics, hobbies, and body-piercing trends. In this retrospective study from Cleveland Clinic, almost half of 157 patients had symptoms for more than 2 years before being referred for patch testing. Similar to immediate hypersensitivity, avoidance is the most important aspect of management for ACD. It is important for allergists to recognize such patients and recommend performance of patch testing.

D.M.L.

Ascha M, Irfan M, Bena J, et al: Pediatric patch testing: a 10-year retrospective study. *Ann Allergy Asthma Immunol*. 2016;117:661-667. ●

Keywords: atopic dermatitis, contact dermatitis, patch testing

REVIEWS OF NOTE

COMMENT: This clinical report published by the American Academy of Pediatrics can serve as a handy reference guide to the "clinical toolbox" for primary care physicians taking care of children with asthma.

C.D.

Dinakar C, Chipps BE: Clinical tools to assess asthma control in children. *Pediatrics*. 2017;139:e20163438

COMMENT: This review examines how technologic interventions could improve the care of black and urban/low-income patients with asthma. The authors performed an analysis of all recent studies on the topic and found that the use of such new technology—including MP3 players, text messaging, computer/Web-based systems, video games, and interactive voice response systems—provides a high level of user satisfaction. These interventions led to improvements in asthma knowledge, medication adherence, and asthma symptoms, although they did not reduce health care utilization. As concluded by the authors, further research is required to better understand the full potential of these tools and how to maximize their effect.

J.J.O.

Baptist AP, Islam N, Joseph CLM: Technology-based interventions for asthma—can they help decrease health disparities? *J Allergy Clin Immunol Pract*. 2016;4:1135-1142.

COMMENT: The difficulties for patients with atopic dermatitis are well-known to us. Estimates of over \$1 billion yearly in direct medical costs related to the disease are daunting. Physical signs are only a part of the burden. Quality of life is affected by pruritus. Stress also contributes to sleep disturbance. The authors call on the practicing allergist to have empathy for these patients. We also have an obligation to educate patients about the disease, manage their expectations, and address their concerns regarding quality-of-life issues. In these ways we can positively impact the lives of our patients with atopic dermatitis.

V.H.-T.

Drucker AM: Atopic dermatitis: burden of illness, quality of life, and associated complications. *Allergy Asthma Proc*. 2017;38:3-8.