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

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FEATURE ARTICLES

Does Cat Ownership Drive Desensitization?

Previous reports have suggested "naturally occurring allergen tolerance" associated with chronic allergen exposure among people with cat allergy who own cats. Allergen tolerance is associated with accumulation of anti-inflammatory IgG_4. This study evaluated the process leading to IgG_4 accumulation in cat owners with chronic allergen exposure.

The study included 24 adults with cat allergy, 9 of whom were cat owners, and 14 nonallergic controls. Frequencies of cat allergen-specific T-cells, allergen-specific IgE and IgG_4 titers, and clinical status were compared among groups.

In cat-allergic subjects who didn't own cats, higher frequencies of Fel d 1- and Fel d 4-specific Th2 cells were associated with higher IgE levels and the presence of asthma. In contrast, among cat-allergic subjects who did own cats, a relatively high frequency of allergen-specific Th2 cells was associated with higher IgG_4 levels and decreased sensitization. Cat owners were more likely to rate their rhinitis as moderate: 22%, compared to 73% of non-cat owners.

Further studies suggested the presence of allergen-experienced B cells with the ability to produce IgG_4 in subjects with cat allergy. In these cells, exposure to cat allergen induced IgG_4 production in Th2 cell-dependent fashion.

These findings in cat-allergic subjects find that both asthma and cat allergen exposure are associated with a high frequency of Th2 cells. The desensitization observed in patients with cat allergy who own cats is related to Th2 cell-dependent IgG_4 production by allergen-experienced B cells. The authors note that allergen immunotherapy may be associated with a similar increase in specific IgG_4 levels.

COMMENT: Many patients say that they're not allergic to their cat even though they have large positive skin tests to cat dander. These researchers studied immune • • •

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The following journals have been selected as the primary focus of review in the preparation of materials within "AllergyWatch®".

- Annals of Allergy, Asthma and Immunology
- Journal of Allergy and Clinical Immunology
- American Journal of Respiratory and Critical Care Medicine
- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
- Journal of Pediatrics
- Journal of Asthma
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal
- Pediatric Allergy and Immunology

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responses in allergic patients who either owned a cat or not, compared to nonallergic controls. Interestingly, allergic patients with cats had a higher frequency of specific Th2 cells and higher IgG_4 levels with lower sensitization. The authors suggest that chronic allergen exposure to B cells generates a stronger IgG_4 response in a Th2-dependent manner, which could result in reduced sensitization. Does this explain why some of our patients with cats don't have many symptoms?

S.M.F.

Renand A, Archila LD, McGinty J, et al: Chronic cat allergen exposure induces a T_H2 cell-dependent IgG_4 response related to low sensitization.
J Allergy Clin Immunol. 2015;136:1627-1635.

Keywords: asthma (adult), cat allergy, immunotherapy

Does Azithromycin Help Childhood Wheezing during Viral URIs?

Airway bacteria and viruses are similarly associated with the occurrence of asthma-like symptoms during the first 3 years of life, suggesting a possible therapeutic role of antibiotics. Although not recommended by current guidelines, antibiotics are widely used for treatment of early asthma-like episodes. This randomized trial evaluated the effects of azithromycin on duration of respiratory episodes in young children with recurrent asthma-like symptoms.

This trial included 72 children aged 1 to 3 years with recurrent asthma-like symptoms, drawn from the Copenhagen Prospective Studies on Asthma in Childhood 2010 cohort. A total of 158 asthma-like episodes lasting at least 3 days were randomly assigned to 3 days of treatment with azithromycin, 10 mg/kg/d, or placebo. Treatment assignments remained masked until the youngest child turned 3 years old. The main outcome of interest was duration of the respiratory episode after treatment.

Azithromycin was associated with a significant reduction in the number of symptomatic days: 3.4 days compared to 7.7 days with placebo. On analysis of the first randomized treatment in each child, the difference was 4.0 versus 7.1 days, respectively. The benefit of azithromycin was greater if treatment started before day 6 of the asthma-like episode, but there was no difference in the risk of subsequent episodes. Adverse events were similar between groups; the study did not include data on bacterial resistance after treatment.

Treatment with azithromycin reduces the duration of asthma-like episodes in young children. Symptom duration is reduced by about 63% with azithromycin versus placebo, even greater if treatment is started early. Azithromycin could become a useful treatment for this common childhood problem.

COMMENT: All one can say is that history truly repeats itself. This study demonstrates the utility of azithromycin in 1- to 3-year-olds with asthma-like symptoms. Added to the recent pediatric cough guidelines for wet cough suggesting the utility of antibiotics (Chang AB, et al: Chest. 2016;149:120-142), will these results lead to an increase in the use of antibiotics in children? A very interesting finding in the study by Stokholm et al is that azithromycin was not only effective in children with bacterial infections, but also those infected by viruses. The authors suggest that this may be a result of azithromycin's abil- • • •

ity to reduce the neutrophilia associated with such infections. They note that further work is needed to better understand the mechanism of azithromycin's efficacy and to determine whether other antibiotics would produce similar results.

J.J.O.

Stokholm J, Chawes BL, Vissing NH, et al: Azithromycin for episodes with asthma-like symptoms in young children aged 1-3 years: a randomised, double-blind, placebo-controlled trial.
Lancet Respir Med. 2016;4:19-26.

Keywords: antibiotics, asthma (child), wheezing

Nondrug Treatments for Asthma: Time to Take Them Seriously?

Especially in light of the known psychological and behavioral associations, nonpharmacologic treatments may have a significant impact on the clinical outcomes of asthma. The authors performed a systematic review of the research literature relevant to nonpharmacologic interventions for asthma.

The review identified 23 randomized, controlled trials of nonpharmacologic interventions for adult patients with asthma. There were nine studies of relaxation-based therapies, five of cognitive-behavioral therapy, three of biofeedback techniques, one of a mindfulness intervention, and five of multicomponent therapies. Because of the use of differing outcome measures, it was difficult to perform meta-analyses, even within groups of studies.

Outcome analyses suggested beneficial effects of several types of interventions. For example, relaxation techniques showed positive effects on lung function, health-related quality of life, and psychological outcomes. However, there were limited data to show the benefits of one form of relaxation over another. Cognitive-behavioral therapy also showed evidence of positive effects on asthma-related quality of life and some psychological outcomes. Because of study heterogeneity and other limitations, the applicability to clinical practice was unclear.

Thus while there is evidence for benefits of nonpharmacologic interventions for adults with asthma, clinical trials of these interventions have important limitations. Relaxation therapies appear to be a promising type of intervention that would be relatively easy to implement in clinical practice. The authors call for further work to "harmonize" the differing types of interventions and the outcome measures used to determine their effectiveness.

COMMENT: Prior research has indicated a link between nonpharmacologic treatments and health outcomes in patients with asthma. Yorke et al performed an extensive literature search and found that relaxation and cognitive behavioral therapies appear to have a consistent positive effect—not just on quality of life measures, but also on physiologic outcomes such as lung function. The authors demonstrate that research in this arena has many deficiencies and stress the need for better methodology in the future.

J.J.O.

Yorke J, Shuldham C, Rao H, Smith HE: Nonpharmacological interventions aimed at modifying health and behavioural outcomes for adults with asthma: a critical review.
Clin Exp Allergy. 2015;45:1750-1764.

Keywords: asthma (adult), complementary therapy

Is Asthma a Risk Factor for Parkinson's Disease?

A previous cross-sectional study reported potential links between asthma and Parkinson's disease, although the temporal and independent nature of this relationship remains unknown. A population database with long-term follow-up was used to assess the risk of later Parkinson's disease among patients with asthma.

From a Taiwanese national health database, the researchers identified 10,455 patients diagnosed with asthma between 1998 and 2008, as well as a group of 41,820 age- and sex-matched controls. Both groups included patients aged 45 years or older; subjects were followed up through 2011. Associations between asthma and subsequent diagnosis of Parkinson's disease were assessed, including the effects of frequency of admissions for asthma exacerbations.

Patients with asthma were three times more likely to develop Parkinson's disease, compared to controls: hazard ratio 3.10, after adjustment for demographic factors, health system use, comorbid conditions, and medication use. The associations were about the same in sensitivity analyses excluding the first year and the first three years of observation. Parkinson's disease risk increased with asthma severity, based on exacerbation frequency: HR increased from 2.92 for patients with no more than one admission per year, to 12.69 with one or two admissions, to 16.43 with more than two admissions.

These population-based data show that patients with asthma are at independently increased risk of later diagnosis of Parkinson's disease. Based on exacerbation rate, there is a dose-dependent relationship between asthma severity and Parkinson's disease risk. The pathophysiologic mechanism of the association remains to be determined.

COMMENT: Using the Taiwan National Health Insurance Research Database, the authors examined between-group comparisons of patients with and without asthma. They found that patients with asthma had an elevated risk of developing Parkinson's disease later in life. They further demonstrated a dose-dependent relationship between greater asthma severity and a higher risk of subsequent Parkinson's disease. From a neurobiologic perspective, asthma-related immunologic dysregulation may explain the association with Parkinson's disease. Certainly, further research is needed including replication of these results.

J.J.O.

Cheng C-M, Wu Y-H, Tsai S-J, et al: Risk of developing Parkinson's disease among patients with asthma: a nationwide longitudinal study.
Allergy. 2015;70:1605-1612.

Keywords: asthma (adult), epidemiology, risk factors

Asthma-COPD Overlap Syndrome: Better Prognosis?

Recent international guidelines have proposed the term asthma-COPD overlap syndrome (ACOS) to describe patients with persistent airflow limitation plus findings typically associated with asthma. Clinical and functional criteria to define ACOS have been proposed but not validated. This study analyzes a stepwise approach to identifying patients with ACOS.

From a Spanish cohort study, the researchers identified 831 well-characterized patients with COPD and up to 1 year of follow-up. The analysis focused on specific characteristics associated with asthma. These included major criteria, ie, a bronchodilator response to salbutamol of greater than 400 mL and 15% and a medical history of asthma; and minor criteria, including IgE greater than 100 IU, history of atopy, two distinct bronchodilator responses of greater than 200 mL and 12%, and blood eosinophils greater than 5%.

Patients who had one major or two minor criteria were considered to have ACOS. A range of baseline characteristic and clinical outcomes were compared for patients who did and did not meet the ACOS criteria.

Fifteen percent of patients met the criteria for ACOS, of whom 98.4% still met the criteria at one-year follow-up. Most patients with ACOS were men, generally with symptomatic mild to moderate disease, who were receiving inhaled corticosteroids. Baseline characteristics were similar for patients with versus without ACOS. Of 67 deaths up to one year's follow-up, 60 were in patients without ACOS. Cumulative survival was 87.3% in the ACOS group versus 94.7% in patients without ACOS.

The prospective study finds that 15% of a cohort of patients with chronic obstructive pulmonary disease meet criteria for ACOS. This group has significantly better survival than patients who do not meet ACOS criteria. The authors present a set of "easily applicable clinical criteria" for use in identifying the presence of ACOS.

COMMENT: Features of both asthma and COPD are common in adults with obstructive airway disease. This study from Spain analyzed a prospective cohort study of COPD patients to evaluate those meeting criteria for ACOS. Of 831 COPD subjects, 15% met criteria for ACOS. Other than the differences used in the diagnostic criteria (reversibility, diagnosis of asthma, eosinophilia, and IgE levels), most other clinical characteristics were similar, including rates of emphysema, smoking pack-years, and disease severity. At 1 year, the ACOS group had lower mortality—a novel finding in this study. Longitudinal studies will be required to determine the importance of differentiating ACOS from COPD.

D.A.K.

Cosio BG, Soriano JB, Lopez-Campos JL, et al: Defining the asthma-COPD overlap syndrome in a COPD cohort.
Chest. 2016;149:45-52.

Keywords: ACOS, asthma (adult), COPD

Short-Term Omalizumab Reduces Fall Exacerbation Rate

Previous studies of inner-city children with asthma have found a lower exacerbation rate with higher doses of inhaled corticosteroids (ICS) or omalizumab, particularly in the fall. This randomized trial evaluated short-term targeted treatment with omalizumab, with or without ICS, to prevent fall exacerbations of asthma.

The randomized, double-blind trial included 513 inner-city children (aged 6 to 17 years) with asthma and one or more recent exacerbations. Over a 4- to 9-month run-in phase, all patients received guideline-based treatment. In a 4-month intervention phase, 318 children were assigned to omalizumab, ICS boost, or placebo; and 195 were assigned to omalizumab or placebo. Treatment started 4 to 6 weeks before the start of school, with outcomes assessed through the first 3 months of the school year.

Outcome analysis included 478 children. The fall exacerbation rate was significantly lower with omalizumab compared to placebo: 11.3% versus 21.0%, odds ratio (OR) 0.48. Exacerbations were not significantly different between omalizumab and ICS boost: 8.4% versus 11.1%. In a prespecified subgroup analysis of children who had an exacerbation during the run-in period, the exacerbation rate was 6.3% with omalizumab versus 36.3% with placebo, OR 0.12; and 2.0% with omalizumab versus 27.8% with ICS boost, OR 0.05.

In a subset analysis, omalizumab was associated with improved interferon-α responses to rhinovirus in peripheral blood mononuclear cells. Larger increases in interferon-α were associated with a lower exacerbation rate: OR 0.14. Adverse event rates were similarly low among treatment groups.

Short-term treatment with omalizumab, starting 4 to 6 weeks before the start of the school year, reduces the fall exacerbation rate among inner-city children with asthma. The effect seems most pronounced in children who experience an exacerbation during guideline-based care. Targeted seasonal treatment may be an effective preventive strategy for high-risk subgroups of asthmatic patients.

COMMENT: Omalizumab has previously been shown to improve asthma exacerbations in children, particularly for seasonal exacerbations. In this study, omalizumab was started 4 to 6 weeks before school and used for only 3 months. The reduction in the risk for exacerbation was not just better than placebo, but also better than ICS boost. The • • •

authors suggest that the role of IgE-triggered asthma, the potential for altering viral-induced interferon-α response, and ensuring compliance with omalizumab injection therapy in the clinic could all help explain the remarkable reduction of exacerbations in this inner-city population.

S.M.F.

Teach SJ, Gill MA, Togias A, et al: Preseasonal treatment with either omalizumab or an inhaled corticosteroid boost to prevent fall asthma exacerbations. J Allergy Clin Immunol. 2015;136:1476-1485.

Keywords: asthma (child), biologics, inner-city, omalizumab

Intrapartum Amoxicillin Does Not Increase Penicillin Allergy in Offspring

In pregnant women colonized with group B *Streptococcus,* intrapartum treatment with intravenous antibiotics is essential to prevent neonatal infection. Penicillin is the drug of choice. Previous studies have suggested increased rates of atopic diseases in children exposed to intrapartum antibiotics. The new study sought to determine whether intrapartum amoxicillin increases the risk of penicillin allergy in children.

The retrospective analysis included a birth cohort of 804 children born at the Mayo Clinic in 2007. Eighty children were reported as having penicillin allergy. Intrapartum exposure to intravenous penicillin for GBS treatment was evaluated for association with penicillin allergy.

Nearly 80% of children with penicillin allergy were white, and over 60% were boys. Reported penicillin allergy was unrelated to intrapartum exposure to penicillin, amoxicillin, or ampicillin. Nor did any of the other factors evaluated—including timing of antibiotic administration, maternal diagnosis of GBS, or mode of delivery—affect the children's risk of developing penicillin allergy.

Children born to mothers receiving penicillin for treatment of GBS are not at increased risk of penicillin allergy. This risk is also unaffected by the presence of GBS, or by cesarean delivery.

COMMENT: Increased interest in predicting which patients will develop allergies has led to studies looking at factors present at the time of childbirth. The authors studied mothers with GBS infection who received intrapartum antibiotics, including amoxicillin, ampicillin, and vancomycin. Unlike prior studies that have shown an association between intrapartum antibiotic use, cesarean delivery, and increased atopy in children, this study reassures us that neither treatment for GBS nor cesarean delivery appears to increase the risk of penicillin allergy in offspring. Further studies would be helpful to explore whether this applies to other antibiotics as well.

V.H.-T.

May SM, Hartz MF, Joshi AY, Park MA: Intrapartum antibiotic exposure for group B *Streptococcus* treatment did not increase penicillin allergy in children. Ann Allergy Asthma Immunol. 2016;116:134-138.

Keywords: penicillin allergy, risk factors

Perioperative Testing: Not Perfect but Good Enough?

Anaphylactic reactions may result from IgE-mediated allergy to several different drugs and other products used during general anesthesia. This study analyzed the results of standardized allergy testing in patients with general anesthesia-induced anaphylaxis, including how the recommendations affected the outcomes of subsequent anesthesia.

The retrospective study included 107 patients referred for evaluation of general anesthesia-induced anaphylaxis between 1995 and 2012. All underwent standardized skin testing using a series of anesthesia-related drugs and other substances, sometimes with drug provocation testing. Patients with confirmed allergy received an allergy alert regarding the implicated allergen and potential cross-reactivity. For those with negative IgE tests and suspected nonallergic drug hypersensitivity, preventive recommendations were made, including premedication with intravenous H_1-blocker and steroids.

An IgE-mediated allergy to anesthesia-related drugs or compounds was confirmed in 53 patients. Grade 3 reactions occurred in about 47% of patients with confirmed allergy, compared to 26% of those with negative allergy test results. Antibiotics were the most frequently identified allergen, including cephalosporins in 15 patients. Fifty-three patients underwent subsequent surgery and general anesthesia: 29 with allergy and 24 with negative test results. Fifty patients tolerated the subsequent anesthesia without incident.

An experience with allergy testing after general anesthesia-induced anaphylaxis is reported. This strategy allows identification and avoidance of culprit and cross-reactive substances in patients with IgE-mediated allergy. When testing indicates nonallergic reactions, premedication can prevent subsequent anaphylaxis in most cases.

COMMENT: Evaluating patients with perioperative anaphylaxis is a time-consuming process, but what are the outcomes after such an evaluation? This retrospective German study evaluated 107 patients with perioperative allergic reactions and identified about 50% as having IgE-mediated reactions. When identified culprits were avoided, 28 of 28 patients tolerated subsequent anesthesia. Twenty-four patients without an identified culprit underwent anesthesia with premedication with antihistamines and steroid as an intervention; 20 of 22 tolerated subsequent anesthesia. Overall, this study adds to the literature showing that an allergy evaluation, even when a culprit cannot be found via skin testing, leads to a relatively low rate of subsequent reactions to anesthesia.

D.A.K.

Trautmann A, Seidl C, Stoevesandt J, Seitz CS: General anaesthesia-induced anaphylaxis: impact of allergy testing on subsequent anaesthesia. Clin Exp Allergy. 2016;46:125-132.

Keywords: anesthesia allergy, diagnosis

No Evidence of Remodeling with Persistent Allergic Rhinitis

Airway remodeling, with increases in airway smooth muscle, extracellular matrix, and vascularity, is a characteristic feature of asthma. There has been little attention to the presence or characteristics of airway remodeling in patients with persistent allergic rhinitis (PAR). This study evaluated the presence and mechanism of upper airway remodeling in severe PAR.

The study included 46 patients with severe PAR and 19 healthy controls. Both seasonal and perennial PAR were associated with eosinophils increased nasal symptom, total visual analog, and total quality-of-life scores. Measurement of Th2 cytokines also showed higher levels of interleukin-5 and interleukin-13 in the PAR patients.

Nasal biopsies showed increased submucosal eosinophils in patients with PAR. However, there were no significant differences in remodeling markers or tissue structure, including angiogenesis, lymphangiogenesis, extracellular matrix deposition, collagen proteins, reticular basement membrane thickness, or glandular percentage area.

The upper airways of patients with severe PAR show evidence of inflammation, but not of tissue remodeling. The findings question current thinking about the relationship between the upper and lower airways, and suggest that, in contrast to allergic asthma, treatments targeting remodeling are not appropriate in allergic rhinitis.

COMMENT: The differences in histology of allergic reactions in the upper and lower airway are defined quite exquisitely in this paper. It appears that both seasonal and perennial allergic rhinitis do not lead to persistent structural changes. However, in a subgroup of patients, persistent nasal turbinate hypertrophy may be refractory to therapy. Further data should be generated regarding patients with nasal polyps to help better understand the pathophysiologic findings associated with this more severe presentation of nasal airway disease.

B.E.C.

Eifan AO, Orban NT, Jacobson MR, Durham SR: Severe persistent allergic rhinitis: inflammation but no histologic features of structural upper airway remodeling.
Am J Respir Crit Care Med. 2015;192:1431-1439.

Keywords: allergic rhinitis, remodeling, unified airway theory

Poor Predictive Value of Food Specific IgE in Atopic Dermatitis

Children with atopic dermatitis (AD) are at increased risk of developing food allergies. Food-specific IgE measurement is commonly performed to assess food sensitization and clinical allergy in infants with AD, but its relation to the development of food allergies is unknown. This study assessed the incidence of food allergy and the predictive value of food-specific IgE testing in infants with AD.

Data were drawn from a multicenter trial of pimecrolimus cream 1%, including more than 1,000 infants aged 3 to 18 months. All had mild-to-severe AD with a family history of allergy, but no history of food allergy. Food allergy incidence was assessed through a 36-month double-blind treatment phase as well as up to 33 months of open-label follow-up. ImmunoCAP specific IgE testing for cow's milk, egg white, peanut, wheat, seafood mix, and soybean was performed at baseline and at the end of each phase of follow-up.

By the end of follow-up, one or more food allergies had developed in 15.9% of infants. Involved allergens were peanut in 6.6% of children, cow's milk in 4.3%, and egg white in 3.9%. Higher levels of milk-, egg-, and peanut-specific IgE were associated with more severe AD, based on Investigator's Global Assessment scores. However, the specific IgE test results were not good predictors of the development of definite food allergy. Positive predictive values were low for all six foods tested, using either published or newly developed specific IgE decision points.

The results question the clinical value of food-specific IgE testing for predicting the risk of developing food allergy in infants with AD. In this large sample, 16% of children with AD developed food allergy during more than 3 years' follow-up. While peanut, milk, and egg allergy are relatively common in this population, seafood, soybean, and wheat allergy are rare.

COMMENT: Current guidelines recommend consideration of food allergy evaluation in children with AD that persists despite optimal management or in the presence of a reliable history of an immediate reaction after ingestion of a specific food. Based on this, food-specific IgE tests are often ordered in children with mild to moderate AD. These tests often show elevated results, sometimes to multiple foods, even though the child ingests some of these foods regularly. Providers and families then find themselves in a dilemma, not knowing whether to eliminate these foods or not. This prospective study of more than 1,000 infants with AD and a family history of atopy study sheds light on that question. Reassuringly, only 15.9% of the children developed a food allergy during a period of greater than 3 years. Furthermore, food-specific IgE testing was not a clinically useful diagnostic substitute for predicting development of food allergy. Providers should be discouraged from prescribing food-elimination diets to children with AD based on food-specific IgE levels alone.

C.D.

Spergel JM, Boguniewicz M, Schneider L, et al: Food allergy in infants with atopic dermatitis: limitations of food-specific IgE measurements.
Pediatrics. 2015;136:e1530-e1538.

Keywords: atopic dermatitis, food allergy, risk factors

Plateau in Childhood Asthma Prevalence

The US prevalence of asthma in children rose rapidly from the 1980s to the mid-1990s. This was followed by a slower increase during the 2000s, during which there were widening racial disparities. This study analyzed nationally representative data to update trends in childhood asthma.

The study used data on asthma prevalence in children aged 0 to 17 years, based on National Health Interview Survey data from 2001 to 2013. Recent trends in asthma prevalence were analyzed, including subgroups of children defined by race/ethnicity and factors known to be associated with asthma.

The data showed a continued increase in childhood asthma prevalence from 2001 to 2009, followed by a plateau and then a decline. Overall estimated prevalence decreased from 9.3% in 2012 to 8.3% in 2013.

Multivariate logistic regression analyses showed differing patterns among various subgroups between 2001 and 2013, including no change in prevalence among non-Hispanic white and Puerto Rican children or among those living in the Northeast and West regions. Asthma prevalence continued to increase among 10- to 17-year-olds, poor children, and those in the South region.

Five- to nine-year-olds, near-poor children, and non-Hispanic black children all showed a rising prevalence followed by a plateau. Prevalence increased then decreased among 0- to 4-year-olds, nonpoor children, Mexican children, and those in the Midwest region. The disparity between non-Hispanic black and white children stopped widening, but prevalence remained highest for Puerto Rican children.

The overall prevalence of childhood asthma has plateaued and even decreased in recent years. The racial disparity between black and white children has stopped increasing, mainly because of a plateau among non-Hispanic black children. Future studies will determine whether the long-term increase in childhood asthma prevalence has ceased or reversed.

COMMENT: It is heartening to know that childhood asthma prevalence may indeed be flattening out in this decade, compared to the last, although it is too premature to uncork the champagne. The other promising finding is the halt in increasing prevalence among non-Hispanic black children, which hints that the racial disparity in asthma prevalence may be closing. There was also a reassuring trend in prevalence in this review of NHIS data among 0- to 4-year-olds, although one must keep in mind the challenges of appropriately diagnosing asthma at this young age.

C.D.

Akinbami LJ, Simon AE, Rossen L: Changing trends in asthma prevalence among children.
Pediatrics. 2016;137:1-7.

Keywords: asthma (child), epidemiology

Different Factors Affect Airway Responsiveness in Later versus Early Life

Airway responsiveness in children might be affected by structural, environmental, or immunologic factors. There are questions about which factors are most important and how they may change with age. These issues were addressed in a long-term follow-up study assessing airway responsiveness at intervals from infancy to young adulthood.

The analysis included an unselected birth cohort of 235 children from the Perth Infant Asthma Follow-up study. Airway responsiveness to histamine was assessed as a dose-response slope at age 1, 6, and 12 months and at 6, 11, and 18 years. Respiratory questionnaires were completed at the same times. Airway responsiveness during infancy was evaluated for association with airway responsiveness and asthma-related outcomes at age 18.

Airway responsiveness was assessed in 203 subjects at 1 month, 137 at 18 years, and 39 at all time points. At 18 years, 13% of participants had doctor-diagnosed asthma and 25% reported wheezing in the previous year. Subjects with asthma at age 18 had increased airway responsiveness at age 6, 12, and 18 years. The dose-response slope at those times was 0.24, 0.25, and 0.56, respectively.

Previous studies have shown that airway responsiveness in early life has a strong effect on asthma in young children. The new results suggest that airway responsiveness later in childhood (age 6) may be a better predictor of asthma at age 18. While airway responsiveness in infancy may reflect intrinsic or inherent factors, later in childhood it may increasingly reflect the effects of environmental exposures.

COMMENT: This landmark study helps better describe the in utero effects leading to early airway hyperreactivity. Subsequent re-emergence of airway hyperreactivity is thought to be related primarily to intercurrent infection and the development of an allergic diathesis. These data are extremely important to help us understand the natural history of wheezing and the determinants of persistent asthma.

B.E.C.

Cox DW, Mullane D, Zhang GC, et al: Longitudinal assessment of airway responsiveness from 1 month to 18 years in the PIAF birth cohort.
Eur Respir J. 2015;46:1654-1661.

Keywords: asthma (child), airway hyperresponsiveness, epidemiology

Severe Asthma in Adults and Children: Baseline Characteristics

Severe asthma is a heterogeneous condition associated with symptoms of cough, wheezing, and breathlessness along with frequent asthma exacerbations. The "Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes" (U-BIOPRED) study seeks to assess the • • •

phenotypes of severe asthma, and ultimately to develop new treatments using state-of-the art "omics" technologies. This paper described the baseline characteristics of adults with severe asthma enrolled in the U-BIOPRED cohort.

The cross-sectional analysis included 441 adults with severe asthma, drawn from 16 centers in 11 European countries. There were 311 nonsmokers with severe asthma and 110 smokers or ex-smokers. They were compared to 88 nonsmokers with mild to moderate asthma and 101 healthy controls.

Patients with severe asthma had an average of 2.5 exacerbations in the previous year, compared to 0.4 for those with mild to moderate asthma. In addition to increased symptoms, patients with severe asthma had poorer quality of life, increased anxiety and depression, higher incidence of nasal polyps and gastroesophageal reflux, and lower lung function. Mean FVC/FEV_1 ratio was 0.64 in nonsmokers and 0.61 in smokers/ex-smokers with severe asthma, compared to 0.72 in subjects with mild to moderate asthma.

Even though they received higher doses of inhaled and/or oral corticosteroids, the patients with severe asthma had higher sputum eosinophil counts: median 2.99% versus 1.05% per year. Exhaled nitric oxide was not significantly increased in patients with severe asthma, although it was higher in patients with nasal polyps.

As in previous studies, adults with severe asthma have a high burden of disease, despite high-dose treatment. The U-BIOPRED cohort will aid in defining the phenotypes and endotypes of severe asthma, with the goal of adding to the limited treatment options.

The U-BIOPRED cohorts provide new insights into the characteristics and burden of severe asthma, including differences between adult and pediatric patients. The baseline characteristics of children and adolescents from the pediatric U-BIOPRED cohort are reported.

The study describes 97 school-aged children with severe asthma and 77 preschool-aged children with severe wheezing, drawn from seven centers in five European countries. Matched groups of children with mild to moderate symptoms were studied for comparison. The children with severe asthma had more frequent exacerbations than controls, despite high-dose treatment: annual median 3.0 versus 1.1 in the school-aged group and 3.9 versus 1.8 in the preschool group.

Nearly all of the children had atopy and normal body mass index; the children with severe wheezing had high exposure to secondhand smoke. In both the school-aged and preschool groups, severe asthma was associated with worse asthma-related quality of life for caregivers as well as children. However, because there was also significant morbidity in the mild-to-moderate cohorts, the two groups were clinically similar overall. Impaired quality of life was associated with poor disease control and airway obstruction.

The baseline findings of the U-BIOPRED cohort lend insights into the phenotype of children with severe asthma, which differs significantly from that in adults with severe asthma. In both groups, integrating clinical data with high-dimensional biomarkers may lead to improvements in clinical management.

COMMENT: The U-BIOPRED child and adult cohorts allow assessment of the determinants of persistent severe asthma over a wide age range. These baseline papers define the distinct contrast between the children and adult cohorts. The papers to follow will hopefully continue to add significant understanding of the mechanism that causes the burden of severe asthma throughout life.

B.E.C.

Shaw DE, Sousa AR, Fowler SJ, et al: Clinical and inflammatory characteristics of the European U-BIOPRED adult severe asthma cohort.
Eur Respir J. 2015;46:1308-1321.
AND
Fleming L, Murray C, Bansal AT, et al: The burden of severe asthma in childhood and adolescence: results from the paediatric U-BIOPRED cohorts.
Eur Respir J. 2015;46:1322-1333.

Keywords: asthma (adult), asthma (child), asthma (severe)

Are Asthma and Confirmed Allergy Truly Increasing in Prevalence?

Previous studies have reported rising rates of asthma and allergies in the population. However, there are few data on progression of the allergic diathesis over time—from positive skin tests, to oculonasal symptoms, to asthma. Changes in allergy and asthma prevalence and in the progression from allergy to asthma were assessed using National Health and Nutrition Examination Surveys (NHANES) data.

The study included data from NHANES II, 1976-80, and NHANES III, 1988-94. Trends in the prevalence of skin test positivity, oculonasal symptoms, and asthma were compared for corresponding age groups from childhood to middle age: eg, subjects who were 6 to 10 years old in NHANES II and 16 to 19 years old in NHANES III.

Asthma prevalence doubled between surveys: from 2.5% in NHANES II to 5.0% in NHANES III. The prevalence of positive skin tests increased 2.2-fold, oculonasal symptoms 3.3-fold, and concurrent asthma, oculonasal symptoms, and positive skin tests 5.3-fold. The percentage of people with positive skin tests to all six tested allergens increased from 0.2% in NHANES II to 2.7% in NHANES III. Correlation coefficients among positive skin test reactions, oculonasal symptoms, and asthma became stronger between the two surveys.

Within the limitations of the analyses, the results show significant increases in allergen sensitization, oculonasal symptoms, and asthma in the US population from the mid-1970s to the mid-1990s. The observed patterns are consistent with increases in sensitization leading to increased allergic symptoms and asthma. Associations between these factors appear stronger in NHANES III than NHANES II.

COMMENT: The NHANES provide important informa-

tion regarding the prevalence of asthma and atopic diseases. This study compared data from NHANES II (1976-80) and NHANES III (1988-94). The largest increases in single as well as combinations of symptoms were seen in children and adolescents, while the middle-age group had the lowest prevalence of increase. A larger portion of the population was sensitized to increasing numbers of allergens, with more people allergic to all 6 allergens tested—a 15-fold increase—from NHANES II to NHANES III. The largest prevalence increases were for cat, Bermuda grass and *Alternaria alternata.* The associations between skin tests and oculonasal symptoms and asthma were stronger in NHANES III. The authors discuss the possible contributions of obesity and exposure to both indoor and outdoor allergens to the increases in prevalence. Further studies are warranted.

V.H.-T.

Meng Q, Nagarajan S, Son Y, et al: Asthma, oculonasal symptoms, and skin test sensitivity across National Health and Nutrition Examination Surveys.
Ann Allergy Asthma Immunol. 2016;116:118-125.

Keywords: atopy, epidemiology, skin testing

One-Step Method for Venom Skin Testing

Because of the risk of adverse reactions, a stepwise approach to intradermal testing for venom allergy is commonly recommended. However, this graded approach is expensive and uncomfortable for the patient. The technique and results of a single-step approach to intradermal testing for venom allergy are reported.

The authors reviewed their approach to single-step intradermal testing in 300 consecutive patients with hymenoptera venom allergy. All had a systemic reaction to at least one sting and at least one positive skin test reaction. The protocol consisted of a 0.02 mL intradermal dose of each of the five commercially available wasp and bee venoms, at the maximum 1.0 μg/mL concentration.

Reactions to venom injection ranged from grade 1 to grade 4, with most patients testing positive to yellowjacket and having more than one positive reaction. Just one patient had an adverse reaction to venom injection, which occurred the following morning. That patient was subsequently started on venom immunotherapy, which was well tolerated.

The experience supports the safety of the single-step venom allergy intradermal testing protocol. This technique has the potential to lead to more efficient, less expensive care for patients with suspected venom allergy.

COMMENT: Standard intradermal testing for venom hypersensitivity utilizes a graded or stepwise assessment, with test concentrations for testing depending on the historic account of the severity of the reaction and/or of emergency department evaluation and therapy. The authors demonstrate that a single-step venom allergy intradermal testing approach using the maximum 1.0 μm/mL concentration of commercially prepared extract is a safe and more economic option for cost-efficient confirmation of venom allergy. While the findings are provocative, further studies are needed to evaluate the sensitivity, specificity, and safety of this approach.

C.C.R.

Quirt JA, Wen X, Kim J, et al: Venom allergy testing: is a graded approach necessary?
Ann Allergy Asthma Immunol. 2016;116:49-51.

Keywords: skin testing, venom allergy

Phenylephrine Is No More Effective Than Placebo

Although phenylephrine hydrochloride is widely used as a nasal decongestant, its efficacy remains unproven. This randomized trial evaluated phenylephrine's safety and efficacy, compared to placebo.

The multicenter study included 575 adults with allergic rhinitis and documented hypersensitivity to fall pollen allergens. During pollen season, patients were randomly assigned to receive modified-release phenylephrine hydrochloride, 30 mg every 12 hours, or placebo for 7 days.

There was no significant difference between treatments for the primary outcome of daily nasal congestion score. Most secondary outcomes, including quality of life, were similar as well. Adverse events leading to emergency treatment occurred in 15.5% of patients, with no difference between groups.

The study questions the efficacy of phenylephrine for treatment of nasal congestion in patients with allergic rhinitis. Patients with this symptom should be advised to use effective, evidence-based over-the-counter or prescription treatments.

COMMENT: Although phenylephrine is widely used as an over-the-counter nasal decongestant, its efficacy has never been proven compared to placebo. This study, performed after efficacy trials were requested by the FDA, demonstrates that phenylephrine is no more effective than placebo for nasal allergy.

C.C.R.

Meltzer EO, Ratner PH, McGraw T: Phenylephrine hydrochloride modified-release tablets for nasal decongestion: a randomized, placebo-controlled trial in allergic rhinitis patients.
Ann Allergy Asthma Immunol. 2016;116: 66-71.

Keywords: allergic rhinitis, pollen allergy

Indoor Allergen Combinations Remain Stable for One Year

It is unclear whether combinations of allergens commonly used for immunotherapy are compatible and stable • • •

over time. This study assessed the stability and compatibility of immunotherapy mixtures containing multiple indoor allergens.

The researchers assessed the immunochemical potency of cat, dog epithelia and dander, dust mite, and cockroach in mixtures at 1:1 and 1:10 strengths during refrigerated storage for up to 1 year. At both concentrations, the extracts showed favorable mixing compatibilities, relative to individual control samples. Cockroach allergen was significantly stabilized by mixing with the other four extracts.

The results show good stability and compatibility of different indoor allergens in combination. The findings support the practice of combining and storing cat, dog, dust mite, and cockroach extracts for use in subcutaneous immunotherapy.

COMMENT: Traditionally, combinations of allergen extracts including cat, dog, mite, and cockroach have been given, although the stability and compatibility of these combinations have not been confirmed. The authors demonstrate that extracts including cat, dog, mite, and cockroach have acceptable stability and compatibility, confirming the practice of combining these extracts. This study enhances our knowledge that these indoor allergens are compatible and stable bedfellows in standard subcutaneous immunotherapy formulations.

C.C.R.

Grier TJ, Hall DB, Duncan EA, Gada SM: Allergen stabilities and compatibilities in immunotherapy mixtures that contain cat, dog, dust mite, and cockroach extracts.
Ann Allergy Asthma Immunol. 2015;115:496-502.

Keywords: immunotherapy (subcutaneous)

Methacholine versus Exercise Challenge for Detecting Asthma in Children

Many children with asthma have exercise-induced bronchoconstriction. This study compared exercise challenge with methacholine challenge testing for detection of asthma in children with postexercise symptoms.

The prospective study included 101 children (aged 10 to 18) with postexercise symptoms. All underwent standardized exercise challenge, followed 1 week later by methacholine challenge testing. Asthma was diagnosed in 43.6% of patients.

Methacholine challenge had 90.9% sensitivity for detection of asthma, compared to 77.3% with exercise challenge. Specificity was 85.2% with methacholine versus 68.4% with exercise challenge; positive predictive value was 80.0% versus 65.4%, respectively. Including methacholine challenge in the diagnostic evaluation confirmed asthma in an additional 24.3% of patients. The discrepancy between tests was reduced when the cutoff value for a positive exercise challenge test was increased from 10% to 17% of FEV_1.

Methacholine challenge appears to be superior to exercise challenge testing for detection of asthma in children with postexercise symptoms. Although the two tests are complementary, methacholine challenge is more sensitive and specific than exercise challenge.

COMMENT: This study teaches us that methacholine challenge is more sensitive and specific than exercise challenge in the diagnosis of asthma in children. The results raise concern that asthma may go undetected in children who are tested only with exercise challenge.

C.C.R.

Zaczeniuk M, Woicka-Kolejwa K, Stelmach W, et al: Methacholine challenge testing is superior to the exercise challenge for detecting asthma in children.
Ann Allergy Asthma Immunol. 2015:115:481-484.

Keywords: asthma (child), exercise-induced bronchoconstriction, methacholine challenge

Screen for Anxiety/Depression in Children with Multiple Allergies

Previous studies have shown associations between allergic diseases and internalizing disorders. However, this research has not addressed multiple allergic diseases or included longitudinal assessment. This study assessed the relationship between multiple allergic diseases and internalizing disorders in school-aged children.

The researchers analyzed a cohort of 546 children from the Cincinnati Childhood Allergy and Air Pollution Study cohort. Allergic diseases at age 4 were evaluated for association with internalizing behaviors, anxiety, and depression at age 7, assessed by the Behavior Assessment for Children, Second Edition.

Children with allergic rhinitis at age 4 were at increased risk of internalizing disorders. On adjusted analysis, odds ratios were 3.2 for elevated internalizing scores, 2.0 for elevated anxiety scores, and 3.2 for elevated depressive scores. Allergic persistent wheezing was also associated with increased internalizing scores: OR 2.7. Multiple allergic disorders were associated with adverse outcomes in "dose-dependent" fashion: ORs for elevated internalizing scores were 3.6 for children with more than one allergic disease and 4.3 for those with allergic rhinitis plus one or more comorbid allergic diseases.

Children with allergic rhinitis and persistent wheezing at age 4 are more likely to have internalizing behaviors at age 7. The risk appears further elevated for children with multiple allergic diseases. The authors discuss the implications for mental health screening and referral of children with allergic diseases.

COMMENT: While allergists are aware that allergic disorders can be associated with anxiety and other mood alterations, this study shows a dose-dependent relationship (two- to fourfold increased odds) between multiple allergic diseases and internalizing disorders in children. Individuals who keep their problems to themselves, or "internalize," can develop disorders such as anxiety or depression. In this study, allergic rhinitis and allergic persistent wheezing were strongly

associated with abnormal anxiety/depression/internalizing scores. Surprisingly, atopic dermatitis was not associated with such behavior, possibly because the authors adjusted for sleep disturbance—a common problem in atopic dermatitis—as a confounding factor. Future studies may need to evaluate whether effective treatment of allergic diseases affects or changes the risk for internalizing disorders.

C.D.

Nanda MK, LeMasters GK, Levin L, et al: Allergic diseases and internalizing behaviors in early childhood.
Pediatrics. 2016;137:1-10.

Keywords: allergic rhinitis, anxiety, depression, wheezing

Subgroup of Milk-Allergic Children Refractory to OIT

Baked milk provides a potential alternative to unheated milk for oral immunotherapy (OIT) in patients with IgE-mediated cow's milk allergy. This study evaluated the outcomes of baked milk OIT in patients who previously failed unheated milk OIT.

The study included 15 children older than 4 who had reactions during a previous trial of unheated milk OIT. Baked milk OIT started at less than the initial eliciting dose, increasing by 50% monthly to reach a primary outcome dose of 1.3 g/d of baked milk protein. Other assessments included basophil reactivity and milk protein-specific IgE binding.

The 1.3 g/d maintenance dose was reached by just 3 of 14 patients. Despite initial progress in some patients, 8 out of 11 OIT failures occurred because of IgE-mediated reactions. Another 3 patients did not complete OIT because of non-IgE-related factors. Challenge thresholds to unheated milk increased up to 12 months, even in patients who were unable to complete baked milk OIT.

The 3 patients who reached the maintenance dose had decreased milk-specific IgE reactivity. Patients who successfully completed OIT had a significantly lower baseline mean difference in induced heated-milk and unheated-milk percentage of CD203c expression.

In this study, baked milk OIT had a low success rate in patients who previously failed unheated milk OIT. Patients who react to baked milk appear to be at high risk of adverse allergic reactions throughout treatment. On basophil activation testing, CD203c might be a useful marker to identify patients more likely to successfully complete baked milk OIT.

COMMENT: In a group of children with cow's milk allergy who previously failed a milk OIT program, baked milk was used for OIT. Interestingly only three patients (21%) met the primary endpoint and were able to tolerate the top dose of 1.3 g/day. Although the study was well-designed, there were only 15 patients; tolerance to milk might have been improved if the maintenance dose of 1.3 g/d was higher. Basophil activation test data showing that patients with CD203C marker were more likely to tolerate successful baked milk OIT compared to those with CD63 expression. The authors suggest that this marker might be useful to predict response to milk OIT.

S.M.F.

Goldberg MR, Nachshon L, Appel MY, et al: Efficacy of baked milk oral immunotherapy in baked milk-reactive allergic patients.
J Allergy Clin Immunol. 2015;136:1601-1606.

Keywords: baked milk, milk allergy, oral immunotherapy

Racial Differences in Response to Systemic Steroids?

Observed racial/ethnic disparities in asthma severity may involve a range of factors, possibly including differences in treatment response. This study evaluated the effects of race/ethnicity on response to depot corticosteroid therapy in children with severe, treatment-resistant asthma (STRA).

The study included 79 children with STRA who had undergone previous detailed assessment, including a home visit at which potentially modifiable factors were addressed. All were admitted to a London hospital for further evaluation including assessment of steroid response. Race/ethnicity was classified as white in 68% of children, Black in 20%, Asian in 6%, and mixed white/black in 5%. Steroid response was evaluated in terms of symptoms and inflammatory markers, before and 4 weeks after administration of intramuscular depot triamcinolone.

Treatment with depot triamcinolone was followed by a significant reduction in median exhaled nitric oxide among white children, from 46.8 to 23.1 ppb; but not in black children, from 52.2 to 34.5 ppb. Based on a decrease to less than 24 ppb, there was no exhaled NO response in 45.3% of white children versus 86.7% of black children. Exacerbation risk was also significantly lower in white children: 17% versus 61%. Improvements in sputum eosinophil count and Asthma Control Test were also significant in white but not black children.

Black children with STRA may not respond to intramuscular triamcinolone as well as their white counterparts. While the mechanisms of this difference remain unclear, based on this study, differences in adherence or access to care do not play a role.

COMMENT: Ethnic minorities have higher morbidity and mortality from asthma; the reasons for these differences may be multifactorial. This UK study evaluated the response at 4 weeks to a depot injection of triamcinolone in children with poorly controlled asthma despite high-dose inhaled corticosteroids. Compared to whites, black children with poorly controlled asthma had a worse baseline FEV_1, were less likely to achieve normal exhaled NO, and had more exacerbations after triamcinolone administration. The study was limited by a disproportionately higher number of white children, compared to black and nonwhite children. Larger studies with a larger minority population are needed to confirm these findings. The fact that the mean ACT score after triamci-

nolone ranged from 13.6 to 16.5 for all groups is surprising and suggests the studied group may not be very steroid sensitive.

D.A.K.

Koo S, Gupta A, Fainardi V, et al: Ethnic variation in response to IM triamcinolone in children with severe therapy-resistant asthma.

Chest. 2016;149:98-105.

Keywords: asthma (severe), race/ethnicity

In EoE, Mast Cells May be Important Too!

Patients with eosinophilic esophagitis (EoE) show an inflammatory infiltrate including abundant intraepithelial mast cells as well as eosinophils. This study assessed the phenotype of mast cells in EoE, including their response to dietary therapy.

The study included 10 adult patients with EoE, all of whom were successfully treated with a six-food elimination. The researchers analyzed esophageal biopsy samples obtained from the patients before and after the dietary intervention, as well as from healthy controls. The effects of the diet on the eosinophil and mast cell infiltrate were assessed, along with the contributions of mast cell activity to the clinical response.

The six-food elimination diet was associated with a significant decrease in mast cell density: from 18.6 to 1.44 cells/hpf. In controls as well as patients, the dominant mast cell phenotype was mast cells with tryptase and chymase (MC_{TC}). The EoE patients had upregulation of mast cell-related proteases, eotaxins, and chemoattractants; these decreased after dietary therapy, regardless of atopic status.

Peak densities of both mast cells and eosinophils were significantly correlated with symptom scores in EoE. Symptoms were also related gene expression of mast cell proteases and eotaxins.

Mast cells and mast cell proteases appear to be significantly involved in the pathophysiology and symptoms of EoE. Like eosinophils, mast cells decrease with effective dietary therapy. Further studies are needed to define the mechanisms of mast cell activation in EoE, and their interactions with other inflammatory cells.

COMMENT: In addition to eosinophils, mast cells have also been found in the mucosa of patients with EoE. This small study evaluated 10 adults with EoE who underwent a 6-week, six-food elimination diet. Mast cells (predominantly MC_{TC} cells) were elevated at baseline and were reduced following diet. Mast cell protease expression was associated with esophageal symptom scores. There was also a correlation between eosinophil infiltration and mast cells. While this study adds more to support a potential role of mast cells in EoE, it is not clear whether mast cells are involved in the pathogenesis of EoE or are simply a byproduct of eosinophilic inflammation.

D.A.K.

Arias Á, Lucendo AJ, Mártínez-Fernandez P, et al: Dietary treatment modulates mast cell phenotype, density, and activity in adult eosinophilic oesophagitis.

Clin Exp Allergy. 2016;46:78-91.

Keywords: EoE, eosinophils, mast cells

REVIEWS OF NOTE

COMMENT: This paper gives insight regarding the relationship between remodeling inflammation and lung function in clinical phenotypes of childhood to adult asthma.

B.E.C.

Saglani S, Lloyd CM: Novel concepts in airway inflammation and remodelling in asthma.

Eur Respir J. 2015; 46:1796-1804.

COMMENT: This fascinating bench-to-bedside update elucidates how exposure to lipopolysaccharides suppresses the responsiveness of airway epithelial cells to TLR4-induced activation by the house dust mite allergen. The authors describe evidence that this suppression is mediated by increased synthesis of the enzyme A20 in airway epithelial cells, causing attenuation of signaling by nuclear factor κB.

C.D.

Holt PG, Sly PD: Environmental microbial exposure and protections against asthma.

N Engl J Med. 2015;373:2576-2578.

COMMENT: This review helps the practicing allergist understand current information regarding the use of electronic cigarettes, as compared to conventional cigarettes. The advantages of e-cigarettes are that they do not contain tobacco, although they may contain nicotine. The authors recommend that we discuss the danger from burning tobacco, as this leads to inhalation of toxic chemicals, which cause damage. Patients can have hypersensitivity to components in the vapor, and contact dermatitis of the oral mucosa can occur to propylene glycol. As far as vaping, toxic aldehydes can be formed, although in lower levels than cigarette smoke. Patients with asthma had improvement in self-reported cough and shortness of breath when quitting or using e-cigarettes to decrease cigarette smoking. Studies investigating the benefits of e-cigarettes are lacking, although they appear to be safe and to improve respiratory health in smokers.

V.H.-T.

Polosa R, Campagna D, Sands MF: Counseling patients with asthma and allergy about electronic cigarettes: an evidence-based approach.

Ann Allergy Asthma Immunol. 2016;116:106-111.