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FEATURE ARTICLES

ACAAI Issues Position Paper on Telemedicine

Telemedicine is a promising tool for extending access to healthcare, although its widespread use in clinical practice has been slow. With the short supply of allergists—only about 3,000 nationwide—telemedicine could play an important role in providing scalable, high-quality specialty allergy care. An American College of Allergy, Asthma, and Immunology (ACAAI) Task Force has developed a position paper defining the scope and practice of telemedicine for allergists.

Telemedicine is defined as the use of technology, typically real-time audio and video, to provide healthcare and health information at a distance. Telemedicine is a promising tool to improve access to allergy specialist care, with the potential to produce significant cost savings in patients with chronic conditions such as asthma and rhinitis. It may be especially important in improving access to care for underserved patients, including those in rural and urban settings.

A study in children with asthma has already shown comparable asthma control with telemedicine versus in-person visits. Coverage and payment for telemedicine still vary by state; the ACAAI supports combined coverage and payment parity for telemedicine services.

Challenges in more fully implementing telemedicine include the need for adequate technology to meet quality standards and guidelines. Practitioners usually must be licensed to practice in the jurisdiction where the patient receives treatment; expedited compact licensure efforts are underway in many states. Telemedicine raises new issues related to credentialing, privileging, and accreditation, and is subject to the same HIPAA privacy and security standards as in office settings. State and federal legislatures are working to develop new laws and regulations regarding • • •

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- 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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telemedicine, including several provisions of the 21st Century Cures Act of 2016.

The ACAAI expresses its support for continued development of telemedicine services to expand access to high-quality specialty care for patients with allergic diseases. The position paper highlights the importance of maintaining or creating patient-centered, longitudinal relationships between allergists and the patients they consult with via telemedicine.

COMMENT: More than 90% of Americans now have internet access, and telemedicine is permissible in all 50 states. The ACAAI Task Force deserves credit for authoring an informative and timely document describing what can be considered as a disruptive influence in healthcare that is moving forward rapidly. There is a clear need to integrate telemedicine into allergy/immunology practice.

D.M.L.

Elliott T, Shih J, Dinakar C, et al: American College of Allergy, Asthma & Immunology Position Paper on the use of telemedicine for allergists.
Ann Allergy Asthma Immunol. 2017;119:512-517.

Keywords: healthcare access, position paper, telemedicine

Epinephrine in the ED – Disparities in Anaphylaxis Care

Guidelines for care of patients with anaphylaxis include prescription of an epinephrine autoinjector and referral to an allergist. These recommendations are important for prevention and management of repeated anaphylactic attacks. This study assessed compliance with and predictors of epinephrine prescribing and allergy referral in a large series of anaphylaxis patients seen in the emergency department (ED).

Using an administrative claims database, the researchers identified 7,790 patients treated for anaphylaxis in US EDs from 2010 through 2014. All had medical and pharmacy coverage for 1 year before and after the event. About 40% of patients were aged 35 to 64 years and nearly 60% were female. About 26% reacted to foods and 13% to medications; the trigger was unknown or unspecified in 58% of cases.

An epinephrine autoinjector was prescribed to about 47% of patients, while 29% had follow-up with an allergist. Factors associated with a lower rate of epinephrine dispensing included age 65 or older, odds ratio (OR) 0.35; having a medication trigger, OR 0.25; cardiac disease, OR 0.85; and Southern region, OR 0.86. Epinephrine prescribing was more likely children younger than 5, OR 2.67; patients reacting to foods, OR 1.40; and those reacting to venom, OR 4.48.

There were similar patterns of association for allergist follow-up. Odds ratios were 0.46 for age 65 or older, 0.66 for medication trigger, 3.15 for age under 5, and 1.39 for food trigger.

Less than half of patients seen in the ED for anaphylaxis are prescribed an epinephrine autoinjector, while about 70% do not receive allergist follow-up. Older age and medication trigger appear to be associated with lower rates of recommended care. Age, trigger, and other factors are associated with lower or higher rates of recommended epinephrine prescribing and specialist follow-up. The investigators conclude, "Post-ED visit anaphylaxis management can be improved, with the potential to decrease future morbidity and mortality risk with venom allergy."

COMMENT: For epinephrine prescribing at discharge from the ED for patients with anaphylaxis, there is a persisting gap between guideline-based management and normative care. The disparity is particularly marked for older patients or those who have cardiac conditions.

D.M.L.

Motosue M, Bellolio MF, Van Houten HK, et al: Predictors of epinephrine dispensing and allergy follow-up after emergency department visit for anaphylaxis. Ann Allergy Asthma Immunol. 2017;119:452-458.

Keywords: anaphylaxis, emergency department, epinephrine

Anxiety in Food-Allergic Moms: 45 Minutes May Make a Difference

Having a child diagnosed with food allergy can provoke high anxiety and stress in parents. The authors previously found that healthcare professionals in the community tend to overestimate the risk of fatal anaphylaxis for food-allergic children. This randomized trial evaluated a brief intervention to reduce anxiety in mothers of children with food allergy,

Two hundred mothers of children with food allergies were randomly assigned to receive the brief intervention or standard care. The intervention consisted of a 45-minute session of cognitive behavioral therapy, which included psychoeducation, addressing the risks of living with anxiety and the risk of fatal anaphylaxis in a food-allergic child; and a behavioral/relaxation component.

Maternal state anxiety was assessed at baseline and after 6 weeks. Other outcomes included state anxiety at 1 year, perceived risk at 6 weeks and 1 year, and salivary cortisol response to a simulated anaphylaxis scenario at 1 year.

There was no significant difference in maternal state anxiety at 6 weeks: mean scores were 31.9 in the intervention group and 34.0 in the control group, both on the higher end of the "low-anxiety" range (20 to 34). However, the psychological intervention significantly reduced state anxiety in mothers with high baseline anxiety: mean 6-week scores were 33.0 in the intervention group versus 37.8 in the control group.

The intervention was associated with a sharp and lasting reduction in the perceived risks of anaphylaxis and fatal anaphylaxis. Cortisol responses to the stressful simulation were also reduced.

A brief psychological intervention can reduce anxiety in mothers of food-allergic children—especially in parents with moderate to high anxiety at baseline. The intervention also corrects inaccurate perceptions of the risks associated with childhood food allergy. The authors note that the intervention was delivered in a routine allergy clinic setting, by personnel with no previous training in cognitive behavioral therapy.

COMMENT: Anxiety regarding food allergy and over-perception of risk of death is common among mothers of food-allergic children. This study randomized mothers of food-allergic children to a session of behavioral therapy (coping thoughts and relaxation techniques) versus usual care. At 1 year, mothers had reduced anxiety and perception of risk. The effect appeared more evident in moms who had high anxiety to begin with. Behavioral therapy was administered by a variety of providers (eg, nurses and residents) who received several hours of training sessions and oversight. While the authors have provided a manual for therapists, it's unknown whether a non-trained group following the manual will get similar results.

D.A.K.

Boyle RJ, Umasunthar T, Smith JG, et al: A brief psychological intervention for mothers of children with food allergy can change risk perception and reduce anxiety: outcomes of a randomized controlled trial.
Clin Exp Allergy. 2017;47:1309-1317.

Keywords: anxiety, behavioral therapy, education, food allergy,

Why Doesn't My Asthma Medicine Work?

Despite availability of effective medications, uncontrolled asthma remains common. The Asthma Control Test (ACT) is widely used to assess the efficacy of asthma medications. This study assessed factors associated with uncontrolled asthma in patients receiving recommended therapies.

The study included 1,299 patients seen at Spanish allergy with uncontrolled asthma (partially controlled or not controlled), based on Global Initiative for Asthma (GINA) 2010 criteria. The patients' mean age was 46.5 years. Approximately 61% were women and 26% were obese. At baseline visits, patients underwent assessment of asthma characteristics and spirometric testing, with treatment optimized according to GINA 2010. Three months later, spirometry was repeated and asthma control was assessed using GINA 2010 and the ACT.

At baseline, 12.0% of patients had well-controlled asthma according to the ACT, despite having uncontrolled asthma according to GINA 2010. Treatment optimization led to a significant increase in asthma control. However, at the second visit, 71.2% of patients still had inadequately controlled asthma: not controlled in 43.5% and partially controlled in 27.7%.

Only 28.1% of patients had well-controlled asthma according to both GINA 2010 and the ACT. The kappa index was low and negative (–0.151), indicating no agreement between the two assessments. Older age, higher body mass index, worse spirometry values, and higher percentage of bronchodilation were associated with worse asthma control.

In this real-world study of patients with uncontrolled asthma, disease control remains poor even with treatment optimization. There is a lack of agreement between GINA

2010 criteria and the ACT, which underestimates asthma control. The study identifies several risk factors for asthma control, which is also affected by treatment adherence and by patients' knowledge of their disease and its treatment.

COMMENT: This study allows us to examine risk factors related to poor asthma control. This outcome may not be reliably defined by the ACT—a very significant observation, in the age of precision medicine. The authors also point out that poor adherence and treatment uncertainties about the use of inhaled corticosteroids are significant contributors to poor outcomes.

B.E.C.

Munoz-Cano R, Torrego A, Batra J, et al: Follow-up of patients with uncontrolled asthma: clinical features of asthma patients according to the level of control achieved (the COAS study). Eur Respir J. 2017;49:1501885.

Keywords: asthma (adult), asthma control

It's All in the Sputum!

Eosinophilic inflammation, measured in sputum, is clearly linked to the risk of asthma exacerbations. Less is known about the association between sputum eosinophils and asthma control. This study assessed the relationship between sputum eosinophils and asthma control in everyday allergy practice.

The retrospective analysis included 187 patients undergoing sputum induction at least twice during follow-up at an asthma clinic. Individual-level changes in sputum eosinophils were analyzed for association with scores on the Asthma Control Questionnaire (ACQ). The researchers also sought to define a minimal important difference in sputum eosinophil count associated with a 0.5 change in ACQ score.

On multivariate analysis, individual variations in sputum eosinophils were independently related to ACQ. The only other factor independently associated with asthma control was FEV_1. Changes in neutrophilic inflammation were unrelated to asthma control.

In patients with intermittent/persistently eosinophilic asthma, a minimal important decrease of 4.3% in percentage of sputum eosinophils was associated with improved asthma control. A minimal important decrease of 3.5%, or 1.8-fold, was associated with worsening of asthma control. The associations were confirmed in a validation cohort of 79 patients.

Individual changes in sputum eosinophils over time are independently associated with asthma control, as measured by the ACQ. The results suggest that treatment intensification is likely to improve asthma control in patients with persistent eosinophilic inflammation despite corticosteroid therapy, but not in patients with noneosinophilic asthma. The authors note that some asthma patients "may tolerate an increase in sputum eosinophils."

COMMENT: This interesting study longitudinally examined the relationship between asthma control and individual variations in sputum eosinophils in patients from a Belgian asthma clinic. Patients underwent two or more sputum inductions. The investigators confirmed that asthma control was associated with changes in sputum eosinophils. They were able to calculate a minimally important increase and decrease in sputum eosinophils associated with a change in ACQ of at least 0.5. The next step is to find an easier way to determine the sputum eosinophil count in the real-world setting. Then, as noted by the authors, we could titrate therapy (ICS and biologics) with greater precision.

J.J.O.

Demarche SF, Schleich FN, Paulus VA, et al: Asthma control and sputum eosinophils: a longitudinal study in daily practice. J Allergy Clin Immunol Pract. 2017;5:1335-1343.

Keywords: asthma (adult), biomarkers, eosinophils

New Marker for Asthma Phenotyping: Airway Basophils

Basophils are thought to be important effector cells in allergic disease, but their role in the pathogenesis of asthma is unknown. This study evaluated the frequency and activation of basophils in sputum specimens from adult asthma patients.

The study included 44 asthmatic patients, mean age 61.5, treated with inhaled corticosteroids for at least 3 months. Assessments included the level and activation of basophils in induced sputum specimens, along with the correlation between sputum basophils and eosinophilic inflammation.

Sputum basophils were significantly elevated in asthma patients, compared to controls. Airway basophils were activated, with higher expression of CD203c compared to blood basophils. Sputum basophil percentage was correlated with eosinophil and mast cell percentages. Sputum basophils were also correlated with blood eosinophils and exhaled nitric oxide, but not with asthma control, serum IgE, percentage FEV_1, or blood basophil percentage. On receiver-operating characteristic curve analysis, sputum basophils were a stronger marker of sputum eosinophil percentage, compared to blood eosinophil count or exhaled NO.

The results show the presence and activation of basophils in the sputum of asthma patients with eosinophilic inflammation despite inhaled corticosteroid therapy. The sputum eosinophil percentage appears to be a strong indicator of sputum and blood eosinophils, and might provide a useful biomarker for monitoring and treatment of eosinophilic asthma.

COMMENT: With the addition of biologic agents to our asthma armamentarium, we are striving to find markers of asthma inflammatory phenotype. This study suggests that airway basophils are activated and strongly correlated with sputum and blood eosinophils. The authors suggest that basophils could be a good biomarker to monitor patients with eosinophilic asthma. Although this is an interesting study, I am hopeful we can find an easier marker to follow in the real world.

J.J.O.

Suzuki Y, Wakahara K, Nishio T, et al: Airway basophils are increased and activated in eosinophilic asthma. Allergy. 2017;72:1532-1539.

Keywords: asthma (adult), basophils, biomarkers, phenotypes

Why Does Tiotropium Reduce Asthma Exacerbations?

The long-acting muscarinic antagonist (LAMA) tiotropium reduces asthma exacerbations when added to inhaled corticosteroids and long-acting beta-agonists (ICS/LABA). The mechanism of this protective effect is unclear; one possibility is a synergistic effect between LAMA and LABA, with receptor cross-talk modifying LABA-induced beta-2 receptor downregulation and tolerance. This study evaluated tiotropium's effect on bronchoprotective tolerance with the LABA indacaterol.

The randomized, open-label, crossover study included 14 nonsmoking patients with persistent asthma. They received 4 weeks of treatment with ICS/LABA plus tiotropium and 4 weeks with ICS/LABA without LAMA. The effects of tiotropium on airway hyperresponsiveness (AHR) were assessed by bronchial challenge using mannitol.

Mannitol sensitivity was not significantly different with ICS/LABA with or without tiotropium. Mannitol AHR was significantly improved with both treatments after single dosing, but the effect was not maintained on repeated dosing. Salbutamol recovery after bronchial challenge was blunted after chronic versus single dosing.

In patients with persistent asthma, the addition of tiotropium does not modify the bronchoprotective tolerance induced by indacaterol. The results suggest that "cross-talk may not be clinically relevant" when using ICS/LABA/LAMA therapy.

COMMENT: Tiotropium has been shown to reduce asthma exacerbations when used as add-on therapy to ICS/LABA. However, its bronchodilator effect is quite modest, suggesting another mechanism. This small crossover study looked at the effect of adding tiotropium to ICS/LABA and its effect on airway hyperresponsiveness assessed by mannitol challenge. Protection against mannitol declined over time in both groups, suggesting that tiotropium did not protect against the well-described bronchoprotective tolerance to LABA. The mechanism of tiotropium's reduction in asthma exacerbations therefore remains unclear.

D.A.K.

Jabbal S, Manoharan A, Lipworth BJ: Bronchoprotective tolerance with indacaterol is not modified by concomitant tiotropium in persistent asthma.
Clin Exp Allergy. 2017;47:1239-1245.

Keywords: add-on therapy, asthma (adult), tiotropium

Autoimmune and Inflammatory Complications of PID

In addition to increased susceptibility to infections, patients with primary immunodeficiencies (PIDs) are predisposed to cancers and immune disorders, including allergy, inflammation, and autoimmune diseases. No studies have focused on the types and incidence of autoimmune and inflammatory conditions associated with PIDs. A national cohort of patients with PIDs were screened for autoimmune or inflammatory complications.

The retrospective study included 2,183 consecutive patients with PIDs, identified from the French national PID registry. Overall, 26.2% of patients had at least one autoimmune or inflammatory complication. Manifestations included most of the known autoimmune diseases, predominantly autoimmune cytopenia and/or thrombocytopenia. Manifestations occurred at any time during the patient's life, with 40% of patients affected by age 50.

Risk of autoimmune cytopenia was elevated at least 120-fold among PID patients compared to the general population. Risk of inflammatory bowel disease was elevated about 80-fold, and all other autoimmune conditions about tenfold. Patients with T-cell PIDs and common variable immunodeficiency were at greatest risk, but the increases were significant for all types of PID. Autoimmune/inflammatory manifestations were associated with shorter survival.

These data confirm the very high rate of autoimmune and inflammatory manifestations in patients with PIDs. The authors call for an in-depth international study of these complications, with the aim of clarifying the risks and assessing the possible benefit of treatments.

COMMENT: It has been well established that PID is associated with increased risks for cancer and other immune diseases. This report includes the largest number of patients using the French national PID registry. Of interest was the finding that autoimmune hematologic and gastrointestinal disorders make up more than half of all the various inflammatory disorders associated with PID. There is a 10-fold increased risk for autoimmune or inflammatory disorders with PID in the general population, increasing to 120-fold in children. It is important to consider these comorbidities when managing our patients with PID.

S.M.F.

Fischer A, Provot J, Jais J-P, et al: Autoimmune and inflammatory manifestations occur frequently in patients with primary immunodeficiencies.
J Allergy Clin Immunol. 2017;140:1388-1393.

Keywords: autoimmune disorders, immunodeficiency, PID

Clustering Approach to Understanding the ACOS Phenotype

Some patients have symptoms of both asthma and chronic obstructive pulmonary diseases, but the phenotype of this so-called asthma-COPD overlap syndrome (ACOS) remains unclear. Pathophysiologic features, including T helper cell polarization, might help in distinguishing patients with ACOS from the asthma and COPD subgroups. The authors used a clustering approach to evaluate the most useful factors in identifying the ACOS phenotype.

The study included 152 patients with asthma and 50 with COPD from a single Japanese center. The asthma patients had higher total serum IgE and peripheral blood eosinophil counts than the COPD group; mean age was 65.6 versus 74.6. Cluster analysis included mRNA expression of T helper cell-related transcription factors, including TBX21 (associated with Th1 differentiation), GATA3 (Th2), RORC (Th17), and FOXP3 (Treg). The study included 1-year follow-up data on asthma and COPD exacerbations.

Four clusters were identified. Cluster 1 included 81% of patients from the COPD group. Cluster 2 reflected the ACOS phenotype, comprising 28% of patients from the asthma group and 14% from the COPD group. Cluster 3 included mainly older adults with asthma, while cluster 4 patients were a younger group with atopic asthma. Rates of moderate to severe exacerbations at 1 year were 26.2% in cluster 1 and 24.0% in cluster 2, compared to 11.8% in clusters 3 and 4 combined. The optimal factors for discriminating cluster 2 from all other groups were total serum IgE of 310 IU/mL or greater, blood eosinophil count of 280 cells/μL or greater, higher ratio of TBX21/GATA3, higher FEV_1/FVC ratio, and smoking history of 10 or more pack-years.

This study identifies some key characteristics of patients with ACOS. The ACOS phenotype is associated with higher total IgE and peripheral blood eosinophilia, despite a Th2-low endotype. The researchers write that their findings "may contribute to the development of stratified medicine in chronic airway disease."

COMMENT: This study found that the cluster of asthma and COPD patients with an overlap phenotype had peripheral blood eosinophilia and higher levels of IgE. Yet the Th1/Th2 balance was distinctly different from that of patients with the allergic asthma phenotype. The authors conclude that this is a step toward better stratification of care in chronic airway disease.

J.J.O.

Hirai K, Shirai T, Suzuki M, et al: A clustering approach to identify and characterize the asthma and chronic obstructive pulmonary disease overlap phenotype. Clin Exp Allergy. 2017;47:1374-1382.

Keywords: asthma, ACOS, COPD, phenotypes

Chronic Obstructive Airway Disease – Does Smoking Really Matter?

Previous attempts at defining the so-called asthma-COPD overlap syndrome (ACOS) have included selected groups of patients with asthma or chronic obstructive pulmonary disease (COPD), rather than addressing chronic obstructive airway disease (COAD) as a whole. This study assessed the characteristics of patients with COAD based on classical diagnostic labels, as well as according to the underlying Th2 inflammatory pattern.

The study included 292 patients aged 40 years or older with COAD, identified from 23 Spanish outpatient clinics. Of these, 94 were classified as nonsmoking asthmatics, 89 with COPD, and 109 with ACOS. Within the ACOS group, 44 were smoking asthmatics and 65 had eosinophilic COPD. Clinical, functional, and inflammatory characteristics were compared among groups. Patients with a blood eosinophil count of 300 cells/μL or greater and/or a sputum eosinophil count of 3% or greater were classified as having a Th2 signature.

The nonsmoking asthma, COPD, and ACOS groups had similar symptoms and exacerbation rates. The underlying inflammatory pattern was Th2-high in 32.2% of patients and Th2-low in 67.8%. Rates of the Th2 signature were 49% in nonsmoking asthmatics and COPD patients with eosinophilia, 30% in smoking asthmatics, and 3% in COPD patients without eosinophilia.

Criteria for ACOS were met by 22% of patients with the Th2-high pattern and 19% with the Th2-low pattern. The Th2-high patients were younger, had a longer history of symptoms, were more likely to have positive skin-prick tests, had more corticosteroid-treated exacerbations, and had higher Th2 biomarkers.

Among patients with COAD, the classical diagnostic categories of asthma, COPD, and ACOS may not be distinguished according to clinical and functional characteristics. In contrast, classification according to the presence of Th2 inflammatory markers may define patients who could benefit from differing clinical approaches. The authors discuss the implications of using Th2 inflammation to guide therapy for COAD.

Little is known about the differences between adult-onset asthma and ACOS, despite the treatment implications of this distinction. Differences between these two phenotypes were evaluated in a Finnish cohort study of adult-onset asthma patients.

The study included 188 patients with adult-onset asthma enrolled in the Seinäjoki Adult Asthma Study, including 12-year follow-up data. Three groups were identified based on smoking history and postbronchodilator spirometry results. There were 122 patients who were never-smokers or had a smoking history of less than 10 pack-years, 32 patients with a smoking history of 10 or more pack-years but a "nonobstructive" pattern, and 34 ACOS patients with a smoking history and an "obstructive" pattern.

Compared to the other two groups, the ACOS patients had lower diffusing capacity, higher blood neutrophil count, and higher interleukin-6 levels. The ACOS group also had lower pulmonary function, greater residual bronchodilator reversibility, and increased comorbidity. Medication use was similar among groups, but the ACOS patients had worse asthma control.

The study defines some important differences between patients with ACOS versus adult-onset asthma. The finding of lower pulmonary diffusing capacity could be a useful clinical tool to differentiate ACOS patients from those with asthma alone.

COMMENT: Taken together, these two articles help us to understand whether the asthma-COPD overlap syndrome actually exists. The accompanying editorial by Miravitlles et al (Eur Respir J. 2017;49:1700506) helps to put it all in perspective. With the advent of triple therapy (LABA, LAMA, ICS), these concepts will be even more important.

B.E.C.

Cosio BG, de Llano LP, Viña AL, et al: Th-2 signature in chronic airway disease: towards the extinction of asthma-COPD overlap syndrome?
Eur Respir J. 2017;49:1602397.
Tommola M, Ilmarinen P, Tuomisto LE, et al: Differences between asthma-COPD overlap syndrome and adult-onset asthma.
Eur Respir J. 2017;49:1602383.

Keywords: asthma (adult), ACOS, COPD, phenotypes

Can We Predict Severe Anaphylaxis?

At a time of increasing anaphylaxis-related hospitalizations, it is important to identify patients at risk of severe or potentially fatal reactions. A large sample of patients with severe or near-fatal anaphylaxis was analyzed to identify risk factors for severe anaphylaxis.

Using an administrative claims database, the researchers identified 38,695 patients with severe anaphylaxis in the United States between 2005 and 2014. Of these, 11.6% were classified as having severe anaphylaxis. Criteria for this outcome included hospital admission in 11.5% of patients, ICU admission in 5.3%, endotracheal intubation in 1.5%, and meeting criteria for near-fatal reactions in 0.45%.

The factor most strongly associated with severe anaphylaxis was age 65 years or older, odds ratio (OR) 3.15. Other independent risk factors were anaphylactic reactions to medications, OR 1.50; cardiac disease, OR 1.56; and lung disease, OR 1.23. The ORs associated with age over 65 were 5.35 for ICU admission, 5.62 for intubation, and 6.71 for near-fatal anaphylaxis.

Older age, reactions to medications, and heart or lung disease are risk factors for severe or potentially fatal anaphylaxis. The researchers note that allergy/immunology consultation within the previous 12 months was associated with a lower risk of hospital or ICU admission on bivariate analysis, but was no longer significant on multivariate analysis.

COMMENT: Patients often ask allergists to predict whether they are at risk of "severe" anaphylaxis. This study found that patients aged 65 or older and those who have cardiac or lung disease were more likely to be admitted, intubated, or have near-fatal outcomes. Medication as a trigger also increased the odds of severe anaphylaxis, as described in prior studies. Interestingly, asthma was less likely to predict hospital or ICU admission—that's in contrast to guidelines and prior studies in which asthma is considered a risk factor for fatality. Allergist/immunology consultation within the last year was associated with lower odds of severe anaphylaxis. This suggests that education provided by allergists may have resulted in use of autoinjectable epinephrine or seeking medical care. The study provides further information that we can use to advise our patients regarding risk of severe anaphylaxis.

V.H.-T.

Motosue M, Bellolio MF, Van Houten HK, et al: Risk factors for severe anaphylaxis in the United States.
Ann Allergy Asthma Immunol, 2017;119:356-361.

Keywords: anaphylaxis, risk factors

Should We Fear the Bottle?

The relationship between mode of infant feeding and the risk of eczema is uncertain. Issues in previous research include a lack of distinction between exclusive versus nonexclusive breastfeeding and direct breastfeeding versus indirect feeding of breast milk, as well as the definition of "mixed" feeding patterns. These issues were addressed in an analysis of data of 6-year follow-up data from the Infants Feeding Practices Study II.

The analysis included data from 1,387 mother-child pairs, including detailed information on infant feeding during the first 6 months plus 6-year follow-up data. At follow-up, the prevalence of skin allergy was 20%. Infants with a mixed feeding pattern during the first months of life—a combination of direct breastfeeding, pumping and feeding breast milk, and formula feeding—were at increased risk of eczema/skin allergy. The adjusted prevalence ratio was 1.46, compared to infants with direct breastfeeding for at least 6 months.

There was a nonsignificant effect (prevalence ratio 1.26) of direct breastfeeding combined with pumped breast milk for the first 3 months, followed by mixed feeding. Eczema risk was unaffected by formula feeding introduced since birth. Paternal eczema and Hispanic race/ethnicity were important risk factors.

Infants with "mixed" feeding patterns may be at increased risk of childhood eczema/skin allergy, compared to those who are directly breastfed. Further studies are needed to assess how the trend toward increased pumping and feeding of breast milk and the use of mixed feeding modes may affect childhood allergy risks. The authors discuss previous findings that pumping may alter some of the constituents of breast milk.

COMMENT: There has been concern that the mode of infant feeding (direct versus indirect breastfeeding versus formula feeding) may play a role in the development of eczema. Soto-Ramírez and colleagues examined the Infant Feeding Practices Study and its 6-year follow-up data. They found that mixed infant feeding (combination of direct breastfeeding, pumping and feeding breast milk and formula) in the first months of life was associated with a higher risk of eczema in the first 6 years, compared to direct feeding at the breast only. The authors note that previously reported reductions in the constituents of pumped breast milk—

including lutein, vitamins C and B6, folic acid, lipase, immune cells, and fat—may be responsible for the association with eczema. Certainly these are worrisome findings that deserve further study.

J.J.O.

Soto-Ramírez N, Kar S, Zhang H, Karmaus W, et al: Infant feeding patterns and eczema in children in the first 6 years of life.
Clin Exp Allergy. 2017;47:1285-1298.

Keywords: breastfeeding, eczema, risk factors

A Potential Surrogate for Tolerance Development in CMA?

Most children with cow's milk allergy (CMA) will outgrow their condition, but little is known about the mechanisms by which natural tolerance develops. Previous reports have suggested that the balance between milk-specific IgE and IgG4 might be an important factor. This study compared IgE and IgG4 antibody binding to cow's milk epitopes in children with persistent CMA versus those who outgrew their allergy.

The study included serum samples, obtained at a median age of 10 months, from 35 children with confirmed CMA. Twenty-two children went on to develop natural tolerance (confirmed by food challenge) at a median age of 51 months. Using a peptide-based immunoassay, the researchers assessed IgE and IgG4 binding to overlapping peptides from five major cow's milk proteins. Findings were compared for children who did and did not acquire natural tolerance.

Baseline sera showed more intense and diverse IgE and IgG4 binding in children with persistent CMA, compared to those who outgrew their allergy. In contrast, children who became tolerant of cow's milk were more likely to have IgE and IgG4 antibodies that recognized the same epitopes. By the time of tolerance development, IgE and IgG4 binding became less intense, particularly to the α-s- and β-casein peptides. The initial differences between IgE and IgG4 binding intensity decreased with the development of natural tolerance.

The findings add to previous evidence that overlap between IgE and IgG4 is potentially important in acquisition of natural tolerance in children with CMA. With further study, the findings may point to new approaches to predicting which children will outgrow their CMA, as well as the development of targeted therapies.

COMMENT: Cow's milk allergy has been reported to occur in as many as 3% of infants, most of whom outgrow their allergy within 1 to 2 years. Previous studies have reported that high levels of specific IgE to cow's milk and/or casein are associated with persistence of CMA and more severe reactions. Furthermore, some studies have indicated a potential role for IgG4 antibodies in the attainment of tolerance, although there have been contradictory results. The study by Caubet et al provides further direction. They found greater intensity and diversity of IgE and IgG4 binding in children with persistent CMA (beyond age 5), compared to those with transient allergy. In children who developed tolerance, both IgE and IgG4 binding intensity decreased, particularly in areas of α-s- and β-casein. We hope that further study in this area will aid in the development of more targeted treatment in food allergy.

J.J.O.

Caubet JC, Lin J, Ahrens B, et al: Natural tolerance development in cow's milk allergic children: IgE and IgG4 epitope binding.
Allergy. 2017;72:1677-1685.

Keywords: cow's milk allergy, food allergy, natural tolerance

Which FPIES Patients Need IV Therapy during Food Challenges?

Food protein-induced enterocolitis (FPIES) is associated with delayed, potentially severe non-IgE-mediated reactions to foods. Oral food challenge (OFC) is essential for confirming resolution of FPIES. Current recommendations call for intravenous access before OFC is performed in this situation. The authors sought to identify risk factors for IV treatment during OFC in patients with FPIES.

The chart review study identified 28 FPIES patients treated at an allergy/immunology clinic between 2000 and 2015. Twenty-eight patients underwent a total of 39 OFCs. Median age was 6 months at diagnosis and 2.6 years at OFC. The researchers compared OFC and patient characteristics for patients with positive and negative OFCs, and for patients who did and did not require intravenous therapy.

The results were positive in 13 of 39 OFCs. Ten patients required no treatment or only oral therapies. The remaining 3 patients—accounting for 7.7% of all OFCs—received intravenous fluids or steroids. All but 1 of the OFCs were associated with reactions of equal or lesser severity than the patient's historical reactions. Food challenges in patients with an initial severe reaction showed a nonsignificant trend toward an increased likelihood of intravenous therapy. Intravenous treatment was more likely in younger children (15 versus 32 months) and in OFCs performed early after FPIES diagnosis (8 versus 28 months).

Although OFCs can elicit severe symptoms in children with FPIES, most reactions resolve without treatment or with oral treatment. In this experience, less than 10% of OFCs require intravenous treatment, and these cases are associated with severe FPIES in young patients. The authors suggest that patient age and time since historical reactions can be considered when deciding on the need for IV placement.

COMMENT: As food allergy continues to be a growing concern, recognition and diagnosis of patients with FPIES remains low. Oral food challenge is necessary to determine resolution of FPIES. This retrospective study found less than one-tenth of patients required treatment with IV fluids • • •

or IV steroids during OFC for FPIES, in contrast to recommendations for universal IV placement. It is important to note that no OFCs were performed in patients with a history of hypotension associated with reaction. No OFC resulted in clinically significant hypotension, no patients were hospitalized, and only one OFC led to a more severe reaction than prior reactions. The authors recommend special consideration for IV access in patients younger than 18 months, those less than 12 months from the prior reaction, or those with severe past FPIES reactions. Allergists may be reluctant to perform OFC in patients with FPIES due to concerns regarding severe reactions. This study should provide reassurance that OFC in these patients should be performed and is relatively safe, although not without risk.

V.H.-T.

Pena LE, Guffey D, Minard CG, et al: The role of intravenous access during oral food challenges in food protein-induced enterocolitis syndrome.
Allergy Asthma Proc. 2017;38:467-473.

Keywords: food allergy, FPIES, oral food challenge

Oral Food Challenge – Is It Safe in the 'Real World?'

There are relatively few data on reactions to oral food challenges (OFCs) in clinical, nonresearch settings. Information on the risk of anaphylactic reactions is especially important. The researchers examined data on the epidemiologic profile of clinical open OFCs performed at US tertiary food allergy centers.

The study included data on 6,377 open OFCs performed between 2008 and 2013, contributed by five centers across the United States. Of these, 6,377 OFCs were performed in children and adolescents. The reported rate of allergic reactions to OFCs was 14%, with a 2% estimated rate of anaphylactic reactions. The rate of nonanaphylactic reactions ranged from 13% to 33%, depending on year and center. Reactions were 16% more frequent in males compared to females.

Overall, treatment with antihistamines was used in 10% of OFCs; epinephrine and steroids were each used in 1% of challenges. In the most recent year, milk, peanut, and egg were the foods most commonly used in OFCs, and were more likely to produce positive reactions than other tested foods.

The study represents the largest report of allergic reactions to "real world" OFCs performed in the United States. The findings suggest that OFCs can be safely performed in nonresearch settings: 86% of challenges result in no reactions and 98% in no anaphylaxis.

COMMENT: As allergists, we have the responsibility to distinguish true allergy from allergen sensitization—a distinction that's especially important for quality of life. This survey of multiple food allergy academic centers throughout the United States investigated reactions during OFCs. The authors commented that for some foods without commercially available stock extract, prick and prick testing of the fresh fruits and vegetables may have changed the decision to perform OFC. Overall, 14% of OFCs resulted in reactions, while only 2% led to anaphylactic reactions. This survey supports the safety of OFCs in clinical settings, when performed by trained allergists.

V.H.-T.

Akuete K, Guffey D, Israelsen RB, et al: Multicenter prevalence of anaphylaxis in clinic-based oral food challenges.
Ann Allergy Asthma Immunol. 2017;119:339-348.

Keywords: food allergy, oral food challenge

Will Anti-IL-31 Become an Option for Itching in Chronic Skin Disease?

Pruritus remains a troublesome and difficult-to-treat problem in patients with atopic dermatitis (AD), chronic urticaria, and other skin diseases. Recent studies have established that interleukin-31 (IL-31) is involved in the pathogenesis of chronic pruritus. The researchers analyze evidence on the role of IL-31 in chronic skin diseases, its possible contribution to pruritus, and the implications for diagnosis and treatment.

A systematic review of the literature identified 45 published papers on IL-31 and its role in pathogenesis of chronic skin diseases and associated pruritus. Animal and human studies have suggested that IL-31 may be involved in AD and other chronic skin diseases, including chronic urticaria, contact dermatitis, chronic urticaria, and cutaneous T-cell lymphoma. Some studies have suggested that IL-31 could be involved in the pathogenesis of pruritus in both its initial and chronic stages. While it's unclear whether IL-31 is related to pruritus intensity or disease activity, it is clearly increased in chronic pruritic skin diseases, and not in similar conditions not associated with itching.

Initial attempts using IL-31 as a therapeutic target have focused on monoclonal antibodies. Studies have reported significant improvement in pruritus with the anti-IL-31 receptor A antibody nemolizumab in patients with moderate to severe AD. The results in terms of itch suppression were best at an 0.5 mg/kg dose given every 4 weeks.

This and other therapies targeting IL-31 might be a useful new approach in the management of chronic skin disorders that are inadequately controlled by conventional treatments. The authors emphasize the need for more research to clarify the effects of blocking the IL-31 cascade in various skin diseases, as well as clinical trials to confirm the safety and efficacy of anti-IL-31 treatments.

COMMENT: Pruritus is frustrating for patients with many atopic diseases. Monoclonal antibodies are being used in the treatment of AD and other diseases. In this review of • • •

published articles, IL-31 levels were often correlated with itching in patients with different skin diseases. Studies of IL-31 or monoclonal antibodies targeting IL-31 receptor A showed promise in the improvement of itching in AD patients. This may give allergists another treatment option, which may ultimately lead to control of pruritus in other "itchy" skin diseases. On a larger scale, IL-31 therapy may lead to improvement in quality of life, with new treatment options in chronic diseases otherwise recalcitrant to conventional treatment.

V.H.-T.

Gangemi S, Quartuccio S, Casciaro M, et al: Interleukin 31 and skin diseases: a systematic review. Allergy Asthma Proc. 2017;38:401-401.

Keywords: atopic dermatitis, interleukin-31, pruritus

Refractory Chronic Urticaria: Cyclosporine and Omalizumab

The biologic agent omalizumab is approved for the treatment of antihistamine-resistant chronic spontaneous urticaria (CSU), while the immunosuppressant drug cyclosporine and other "last-line" agents are not. The authors review the evidence for these two options for refractory CSU.

Six randomized controlled trials have analyzed the use of omalizumab for refractory CSU. Omalizumab 75 mg was effective in 1 of 3 trials, but all studies reported benefits at doses of 150, 300, and 600 mg. A meta-analysis concluded that omalizumab 300 mg was the most effective dose.

Four studies have evaluated modified cyclosporine for patients with refractory CSU. All doses studied, ranging from 1 to 5 mg/kg/d, were found to be effective. One study reported reductions in biomarkers thought to be involved in the pathophysiology of CSU.

The evidence suggests that both omalizumab and cyclosporine are effective treatments for antihistamine-resistant CSU. The authors note that the omalizumab trials were better designed than the cyclosporine studies. They also discuss the differences between these two options in terms of patient monitoring and adherence. The authors conclude, "Both drugs are feasible options in resistant CSU, given their effectiveness and safety profile."

COMMENT: This review presents both cyclosporine and omalizumab as effective treatment options for antihistamine-resistant chronic urticaria. However, as pointed out in our practice parameters, the randomized controlled trials involving cyclosporine suffered from methodologic limitations (J Allergy Clin Immunol. 2014;133:1270-1277), while the seven randomized controlled trials involving omalizumab were methodologically sound with a low risk of bias (J Allergy Clin Immunol. 2016;137:1742-1750). The authors conclude there is a need for a study comparing the effectiveness of cyclosporine and omalizumab in patients with refractory CSU.

D.M.L.

Koski R, Kennedy KK: Treatment with omalizumab or cyclosporine for resistant chronic spontaneous urticaria.
Ann Allergy Asthma Immunol. 2017;119:397-401.

Keywords: biologics, chronic spontaneous urticaria

Pneumonia: A Big Deal, Especially in NYC

Mortality from pneumonia is higher in New York City (NYC) than in the rest of the United States. The settings in which pneumonia are acquired are unclear; this information has important implications for prevention and treatment. The authors analyzed the burden of hospitalizations for pneumonia acquired in different settings in NYC.

The retrospective study included data from a New York State hospital discharge reporting system for 2010-14. Adult hospitalizations for pneumonia were identified and, based on clinical guidelines, classified into mutually exclusive categories of community-acquired (CAP), healthcare-associated (HCAP), hospital-acquired (HAP), and ventilator-associated pneumonia (VAP).

Of more than 4.6 million hospitalizations in NYC during the study period, 6.2% were associated with pneumonia. Of these cases, 54.3% were classified as CAP, 30.2% as HCAP, 14.0% as HAP, and 1.6% as VAP. In-hospital death occurred in 12.2% of pneumonia hospitalizations. This rate increased from 7.9% for CAP to 15.5% for HCAP, 20.7% hospital-acquired (HAP), and 21.6% for ventilator-associated pneumonia.

Age-adjusted pneumonia hospitalization rates were higher in men, in older patients, in the Bronx compared to Manhattan, in neighborhoods with a higher poverty rate, and in the winter months. Some type of immunocompromising condition was involved in 49.5% of pneumonia hospitalizations, increasing to over 55% for HCAP and HAP. Median length of stay was 5 days for CAP, 7 days for HCAP, 16 days for HAP, and 22 days for VAP.

Most pneumonia hospitalizations in NYC are acquired in community settings (CAP and HCAP), while those acquired in noncommunity settings (HAP and VAP) account for a disproportionate number of deaths. The authors discuss the implications for public health efforts to reduce the high burden of community- and noncommunity-acquired pneumonia in NYC.

COMMENT: Pneumonia and influenza together rank eighth in the United States as a cause of death, while in NYC they rank third. This study looked at the epidemiology of different forms of pneumonia in NYC. Six percent of hospitalizations were associated with pneumonia, and 54% of these were for CAP. Deaths were five times more frequent with pneumonia than without. More than 25% of pneumonia-associ- • • •

ated hospitalization deaths were due to HAP or VAP, even though these accounted for only 15% of pneumonias. About half of pneumonias occurred in patients considered "immunocompromised," based on a very broad definition. Clearly, both communities and healthcare systems need to do more to address the large burden of pneumonia.

D.A.K.

Corrado RE, Lee D, Lucerco DE, et al: Burden of adult community-acquired, health-care-associated, hospital-acquired, and ventilator-associated pneumonia: New York City, 2010-2014. Chest. 2017;152:930-942.

Keywords: epidemiology, inner-city, pneumonia

How Best to Manage Idiopathic CD4 Lymphocytopenia?

Patients with idiopathic CD4 lymphocytopenia (ICL) have an unexplained deficit of circulating CD4 T cells (less than 300/mm^3 or 20% of total T cells), placing them at risk of opportunistic infections. Questions remain about the clinical presentation, treatment, and outcomes of this rare disease. The authors present a single-center experience of 24 patients with ICL.

The patients were 14 women and 10 men, mean age 45 years, seen at the authors' immunology clinic between 1993 and 2014. Mean CD4 T cell count at diagnosis was 119/mm^3 and CD8 T cell count 219/mm^3. At presentation, 7% of patients had opportunistic infections, 41% had malignancies, 20% had autoimmunity, and 13% had demyelinating or other neurologic diseases.

Treatment with interleukin-2 led to resolution of severe resistant warts in 3 patients and of mycobacterial lung disease in 1. Eleven patients received maintenance therapy with trimethoprim-sulfamethoxazole; none had further infections requiring hospitalization.

The findings provide insight into the presentation and management of ICL. Most patients have opportunistic infections, although some appear healthy. Immunologic characteristics include very low CD4 T cells, deficient CD8 T cells and natural killer cells, and impaired lymphocyte proliferation. Other than prophylactic antibiotics—especially when CD4 cell counts are less than 200/mm^3—there is no standard treatment for this rare disorder.

COMMENT: In patients with opportunistic infections, lymphocyte subsets are often part of the immune workup. In this retrospective study, patients with ICL commonly had human papillomavirus mucocutaneous lesions. More than half of the patients also had low CD8+ T cells and natural killer cells. Forty-one percent of the patients had lymphoma or solid tumors—higher than previously reported. Treatment with interleukin-2 in some patients with resistant warts or pulmonary mycobacterial infection led to improvement in CD4+ T cell numbers. Among patients treated with prophylactic antibiotics, there were no further hospitalizations. This study reminds us about the importance of prophylactic antibiotics and monitoring for malignancy in our patients with ICL.

V.H.-T.

Yarmohammadi H, Cunningham-Rundles C: Idiopathic CD4 lymphocytopenia: Pathogenesis, etiologies, clinical presentations and treatment strategies. Ann Allergy Asthma Immunol. 2017;119:374-378.

Keywords: antibiotics, immunodeficiency disorders, ICL

May the Forest Be with You

Specific IgE to galactose-α-1,3-galactose (alpha-gal) can cause delayed anaphylaxis after red meat ingestion, with sensitization occurring via previous tick bites. This study assessed the prevalence of alpha-gal-specific IgE (sIgE) positivity in a population of forest service workers.

A cohort of 300 forest service employees and hunters in southwest Germany underwent ImmunoCAP measurement of alpha-gal-sIgE. At a cutoff of 0.10 kUA/L or higher, 35.0% of the study population had type I sensitization to alpha-gal. The prevalence of alpha-gal-sIgE levels of 0.35 kUA/L or greater was 19.3%. The presence of alpha-gal-sIgE was significantly associated with total IgE level and recent tick bites. Of subjects meeting the higher alpha-gal-sIgE cutoff, 8.6% had experienced delayed anaphylaxis to mammalian meat. Forest service employers were 2.5 times more likely to be positive for alpha-gal-sIgE. The prevalence of alpha-gal sensitization was no different in the current forest service sample compared to a historical cohort.

Forest service employees have a high prevalence of alpha-gal-sIgE, associated with recent tick bites and a high rate of delayed anaphylaxis to red meat ingestion. The researchers note that alpha-gal levels vary seasonally, and that atopy appears to be a predisposing factor for developing of alpha-gal-sIgE.

COMMENT: The prevalence of alpha-gal syndrome is quite variable. This sero-epidemiologic study defines a high-risk population of forest service workers, lumbermen, and hunters—with a median of three tick bites per year!

D.M.L.

Fischer J, Lupberger E, Hebsaker J, et al: Prevalence of type I sensitization to alpha-gal in forest service employees and hunters. Allergy. 2017;72:1540-1547.

Keywords: alpha-gal syndrome, occupational allergy, red meat allergy

Home Dampness Linked to Respiratory Symptoms

Dampness in the home is associated with respiratory symptoms in children. Less is known about this association in adults, or about the relationship between dampness • • •

and chronic rhinosinusitis (CRS). These issues were addressed using data from the Global Allergy and Asthma European Network survey.

The researchers analyzed data from 26,577 adults in Sweden, with questions including respiratory symptoms, smoking, education, and environmental exposures, including dampness. Chronic rhinosinusitis was defined using EP^{3}OS criteria; home dampness was scored in terms of water damage, damp floors, or visible mold in the past year.

Dampness at home was reported by 11.3% of respondents. On adjusted analysis, home dampness was associated with CRS, odds ratio (OR) 1.71; allergic rhinitis, OR 1.24; current asthma, OR 1.21; wheezing, OR 1.37; nocturnal dyspnea, OR 1.80; nocturnal cough, OR 1.34; and chronic bronchitis, OR 1.64. The higher the dampness score, the higher the risk of CRS and most other respiratory conditions.

Home dampness is independently associated with CRS and some other respiratory diseases and symptoms in Swedish adults. Studies in patients with confirmed CRS and expert assessment of dampness would help to confirm the associations.

COMMENT: The impact of dampness and mold on asthma has been well established, while their impact on the upper airway is quite limited. The GA^{2}LEN group's survey was used to assess home dampness as a risk factor for CRS, allergic rhinitis, and asthma. Dampness at home was associated with respiratory symptoms, with the strongest signal for nocturnal dyspnea, chronic bronchitis, and CRS. The exact mechanism(s) by which dampness and molds impact the airways is unknown. The authors stress that the association is likely not solely due to allergy, but also secondary to nonallergic mechanisms such as toxins or irritant exposure.

J.J.O.

Ahlroth Pind C, Gunnbjörnsdottir M, Bjerg A, et al: Patient-reported signs of dampness at home may be a risk factor for chronic rhinosinusitis: a cross-sectional study. Clin Exp Allergy. 2017; 47: 1383-1389.

Keywords: chronic rhinosinusitis, dampness, mold

REVIEWS OF NOTE

COMMENT: This European Academy of Allergy and Clinical Immunology position paper provides a state-of-the-art exploration of the nonallergic rhinitis (NAR) literature. It examines our current understanding of NAR phenotypes, provides recommendations for diagnosis and treatment, and closes with discussion of the unmet needs associated with this illness. This is a great resource for clinicians grappling with NAR.

J.J.O.

Hellings PW, Klimek L, Cingi C, et al: Non-allergic rhinitis: Position paper of the European Academy of Allergy and Clinical Immunology. Allergy. 2017;72:1657-1665.

COMMENT: In this Lancet Commission, an assembled group of experts provides a view of "where we are and where we need to go" in our attempt to resolve the public health problem of asthma. As the authors note, the article is not intended as a comprehensive review of asthma, but rather the collective view and opinions of an international expert panel. It is truly an amazing document that begins with historical landmarks regarding our present understanding of asthma, stressing the utility of phenotypic discriminators in the treatment of asthma (with attention to biologic therapies), along with future directions in asthma research. It's a great read.

J.J.O.

Pavord ID, Beasley R, Agusti A, et al: After asthma: redefining airways disease. Lancet. 2018;391:350-400.

COMMENT: Cough is a common chronic problem. This editorial outlines new pharmacologic treatment approaches.

B.E.C.

Birring SS: The search for the hypersensitivity in chronic cough. Eur Respir J. 2017;49:1700082.

COMMENT: This article provides a practical guide to identifying eosinophilic asthma.

B.E.C.

Buhl R, Humbert M, Bjermer L, et al: Severe eosinophilic asthma: a roadmap to consensus. Eur Respir J. 2017;49:1700634.

COMMENT: Here are three important recent articles dealing with management of chronic obstructive pulmonary disease.

B.E.C.

Vogelmeier CF, Criner GJ, Martinez FJ, et al: Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD Executive Summary. Eur Respir J. 2017;49:1700214.

Wedzicha JA, Miravitlles M, Hurst JR, et al: Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2017;49:1600791.

Wedzicha JA, Calverley PMA, Albert RK, et al: Prevention of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2017;50:1602265.