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AllergyWatch®

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

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The LEAP Study: A Triumph for Patients and Our Specialty

AFTER a decade of rapidly increasing prevalence in Western countries, peanut allergy is now appearing in Africa and Asia as well. Previous guidelines have recommended exclusion of peanut and other allergenic foods from the diets of high-risk infants. Subsequent research found a dramatically lower risk of peanut allergy in countries where peanut-based foods are introduced earlier in life. A randomized trial was performed to evaluate early introduction of peanut for primary and secondary prevention of peanut allergy in high-risk infants.

The "Learning Early About Peanut Allergy" (LEAP) trial included 640 infants at one UK center. All were considered at high risk of peanut allergy, with severe eczema and/or egg allergy at baseline. Enrolled at age 4 to less than 11 months, the infants were stratified according to the results of skin-prick testing to peanut extract. Ninety-eight infants had pre-existing sensitization, with a 1 to 4 mm wheal response to peanut.

In open-label fashion, infants were assigned to peanut consumption, at least 6 g of peanut protein per week, or avoidance of peanut-based foods until 5 years of age. At that time, the proportion of children with peanut allergy was compared between groups.

On intention-to-treat analysis of children with initially negative skin-prick test results, the prevalence of peanut allergy at 5 years was 13.7% for those assigned to peanut avoidance versus 1.9% for those assigned to early peanut introduction. Among those initially sensitized to peanut, allergy prevalence was 35.3% with peanut avoidance versus 10.6% with peanut consumption. Early introduction of peanut was effective in both primary prevention, 6.0% versus 1.0%; and secondary prevention, 33.1% versus 6.8%. ►►

CONTENTS

2015 Editor-in-Chief Disclosure:
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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 Asthama
- 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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Serious adverse events were similar between groups. Early peanut introduction was associated with increased levels of peanut-specific IgG4 antibody, whereas children assigned to avoidance were more likely to have elevated peanut-specific IgE. Children with a larger skin-prick test result and lower ratio of peanut-specific IgG4:IgE were more likely to develop peanut allergy.

The LEAP study supports early peanut consumption to reduce the development of peanut allergy in infants at high risk. This dietary intervention appears effective for both primary and secondary prevention, with immunologic changes consistent with those produced by successful allergen immunotherapy. A follow-up study will determine whether the protective effect persists after prolonged cessation of peanut consumption.

COMMENT: *By introducing regular peanut consumption between age 4 and 6 months, these investigators showed that peanut allergy can be prevented in high-risk infants. This work will no doubt catalyze a change in the epidemiology of peanut allergy, and it represents a triumph of collaborative clinical research funded by the federal government. There may well be many thousands fewer peanut allergic people 10 years from now than there would have been without the LEAP study, and the intervention responsible is not an expensive biotech product, but rather an everyday food. Can you think of a more cost-effective way to spend taxpayer dollars on research? S.A.T.*

Du Toit G, Roberts G, Sayre PH, et al: Randomized trial of peanut consumption in infants at risk for peanut allergy.
N Engl J Med. 2015;372:803-813. ♦♦

Study Shows Rising Rate of Drug-Induced Fatal Anaphylaxis in US

ADMISSIONS for anaphylaxis have increased in the United States. In Australia--which, like the United States, has a high rate of severe anaphylaxis--the incidence of fatal anaphylaxis has doubled in recent years. This study analyzed the features and time trends of fatal anaphylaxis in the United States.

Using the US National Mortality Database from 1999 through 2010, the researchers used ICD-10 codes to identify anaphylaxis deaths. They analyzed temporal trends in fatal anaphylaxis, as well as associations with demographic characteristics.

The analysis identified a total of 2,458 anaphylaxis-related deaths during the 12-year period studied. Medications were the most common cause of fatal anaphylaxis, reported in 58.8% of cases. This was followed by "unspecified," 19.3%; venom, 15.2%; and foods, 6.7%.

The incidence of fatal drug-induced anaphylaxis approximately doubled during the study period: from 0.27 cases per million in 1999-2001 to 0.51 per million in 2008-10. In about three-fourths of cases of drug-induced fatal anaphylaxis, no specific culprit drug was identified. Where a drug was specified, antibiotics were most common, followed by radiocontrast agents and antineoplastic drugs.

African American and older patients were more likely to have fatal anaphylaxis from medications, foods, and unspecified allergens. Fatal anaphylaxis from venom was also associated with white race, older age, and male sex. Among African Americans, the fatal anaphylaxis rate increased sharply during the study period: from 0.06 to 0.21 per million. The incidence of "unspecified" fatal anaphylaxis decreased from 0.30 to 0.09 per million.

The study suggests an increase in medication-related deaths caused by anaphylaxis in the United States in recent years. The authors believe these trends likely reflect increased medication and radiocontrast use, along with enhanced diagnosis and coding changes. The study also finds "strong and disparate associations" between race and specific causes of fatal anaphylaxis. ►►

COMMENT: *Recent reports have suggested that anaphylaxis may be underrecognized and undertreated. Since there is no central recording database for anaphylaxis reporting in the United States, these authors used coding information to show that antibiotics were the most frequent cause of fatal anaphylaxis. Interestingly, the rates for fatal drug-induced anaphylaxis doubled over the 10-year study period. The main limitation of this study is the specificity of coding data. However, the report is helpful since it increases awareness of potential anaphylaxis--particularly in hospitalized elderly patients receiving antibiotics, radiocontrast media, and anesthesia.*
S.M.F.
Jerschow E, Lin Y, Scaperotti MM, et al: Fatal anaphylaxis in the United States, 1999-2010: temporal patterns and demographic associations.
J Allergy Clin Immunol. 2014;134:1318-1328. ♦♦

Inhaler Reminders Improve Adherence in Asthma

POOR adherence is a major barrier to effective asthma treatment. Reliable interactive reminders to prompt patients to take inhaled medications are now available, but few studies have looked at how they affect adherence. This randomized trial compared inhaler reminders with doctor-patient discussions to enhance adherence in primary care patients with asthma.

The cluster randomized trial included 143 patients with moderate to severe asthma, enrolled by 43 Australian general practitioners. On the physician level, the study compared the effects of inhaler reminder feedback (IRF) and/or personalized adherence discussions (PADs) with active usual care alone. Enrolled patients had prescribed combination controller inhalers with a suboptimal Asthma Control Test (ACT) score of 19 or less. The patients' mean age was 40 years, with a mean ACT score of 14.6 and mean fluticasone propionate dose of 718 μg.

The IRF devices were monitors installed on fluticasaone/salmeterol inhalers that recorded adherence. Recordings were made covertly in non-IRF clusters, while the IRF groups received adherence feedback, including twice-daily reminders for missed doses. In the PAD groups, physicians received training in discussing medication adherence. The primary outcome was ACT scores, evaluated every 2 months. Severe exacerbations were assessed as well.

Through 6 months, adherence was 73% of prescribed daily doses for patients assigned to IRF versus 46% in the non-IRF groups. There was no significant difference in adherence between the PAD and non-PAD groups. Participants showed overall improvement in asthma control--mean ACT score change of 4.5--with no significant difference between groups. Severe exacerbation rates were 11% in IRF groups versus 28% in non-IRF groups. The difference was significant after adjustment for exacerbation history.

The IRF intervention evaluated in this study, using electronic monitors attached to inhalers, effectively improves medication adherence in primary care patients with asthma. The IRF devices are superior to a behavioral intervention or usual care, although the difference may not be apparent in daily asthma control scores. The authors plan a larger follow-up study, including patients with lower background controller doses.

COMMENT: *Adherence to recommended treatment regimens is challenging for patients with chronic illnesses--particularly asthmatics who require inhaler devices. This real-world study compared focused patient discussions and/or an inhaler reminder feedback device to usual care. Interestingly, the IRF technology was superior to behavioral discussions in improving adherence. There was no significant improvement in overall asthma control with either intervention. New technology can improve adherence to asthma therapy, the authors suggest.*
S.M.F.
Foster JM, Usherwood T, Smith L, et al: Inhaler reminders improve adherence with controller treatment in primary care patients with asthma.
J Allergy Clin Immunol. 2014;134:1260-1268. ♦♦

Can 'Google Trends' Predict Allergic Rhinitis Outbreaks?

THE web-based surveillance tool Google Trends has proven useful in predicting disease outbreaks, including influenza. This tool might have useful applications for allergic diseases as well. The authors evaluated the utility of Google Trends for predicting the "real world" epidemiology of allergic rhinitis (AR).

Using Google Trends, the researchers evaluated seasonal searching trends for AR in the United States from 2008 to 2014. The results showed a repeated seasonality effect, with AR searches peaking in late April and early May. After a decline in summer, there was a second small peak in AR searches in September.

Searches for AR were closely related to trends for other terms, including "pollen count," "loratadine," and "cetirizine." There were also significant associations with mean serial total pollen counts at locations across the United States. The patterns on Google Trends were also supported by monthly prevalence of nasal symptoms in AR reported in NHANES III, and by data on antihistamine sales.

Google Trends provides useful information on patterns of web searches for AR and related terms, reflecting the real-world epidemiology of this common disease. The results suggest that Google Trends might have value in predicting outbreaks of AR, as for other diseases.

COMMENT: *In this study, the web-based surveillance tool Google Trends proved a valuable epidemiologic measure for allergic rhinitis. It is likely that the design of epidemiology studies will look quite different in the future. More to come....*
J.J.O.
Kang M-J, Song W-J, Choi S, et al: Google unveils a glimpse of allergic rhinitis in the real world.
Allergy. 2015;70:124-128. ♦♦

Nasal Cytokines during a Cold Help Predict Asthma Exacerbation

VIRAL upper respiratory infections (URIs) have been linked to an increased risk of asthma exacerbations, although the mechanism of this association remains unclear. Recent studies raise the possibility that cytokine signatures in the upper airway during common colds might predict virus-induced events leading to asthma exacerbations. This hypothesis was addressed in a study testing nasal lavage specimens obtained during and after acute URI episodes.

The researchers analyzed nasal lavage fluid obtained from 59 patients, 46 of whom had asthma, during and after acute URI episodes. A wide range of analytes potentially relevant to asthma exacerbations--including cytokines involved in antiviral responses, cell recruiting, and injury remodeling--were analyzed.

Across the broad range of cytokines tested, overall responses during acute URI symptoms were similar for asthmatic and control subjects. However, among asthma patients, certain cytokine responses were elevated in those who had exacerbations during the first 3 weeks of the cold. These changes included a 1.7-fold increase in vascular endothelial growth factor (VEGF), a 5.1-fold increase in tumor necrosis factor-α (TNF-α), and a 4.7-fold increase in interleukin-1β. On receiver operating characteristic curve analysis, elevated VEGF and TNF-α levels were associated with shorter times to exacerbation.

Thus for patients with asthma, increased proinflammatory cytokine responses--especially VEGF and TNF-α--may contribute to virus-induced asthma exacerbations. The results may suggest possible new approaches using cytokine profile assessments to assess asthma exacerbation risk during URIs.

COMMENT: *Rhinovirus is known to trigger asthma exacerbations in children and adults. However, colds will not always trigger an exacerbation. This study evaluated adults with acute URIs, including asthmatics and controls, and analyzed nasal lavage levels for a variety of cytokines. Higher levels of VEGF and TNF-α during an acute cold were associated with the likelihood of a subsequent asthma exacerbation and earlier time to exacerbation. While these findings are not quite ready for prime time, in the future perhaps analyzing nasal cytokines using a simple and rapid test during a cold might be helpful in tailoring asthma management.*
D.A.K.

Manthei DM, Schwantes EA, Mathur SK, et al: Nasal lavage VEGF and TNF-α levels during a natural cold predict asthma exacerbations.
Clin Exp Allergy. 2014;44:1484-1493. ♦♦

Relapses after Asthma ED Visits Relatively Common

PREVIOUS studies have reported substantial rates of relapse after emergency department (ED) visits for acute asthma. Although various types of risk factors for asthma relapse after ED discharge have been suggested, these studies have had important limitations. Rates of and risk factors for asthma relapse after ED visits were assessed in a prospective, multicenter cohort study.

The study included 807 adults, aged 18 to 55 years, treated for acute asthma at 20 Canadian EDs between 2003 and 2007. The patients' median age was 30 years; 58% were women. Management in the ED was at the discretion of the treating physician. At discharge, a study nurse offered a short course of prednisone: 50 mg for 5 to 7 days.

Structured interviews were performed in the ED and by telephone at 4 weeks' follow-up. Relapse rates and associated risk factors were evaluated. Relapse was defined as worsening asthma leading to any unscheduled medical visit.

There was an 18% relapse rate within 4 weeks of ED discharge. Women were at higher risk of relapse than men: 22% versus 12%, adjusted odds ratio (OR) 1.9. Risk was also increased for patients with symptoms present at least 24 hours before the ED visit: 19% versus 13%, OR 1.7.

Relapse risk was also higher for patients ever using oral corticosteroids, 21% versus 12%; current use of a combined inhaled corticosteroid (ICS) plus long-acting β-agonist (compared to ICS monotherapy), OR 1.9; and owning a spacer device, 24% versus 15%. Adjusted ORs for these risk factors were 1.5, 1.9, and 1.6, respectively.

The study finds nearly a 20% rate of relapse within 4 weeks after an ED visit for acute asthma. This high relapse risk is despite guideline-recommended anti-inflammatory therapy. The identified risk factors--including female sex, prolonged symptoms, and certain treatment-related variables--may help in targeting high-risk patients for more aggressive interventions.

COMMENT: *This Canadian prospective study evaluated the rate and risk factors for asthma relapse, requiring a healthcare visit, after ED visits for asthma. About 1 in 5 of the 807 subjects had a relapse, even though all received a 5-day course of oral steroids. Some identified risk factors were obvious: prior oral steroid use and current use of ICS/LABA, likely reflecting more severe disease, and longer symptoms before presentation. One of the strongest risk factors was female gender, which does not seem to have a clear explanation. Most patients were cared for by family physicians, but there were no questions regarding specialty care, which is more common in the United States. Would allergist care reduce this risk? One would certainly hope.*
D.A.K.

Rowe BH, Villa-Roel C, Majumdar SR, et al: Rates and correlates of relapse following ED discharge for acute asthma: a Canadian 20-site prospective cohort study.
Chest. 2015;147:140-149. ♦♦

Yeast in the Dust--It May Be Good For You!

EXPOSURE to damp conditions and mold during infancy may affect the risk of childhood asthma and allergic disease. There have been few detailed studies of diverse fungal exposures during infancy and their relation to later disease risk. A birth cohort study with long-term follow-up evaluated the effects of early exposure to fungi on allergic disease risk.

The study included 408 children with a family history of allergic disease or asthma, recruited in 1994-96. Culturable fungi were measured in bedroom air and dust and in outdoor air when the children were 2 to 3 months old. Children were followed up to age 13 for the occurrence of asthma and allergy. These outcomes were analyzed in relation to fungal concentrations measured in infancy, with adjustment for other predictors and potential confounders.

Children with higher exposure to yeasts in bedroom floor dust during infancy were less likely to develop wheezing or to become sensitized to fungi. They were also less likely to develop asthma by age 13 years: hazard ratio (HR) 0.86. Visible dampness was unrelated to asthma risk.

Exposure to *Cladosporium* in outdoor air and to *Aspergillus* in dust were associated with an increased risk of rhinitis. Risk of mold sensitization was lower for children with higher exposure to dustborne yeast, but was unaffected by total exposure to airborne fungi. Children with a maternal history of fungal sensitization who were exposed to *Alternaria* and *Aspergillus* were more likely to become sensitized to fungi by age 12.

Infants with higher exposure to yeasts in dust appear to have lower asthma and allergy risks later in childhood. The results suggest that exposure to dustborne versus airborne yeasts may have differing effects on allergic disease outcomes. The researchers call for further studies to identify the "fungal components associated with immunoprotective effects."

COMMENT: *The role of environmental exposure in infancy and its relationship to the development of allergic disease has received much attention. This study from a Boston birth cohort adds to this evidence by looking at yeast and fungal exposure and development of allergic disease. Interestingly, elevated levels of yeast in dust were associated with lower wheeze, reduced risk of asthma, and less mold sensitization. Some specific fungi were positive risk factors for various outcomes. Visible dampness was not associated with asthma. This study suggests that yeast may have some immunoprotective effects on allergic diseases. Determining the yin and yang of these effects will require further studies.*
D.A.K.

Behbod B, Sordillo JE, Hoffman EB, et al: Asthma and allergy development: contrasting influences of yeasts and other fungal exposures.
Clin Exp Allergy. 2015;45:154-163. ♦♦

Icatibant shows Promise in ACE Inhibitor-Induced Angioedema

WITH the extensive use of angiotensin-converting enzyme (ACE) inhibitors, ACE inhibitor-induced angioedema affects a comparatively large number of patients. Predominantly affecting the upper aerodigestive tract, this is a potentially life-threatening condition with no approved treatment. The selective bradykinin B2 receptor antagonist icatibant was evaluated for treatment of ACE inhibitor-induced angioedema.

The randomized, phase 2 trial included 30 patients at four German centers with ACE inhibitor-induced angioedema of the upper aerodigestive tract. In double-blind fashion, they were assigned to treatment with subcutaneous icatibant, 30 mg; or current standard (off-label) treatment: intravenous prednisone, 500 mg, plus clemastine, 2 mg.

Of 27 patients treated according to the study protocol, all had complete resolution of edema. Median time to complete resolution was significantly shorter with icatibant: 8.0 hours, compared to 27.1 hours with standard treatment. Rescue therapy with icatibant and prednisolone was used in 3 patients initially assigned to standard treatment. One of these patients required tracheostomy.

Edema resolved within 4 hours for 5 of 13 patients with icatibant versus 0 of 14 with standard treatment. Icatibant was also associated with a shorter time to onset of symptom relief: 2.0 versus 11.7 hours, respectively.

Icatibant yields faster recovery in patients with ACE inhibitor-induced angioedema, compared to current off-label treatment with glucocorticoids and antihistamines. Time to complete resolution of edema is 70% faster with icatibant. The results are consistent with evidence suggesting that ACE inhibitor-induced angiodema is mediated by bradykinin, and therefore would not be expected to respond to antihistamines.

COMMENT: *Angioedema induced by ACE inhibitors is uncommon, but still accounts for one-third of all cases of angioedema treated in the emergency room. Although previous studies have demonstrated icatibant's effectiveness in aborting acute attacks of hereditary angioedema, it is exciting to find similar temporal improvement in a phase 2 study of subcutaneous icatibant in patients with ACE inhibitor-induced angioedema. It is particularly important since the current standard of therapy for this condition is off-label parenteral steroids and antihistamines, neither of which has significant clinical benefit in bradykinin-mediated angioedema. It remains to be seen whether the extremely high cost of icatibant will affect its use for bradykinin-induced angioedema due to ACE inhibitor therapy.*
C.D.

Baş M, Greve J, Stelter K, et al: A randomized trial of icatibant in ACE inhibitor-induced angioedema.
N Engl J Med. 2015;372:418-425. ♦♦

Maybe Mom Was Right--Take Your Cod Liver Oil

OXIDATIVE stress appears to play an important role in the immune and inflammatory responses involved in asthma. The antioxidant host defense system involves endogenous antioxidant activity as well as exogenous nonenzymatic antioxidants. The current study examined both factors for association with adult-onset asthma.

Participants were drawn from the Shanghai Women's Asthma and Allergy Study, including 40- to 70-year-old women free of prevalent asthma at baseline. Women developing asthma over 8 years' follow-up were matched to two asymptomatic controls. Baseline samples were used to compare markers of host antioxidant defense, including urinary F2-isoprostanes; plasma levels of various antioxidant micronutrients, such as tocopherols, xanthenes, carotenes, and lycopene; and markers of antioxidant enzyme activity, including platelet-activating factor acetylhydrolase (PAF-AH) and superoxide dismutase.

Of 65,372 women included in the analysis, 150 developed asthma during follow-up: an incidence of 0.24%. Cases and controls had similar baseline F2-isoprostane levels. However, a higher α-tocopherol concentration and PAF-AH activity were associated with lower asthma risk. Adjusted odds ratios were 0.52 for doubling of baseline α-tocopherol and 0.63 for doubling of PAH-AF. For both enzymatic and nonenzymatic antioxidants, effects were modified by workplace smoking exposure and family history of asthma.

Levels of α-tocopherol and activity of PAF-AH are both associated with a lower incidence of adult-onset asthma. These indicators of host antioxidant defense might be useful targets for primary asthma prevention, the authors suggest. They discuss the results in context of previous negative trials of antioxidant supplementation.

COMMENT: *This nested case-control study over an 8-year period helps us understand that increased endogenous antioxidant enzymatic activity of PAF and increased antioxidant plasma α-tocopherol concentrations are associated with a decrease in incident asthma in adults. These data are intriguing--but clearly not a call for increased vitamin E supplementation to prevent asthma, as previous data have not been consistent. It is important that appropriate studies be done to determine if targeting antioxidant defense may be a future strategy for primary asthma prevention. See the accompanying editorial by Quon and Goss(Am J Respir Crit Care Med. 2015;191:4-5).*
B.E.C.

Larkin EK, Gao Y-T, Gebretsadik T, et al: New risk factors for adult-onset incident asthma: a nested case-control study of host antioxidant defense.
Am J Respir Crit Care Med. 2015;191:45-53. ♦♦

Combination Approach Improves Asthma Prediction in Preschoolers

SOME reliable test for asthma diagnosis in the large population of preschool children with wheezing is needed. Based on symptoms and other clinical data, the Asthma Predictive Index (API) has been used for early diagnosis, but has important limitations. This study evaluated a combination approach--including the API, measurement of exhaled volatile organic compounds (VOCs), and expression of inflammation genes--for asthma diagnosis in young children.

The Asthma Detection and Monitoring study included 202 Danish children with recurrent wheezing. The children, aged 2 to 4 years at baseline, were followed up to age 6, at which time a diagnosis of asthma versus transient wheezing was made. The API was assessed at baseline, along with biomarkers in exhaled breath condensate, exhaled VOCs, gene expression, and airway resistance. Area under the receiver operating characteristic curve (AUC) analysis was performed to determine which biomarkers provided additional predictive value for early asthma diagnosis.

At age 6, asthma was diagnosed in 76 of 198 children. Added to clinical information, measurement of exhaled VOCs significantly improved asthma prediction. Area under the curve was 89%, with an increase of 28%; positive predictive value (PPV) was 82% and negative predictive value (NPV) 83%. These values were confirmed in a validation set.

Gene expression of toll-like receptor 4, catalase, and tumor necrosis factor-α also improved prediction, with an AUC of 75% (increase of 17%), PPV of 76%, and NPV of 73%. However, these values were not confirmed on validation. The addition of biomarkers in exhaled breath condensate and pre- and post-bronchodilator airway resistance did not improve asthma prediction. A final model comprising API, VOCs, and gene expression has an AUC of 95%, PPV of 90%, and NPV of 89%.

Added to clinical information in the API, data on exhaled VOCs and possibly on inflammatory genes can improve the early diagnosis of asthma in preschoolers with recurrent wheezing. Further study is needed to confirm the clinical relevance of this approach, including its effects on treatment and outcomes.

COMMENT: *Wheezing is present in approximately 40% of preschool children. In the past, the API has been used to help predict who is more likely to not progress to persistent asthma. This study helps us understand that a combination of VOCs, expression of inflammatory genes and the API predict asthma in approximately 90% of preschool children. Similar data have been published by Robin Taylor (J Allergy Clin Immunol. 2011;128:927-934) showing that exhaled NO at age 3 associated with a positive API is highly predictive of asthma. These data are important and must be repeated in order to define appropriate diagnostic tests for clinical practice.*
B.E.C.

Klaassen EMM, van de Kant KDG, Jöbsis Q, et al: Exhaled biomarkers and gene expression at preschool age improve asthma prediction at 6 years of age.
Am J Respir Crit Care Med. 2015;191:201-207. ♦♦

Assessing Alternative Medicine Beliefs May Help Improve ICS Adherence

SEVERAL factors may contribute to low adherence to inhaled corticosteroids (ICS) in asthma patients. Previous studies have reported lower ICS adherence in patients who endorse complementary and alternative medicine (CAM) therapies. Negative beliefs about ICS and endorsement of CAM are more common in black versus white adults. These factors and their relation to uncontrolled asthma were assessed in an urban minority population.

For the study, the authors developed a brief questionnaire with low literacy demands: the Complementary and Alternative Management for Asthma (CAM-A) questionnaire. The CAM-A, which identified negative ICS beliefs and CAM endorsement, underwent psychometric testing in a mainly low-income, African American population of 304 subjects. In a second phase, 33 primary care visits were audio-recorded to evaluate the CAM-A's value in prompting clinical discussions about ICS and CAM beliefs.

Psychometric testing identified 17 items relative to ICS beliefs or CAM endorsement. The CAM-A showed high reliability for both sets of items. The study population had a 93% rate of CAM endorsement, with a 68% rate of negative ICS beliefs and a 69% rate of uncontrolled asthma. Low education and CAM endorsement were the two main factors associated with uncontrolled asthma: uncontrolled asthma increased by 1.41 for each 1-unit increase in a cumulative CAM endorsement score.

On qualitative analysis of the interviews, the CAM-A appeared useful in prompting discussions of these issues with patients. When using the questionnaire, providers were more likely to learn something new about the patient's asthma self-management and more likely to discuss ICS use or nonpharmacologic approaches.

In this urban minority population, negative beliefs about ICS and endorsement of CAM are associated with uncontrolled asthma. The CAM-A questionnaire may help in identifying beliefs and behaviors contributing to poor ICS adherence, and may promote discussion of these topics in primary care visits.

COMMENT: *Use of CAM treatments seems to be increasing recently, particularly in patients with chronic illnesses such as asthma. These researchers developed a psychometric testing questionnaire to determine patients' feelings about the use of CAM compared to conventional ICS and how these attitudes affect asthma control. The finding that patients with uncontrolled asthma had higher rates of CAM endorsement and negative ICS beliefs should not be surprising. The authors recommend that we ask our asthmatic patients directly about their use of CAM, to help dispel beliefs and behaviors that might undermine adherence to our medical advice.*
S.M.F.

George M, Topaz M, Rand C, et al: Inhaled corticosteroid beliefs, complementary and alternative medicine, and uncontrolled asthma in urban minority adults.
J Allergy Clin Immunol. 2014;134:1252-1259. ♦♦

Mango or Pineapple Flavor? Increasing E-Cigarette Use in Teens

USE of electronic cigarettes (e-cigarettes) is increasing rapidly, including among adolescents. Teens who smoke e-cigarettes are more likely to smoke tobacco cigarettes as well, but the characteristics of these dual users remain unclear. Risk factors for e-cigarette use and dual use of e-cigarettes and tobacco cigarettes were assessed in a survey of high school students.

The school-based survey included 1,941 students, mean age 14.6 years, in Hawaii. In addition to their use of e-cigarettes and tobacco cigarettes, participants were asked about use of other substances and potential psychosocial risk (eg, sensation seeking) and protective factors (eg, parental support).

Seventeen percent of teens used e-cigarettes only, 12% used e-cigarettes and tobacco cigarettes, and 3% used tobacco cigarettes only. The dual users and tobacco-only smokers had higher scores for smoking-related risk factors and lower scores for protective factors, compared to students who used neither product or e-cigarettes only. Those who used e-cigarettes only scored higher on risk factors than nonusers, but lower than dual users. Youth who used e-cigarettes--alone or in addition to tobacco cigarettes--were more likely to perceive e-cigarettes as healthier than tobacco cigarettes.

About 30% of Hawaiian high school students surveyed report using e-cigarettes, with many of them using tobacco cigarettes as well. Risk factors for smoking appear "intermediate" for young people who use e-cigarettes only, suggesting that e-cigarettes are attracting "medium-risk" teens who would otherwise be less likely to smoke. Longitudinal studies are needed to see how e-cigarettes affect later smoking behavior and other types of substance use.

COMMENT: *In this study, more than two-thirds of high school students surveyed in Hawaii considered e-cigarettes to be healthier than cigarettes. Almost 3 out of every 10 adolescents had ever used e-cigarettes, one of the largest prevalence rates hitherto published. There was also a substantial prevalence of dual use of cigarettes and e-cigarettes, raising the alarming question on whether this was a consequence of "renormalization" of smoking. Interestingly, flavors available in Hawaii during the study period included mango and pineapple!*
C.D.

Wills TA, Knight R, Williams RJ, et al: Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents.
Pediatrics. 2015;135:e43-e51. ♦♦

In Young Children, Allergy Tests Disagree

SKIN prick testing (SPT) and specific IgE (sIgE) measurement are important for objective diagnosis of allergy in young children. Although these two tests are commonly used interchangeably, their degree of ➤➤

correlation in young children remains unclear. This study evaluated the agreement between SPT and sIgE results in preschool-aged children.

The study included 389 children with a maternal history of asthma, drawn from a Danish birth cohort study (the Copenhagen Prospective Study on Asthma in Childhood$_{2000}$). At age 0.5, 1.5, 4, and 6 years, the children underwent simultaneous SPT and sIgE testing for 16 common food and inhalant allergens. Agreement between the two tests for diagnosis of allergic sensitization was assessed at each time point.

By sIgE testing, the prevalence of inhalant allergen sensitization increased from 0.6% at 0.5 years to 4.2% at 1.5 years, to 18.1% at 4 years, to 24.8% at 6 years. By SPT, the rates were 1.5%, 3.8%, 8.4%, and 15.4%, respectively. The prevalence of food sensitization diagnosed by sIgE also increased over time: from 7.8% to 12.1% to 15.0% to 18.9%.

However, by SPT, the prevalence of food sensitization decreased from 5.3% at 0.5 years to 5.1% at 1.5 years, to 3.7% at 4 years, to 3.0% at 6 years. Overall agreement between the two tests was rate poor to moderate, with κ-coefficients of 0.60 or less. For food allergens, agreement decreased from moderate to slight with increasing age.

The results show "substantial disagreement" between the results of SPT and sIgE measurement in young children at risk of allergic disease. For sensitization to foods, the discrepancy widens over time from infancy to school age. The choice of test appears to have a major impact on diagnosis of IgE-mediated allergy in young children.

COMMENT: *These authors examined the concordance between SPT and sIgE measurement, via the ImmunoCAP assay, in a group of children aged 6 months to 6 years. They found substantial disagreement between these two diagnostic tests--a very bothersome outcome! This is a reminder that specific IgE test modalities are not interchangeable.*
J.J.O.

Schoos A-MM, Chawes BLK, Følsgaard NV, et al: Disagreement between skin prick test and specific IgE in young children.
Allergy. 2014;70:41-48. ♦♦

Does Traffic Exposure Increase Children's Allergy Risk?

PREVIOUS studies have linked early exposure to traffic-related air pollution to an increased risk of sensitization and allergic disease in children. The authors report a prospective epidemiologic study of exposure to traffic exhaust during infancy and allergy-related outcomes in early childhood.

The Cincinnati Childhood Allergy and Air Pollution Study enrolled infants with a parental history of aeroallergen sensitization. Air pollution monitoring data (with a land use regression model) were used to assess diesel exhaust particle (DEP) exposure during infancy. Each year, the children underwent skin prick testing for sensitization to 15 aeroallergens. The presence of allergic rhinitis--defined as at least one positive skin prick test with sneezing and a runny nose--was assessed at age 4 years.

Follow-up to age 4 was available for 634 children. The overall prevalence of AR increased from 6.9% at 1 year to 21.9% at 4 years. There were borderline associations between high DEP exposure in infancy and aeroallergen sensitization at age 2 and 3 years: odds ratio 1.40 and 1.35, respectively. However, DEP exposure was unrelated to AR.

In contrast, responses to specific aeroallergens were associated with AR. Odds of AR at age 4 were significantly increased with each 1 mm² increase in wheal responses to timothy grass and *Alternaria* at age 2, and with similar increases in wheal area to fescue, dog, and *Penicillum* at age 4. Models using these specific allergens were superior to models summing the wheal areas of all aeroallergens.

The study reports a "positive trend" toward an increased risk of early aeroallergen sensitization with higher DEP exposure in infancy. Wheal responses to specific aeroallergens at age 2 and 3 are significantly associated with the development of AR at age 4. The results suggest the potential to improve asthma risk stratification in young children.

COMMENT: *Studies have investigated the relationship between exposure to pollution and atopy. This was the first prospective study, in young children with parental history of aeroallergen sensitization, looking at early-life exposure to DEP and subsequent sensitization to aeroallergens. This study found that increases in wheal size to timothy grass pollen and* Alternaria *in young children were significantly associated with increased risk of development of AR. The findings support other studies showing that exposure to pollution increases the risk of developing atopic disease.*
V.H.-T.

Codispoti CD, LeMasters GK, Levin L, et al: Traffic pollution is associated with early childhood aeroallergen sensitization.
Ann Allergy Asthma Immunol. 2015;114:126-133. ♦♦

Food Allergy and Parents' QOL--A Closer Look

PREVIOUS studies--focusing mainly on mothers--have suggested poorer health-related quality of life (QOL) in parents of children with food allergy. This study further examined differences in food allergy-related QOL and psychological empowerment in mothers and fathers.

The study included 876 families of children enrolled in the Chicago Family Cohort food allergy study. Sixty-four percent of the children were boys, and 48% were between 2 and 5 years old; the parents were mainly white, upper-income married couples. The study included strict criteria for diagnosis of food allergy, including clinical history, skin prick testing, and specific IgE measurement. Parents completed specific assessments of family empowerment and food allergy-related QOL and burden. Quality of life was compared for mothers ➤➤

and fathers, and relationships between parental empowerment and QOL were assessed.

Empowerment was higher and food allergy-related quality of life was lower in mothers compared to fathers. This was so across allergy severity levels, allergy type, and comorbid disease status. However, neither mothers nor fathers showed a significant association between empowerment and QOL

There were no differences in parental empowerment across different types of food allergy. However, QOL was significantly reduced for parents of children with milk or egg allergy. Parental fears of exposure to allergen outside the home had the largest impact on QOL.

Mothers of children with food allergy have lower QOL but higher empowerment than fathers. The QOL impact appears greatest for parents of children with milk or egg allergy. Despite feeling empowered to care for their child, fears that the child will be exposed to allergens in situations outside the control continues to have a major impact on QOL for parents.

COMMENT: *Patients and families with food allergy have decreases in QOL due to anxiety, among other factors. Differences were seen in QOL of mothers as compared to fathers, even though mothers reported greater empowerment. Families of children with milk and egg allergy had lower QOL. The authors remind us that efforts such as improved food labeling, school laws for provision of undesignated epinephrine, and support groups may help our patients and families affected by food allergy. This study is an important call to allergists that addressing the allergy alone is not sufficient to help these families in their day-to-day lives.*
V.H.-T.
Warren CM, Gupta RS, Sohn M-W, et al: Differences in empowerment and quality of life among parents of children with food allergy.
Ann Allergy Asthma Immunol. 2015;114:117-125. ♦♦

Pets and Asthma--Still No Consensus!

PREVIOUS studies have suggested that children exposed to pets at home are at lower risk of allergy, but the relationship with asthma risk is still unclear. Data from a large UK birth cohort study were used to analyze the effects of pet ownership during pregnancy and childhood on asthma and atopy at age 7.

The study included 3,768 children from the Avon Longitudinal Study of Parents and Children. Pet ownership was assessed six times between pregnancy and age 7. Associations between pet exposure and atopy (based on skin prick tests to grass, house dust mite, and cat) and with atopic and nonatopic asthma at age 7 were assessed. The analysis included adjustment for the child's sex, the mother's history of asthma or atopy, the mother's smoking during pregnancy, and family adversity.

Continuous pet ownership, before and after age 3, was associated with a significant reduction in the risk of asthma at age 7: odds ratio (OR) 0.48. However, children exposed to pets tended to have a higher rate of nonatopic asthma--especially for rabbits, OR 1.61, and rodents, OR 1.86. Sensitization to tested allergens was consistently lower for children with pets, except for a higher rate of rodent sensitization in children with rodents as pets. All types of pets--including cats, dogs, rabbits, rodents, and birds--were associated with differing effects on atopic versus nonatopic asthma.

Children exposed to pets during pregnancy and childhood are less likely to have aeroallergen sensitization and atopic asthma at age 7. However, pet ownership--especially rabbits and rodents--is associated with increased odds of nonatopic asthma. It is unclear whether the pet-related increase in nonatopic asthma is a "causal effect or trigger mechanism."

COMMENT: *In essence, this study brings further complexity in responding to parents who ask, "Do pets in the home increase the risk of asthma?" It would appear that pets reduce the likelihood of atopic asthma; however, they increase the risk of nonatopic asthma. This will likely be perceived by the parents as clear as mud.*
J.J.O.
Collin SM, Granell R, Westgarth C, et al: Pet ownership is associated with increased risk of non-atopic asthma and reduced risk of atopy in childhood: findings from a UK birth cohort.
Clin Exp Allergy. 2015;45:200-210. ♦♦

Can Cytokines Aid in Stratifying Atopic Eczema?

CHILDREN with atopic eczema/dermatitis syndrome (AEDS) are an important population in allergy/immunology practice. Many questions remain about the pathogenesis of this condition, including the associated cytokine profile. This study evaluated levels of interleukin (IL)-17, IL-23, and IL-30 in children with atopic and nonatopic AEDS, including the association of cytokines with disease severity.

The study included 181 children with AEDS and 93 healthy controls, Based on skin prick tests and specific IgE measurements, AEDS was classified as atopic in 104 patients and nonatopic in 77. Levels of IL-17, IL-23, and IL-30 were compared for children with AEDS versus controls and children with atopic versus nonatopic AEDS. Associations with disease severity, based on the Score Atopic Dermatitis (SCORAD) index, were assessed as well.

Serum IL-17 and IL-23 levels were significantly higher in children with AEDS compared to controls: 63.21 versus 29.3 pg/mL for IL-17 and 211.93 versus 111.3 pg/mL for IL-23. Serum IL-10 was lower in children with AEDS: 3.21 versus 4.95 pg/mL. In addition, IL-17 and IL-23 levels were higher in children with atopic versus nonatopic AEDS. Serum IL-10 levels were not significantly different between the two AEDS subgroups.

In both AEDS subtypes, IL-17 and IL-23 were significantly correlated with the SCORAD index while IL-10 was negatively correlated with SCORAD. Serum IL-17 and IL-23 were also positively correlated with total IgE levels in the children with atopic AEDS. Within the atopic AEDS group, children with allergic diseases ➤➤

such as asthma and rhinitis had further increases in IL-17 and IL-23, compared to children with allergic sensitization only.

The results show differences in IL-17, IL-23, and IL-10 levels in children with AEDS versus controls, and in IL-17 and IL-23 levels for children with atopic versus nonatopic AEDS. The findings suggest that the IL-17/IL-23 axis may be relevant to the pathogenesis of AEDS, and an informative marker of the "atopic march" and disease severity in these children.

COMMENT: *Parents often ask about the severity of their children's atopic disease--a topic that is often difficult, if not impossible, to accurately address. This study investigated levels of IL-17, IL-23 and IL-10 in children with AEDS, specifically comparing patients with and without IgE sensitization. In IgE-sensitized children, IL-17 and IL-23 levels were higher compared to both healthy controls and children without atopy, especially those with more severe disease. Higher levels of IL-17 and IL-23 were seen in patients with IgE sensitization who also had asthma and/or rhinitis. On the other hand, IL-10 was lower in patients with atopic forms of AEDS, compared to healthy controls. Lower levels of IL-10 were seen with more severe disease. The study raises the question of whether we may be able to more accurately define the severity of AEDS based on cytokine levels, as well as the potential effects of treatment on these levels.*
V,H.-T.
Leonardi S, Cuppari C, Manti S, et al: Serum interleukin 17, interleukin 23, and interleukin 10 values in children with atopic eczema/dermatitis syndrome (AEDS): association with clinical severity and phenotype.
Allergy Asthma Proc. 2015;36:74-81. ♦♦

Should Measuring Exhaled Nitric Oxide Be Standard Practice?

ROUTINE outpatient asthma management includes clinical evaluation, spirometry, and symptom assessment. However, these do not provide information on ongoing airway inflammation, which is a key factor affecting asthma control. Exhaled nitric oxide measurement has been recommended for assessment of asthmatic airway inflammation, but its impact on treatment decision-making remains unclear. This study evaluated the impact of exhaled NO measurements of treatment decisions in an asthma specialty clinic.

The study included 50 children and adults, aged 7 to 60 years, receiving outpatient follow-up care for asthma. After routine evaluation, including the Asthma Control Test, patients underwent a single exhaled NO measurement. Study clinicians--four Board-certified allergists and a nurse practitioner--estimated the degree of airway inflammation and made treatment recommendations.

The clinicians were then informed of the exhaled NO results, and any subsequent changes in treatment recommendations were noted. The cost effects of including exhaled NO measurement in ongoing patient care were estimated as well.

Clinicians generally underestimated airway inflammation on the basis of routine evaluation, estimating a low exhaled NO level in 68% of patients, a medium level in 28%, and a high level in 4%. Measured exhaled NO levels were low in 58% of patients, intermediate in 20%, and high in 22%. The clinical estimates were incorrect in half of patients.

After receiving the exhaled NO results, the clinicians altered their treatment recommendations in 36% of patients. Medication was added or the dose increased in 10 patients, while medications were eliminated or decreased in 8 patients. Adding exhaled NO measurement to standard care was estimated to reduce annual asthma costs by $629 per patient.

The results suggest that assessing airway inflammation by exhaled NO, in addition to routine evaluation, affects treatment recommendations for many asthma patients seen at a specialty clinic. This test may have important effects on long-term asthma management, potentially reducing the costs and morbidity associated with exacerbations.

COMMENT: *Considered routine by some of us, occasionally useful by others, and outright rejected by still others, exhaled NO measurement has not settled into a stable niche as an aid to the diagnosis and management of asthma. Sponsored by a leading exhaled NO device company, this study is limited by its small size. However, it does suggest that exhaled NO measurement may be a practical way to improve our assessment of inflammation in uncontrolled asthma, and may also be cost effective when used appropriately.*
C.C.R.
LaForce C, Brooks E, Herje N, et al: Impact of exhaled nitric oxide measurements on treatment decisions in an asthma specialty clinic.
Ann Allergy Asthma Immunol. 2014;113;691-623. ♦♦

CLINICAL TIDBITS

Omalizumab for Poor Adherence?

SOME form of directly observed therapy might be useful in patients with uncontrolled asthma related to poor adherence with inhaled corticosteroid (ICS) therapy. This randomized trial assessed the effects of anti-IgE therapy with omalizumab for patients with low adherence and poorly controlled asthma.

The study included 17 patients, mean age 16 years, with persistent allergic asthma and less than 50% adherence to ICS therapy. All had an FEV_1 of 60% predicted or higher, with an adenosine provocation concentration causing a 20% decrease in FEV_1 (PC_{20}) of 60 mg/mL or less. In double-blind, crossover fashion, patients were assigned to 4 months of double-blind treatment with omalizumab or placebo, while continuing on ICS therapy.

Mean baseline PC_{20} was 14.1 mg/mL. The PC_{20} changed by 3.1-fold during omalizumab treatment, compared to 0.9-fold during placebo. Six patients had exacerbations requiring oral corticosteroids during placebo treatment, compared to none during omalizumab. ➤➤

Omalizumab may be an option for patients with poorly controlled asthma related to low ICS adherence. The very high cost of omalizumab would be a barrier to this approach, however.

COMMENT: *Poor adherence to ICS therapy for asthma is both common and costly in terms of morbidity and even mortality. The results of this 4-month study suggest that omalizumab may be worth considering in refractory asthma, even in poorly adherent patients. Were it not for omalizumab's very high cost, it would almost certainly be more widely used as "directly observed therapy" in poorly adherent, moderate to severe asthmatic patients.*
C.C.R.
Hendeles L, Khan YR, Shuster JJ, et al: Omalizumab therapy for asthma patients with poor adherence to inhaled corticosteroid therapy.
Ann Allergy Asthma Immunol. 2015:114;58-62. ♦♦

Allergic Rhinitis: Clinical Practice

SEASONAL or perennial allergic rhinitis is a major problem, affecting 15% to 30% of US adults and children. Up to 40% of patients with allergic rhinitis currently have or will develop asthma. A clinical practice vignette outlines the clinical problem and approach to diagnosis and treatment of allergic rhinitis.

Allergic rhinitis is commonly diagnosed on clinical grounds, based on the symptoms and response to antihistamines or nasal glucocorticoids. The relative advantages and disadvantages of skin tests and specific IgE measurement are discussed. Nonallergic forms of rhinitis must sometimes be considered.

The authors outline recommended medication approaches for patients with different types of symptoms: episodic, mild seasonal or perennial symptoms, or moderate to severe symptoms. One-third of children and nearly two-thirds of adults do not have a good response to drug therapy, and may be candidates for allergen immunotherapy. Areas of uncertainty include the appropriate use of immunotherapy and the role of allergen avoidance.

The article presents useful information on the clinical approach to allergic rhinitis for the nonspecialist. It features an illustrated discussion of the process of allergic sensitization, the mechanism of nasal reaction on re-exposure, and the development of symptoms in response to allergen exposure.

COMMENT: *Using a case vignette of a 35-year-old woman presenting with a combination of perennial and seasonal allergic rhinitis, the authors discuss the evaluation and management of allergic rhinitis. Their approach uses both the Allergic Rhinitis and Its Impact on Asthma (ARIA) Guidelines and the Rhinitis Practice Parameter as evidence-based references. This is an excellent article to hand out to medical trainees.*
C.D.
Wheatley LM, Togias A: Allergic rhinitis.
N Engl J Med. 2015;372:45-63. ♦♦

Costs of COPD on the Rise

PREVIOUS studies have estimated that approximately 15 million US adults have been diagnosed with chronic obstructive pulmonary disease (COPD), which is a major reason for hospital admissions and outpatient and emergency department visits. This study estimated national and state-level costs for COPD.

The researchers analyzed data from the 2006-2010 Medical Expenditure Panel Survey, Centers for Medicare and Medicaid Services 2010 data, and other sources. For 2010, total national medical costs attributable to COPD and its sequelae were estimated at $32.1 billion. With the addition of $3.9 billion in absenteeism costs, the total burden of COPD costs was $36 billion.

Fifty-one percent of the medical costs of COPD were paid by Medicare, 25% by Medicaid, and 18% by private insurance. Based on census data, COPD costs were projected to increase to $49.0 billion in 2020. Total costs were highest in California, $2.8 billion, and lowest in Wyoming, $49.1 million. Florida had the highest medical costs, $2.5 billion, and Alaska the lowest, $42.5 million.

The data suggest that national and state-level costs for COPD are high and rising. Savings might be achieved through evidence-based steps to prevent smoking and reduce COPD complications.

COMMENT: *Chronic obstructive pulmonary disease is relatively common and costly. This study provided updated information on annual costs as well as new, state-specific costs using data from the US Medical Expenditure Panel Survey. The authors determined that in 2010, the annual US cost of COPD was $36 billion and is expected to increase over the next 10 years. Medical costs varied dramatically at the state level. Asthma and COPD are both costly diseases, but COPD can be almost entirely prevented. These economic data may help state public health officials promote activities to reduce COPD.*
D.A.K.
Ford ES, Murphy LB, Khavjou O, et al: Total and state-specific medical and absenteeism costs of COPD among adults aged ≥ 18 years in the United States for 2010 and projections through 2020.
Chest. 2015;147:31-45. ♦♦

Siblings of Peanut-Allergic Children: Exposure and Allergy

STUDIES have reported an increased prevalence of peanut allergy among siblings of affected patients. Assuming higher risk, parents may avoid peanut exposure in siblings. This registry study assessed peanut exposure and diagnosis of peanut allergy in siblings of peanut-allergic children.

Using the Canadian Peanut Allergy Registry, the researchers identified 922 siblings of children with peanut allergy, reported by 748 families. Overall, 13.6% of siblings had never been exposed to peanut. Seventy percent of these never-exposed siblings were born ➤➤

after the index patient.

Nearly 9% of siblings were reported as having peanut allergy. However, close to half of these children had never had a reaction to peanut. Five diagnosed siblings-all but 1 diagnosed after the index case--had no confirmatory testing. Siblings born after the index child were more likely to have no history of peanut exposure, and appeared more likely to be diagnosed with peanut allergy with no relevant history or testing.

More than 10% of siblings of children with peanut allergy, especially younger siblings, have never been exposed to peanut. Education and guidelines are needed to recommend against such unnecessary peanut avoidance.

COMMENT: *This study reinforces that we should be counseling the parents of peanut-allergic children not to assume that their other children will also be allergic to peanut. They should also be advised not to delay peanut introduction.*
J.J.O.
Lavine E, Clarke A, Joseph L, et al: Peanut avoidance and peanut allergy diagnosis in siblings of peanut allergic children.
Clin Exp Allergy. 2015;45:349-354. ♦♦

C-Section Linked to 'Moderate' Increase in Asthma Risk

There are conflicting reports as to whether delivery by cesarean section is associated with an increased risk of asthma later in life. A new meta-analysis was performed to clarify the effects of mode of delivery--including elective and emergency cesarean section and different types of vaginal delivery--on asthma risk.

The meta-analysis included 26 studies providing data on the relationship between delivery type and asthma risk. On overall analysis, cesarean section was associated with a moderately increased risk of asthma: summary odds ratio (OR) 1.16, with no significant heterogeneity. Similar risk increases were found for elective and emergency cesarean section: OR 1.21 and 1.25, respectively. There was a small increase in asthma risk for children born by instrumental vaginal delivery--OR 1.07--but with significant heterogeneity.

The findings suggest about a 20% increase in later asthma risk among children born by either elective or emergency cesarean section. Although the mechanism of this association requires further study, rising rates of cesarean section worldwide might have contributed to the increased prevalence of asthma.

COMMENT: *Caesarean section has increased from 5% of deliveries in the 1970s to greater than 50% in 2015. A previous meta-analysis reported that C-section was associated with an increased likelihood of developing childhood or adult asthma, although with significant heterogeneity limiting generalizability. This updated meta-analysis demonstrates that C-section, whether emergency or elective, is related to a 20% increase in the risk of asthma. The relationship is attributed to the impact of delivery method on the infant's gut microbiome. However, further evaluation is needed, given the increasing prevalence of both asthma and C-section in recent decades.*
C.C.R.
Huang L, Chen Q, Zhao Y, et al: Is elective cesarean section associated with a higher risk of asthma? A meta-analysis.
J Asthma. 2015;52:16-25. ♦♦

REVIEWS OF NOTE

COMMENT: *Here's an excellent and comprehensive review that succinctly captures pertinent and up-to-date information about community acquired pneumonia, from causes to outcomes. This well-written manuscript is a handy reference guide to a common and vexing clinical problem.*
C.D.
Musher DM, Thorner AR: Community-acquired pneumonia.
N Engl J Med. 2014;371:1619-1628. ♦♦

COMMENT: *Interlekin-17 has been implicated in asthma pathogenesis, not only for structural alterations in endothelial cells and smooth muscle but also the induction of neutrophilic airway inflammation and steroid sensitivity. This review helps focus our understanding of this very important cytokine.*
B.E.C.
Chesné J, Braza F, Mahay G, et al: IL-17 in severe asthma: where do we stand?
Am J Respir Crit Care Med. 2014:190;1094-1101. ♦♦

COMMENT: This is an excellent review of both the easy- and difficult-to-control factors operative in the early-life origins of chronic respiratory disease.
Carraro S, Scheltema N, Bont L, Baraldi E: Early-life origins of chronic respiratory diseases: understanding and promoting healthy ageing.
B.E.C.
Eur Respir J. 2014;44:1682-1696. ♦♦

COMMENT: *Recent studies have indicated the possibility that acetaminophen use may be a factor in the rise in prevalence in asthma. This is an excellent review on the topic, reinforcing the need for further, well-controlled studies to bring closure to this question.*
J.J.O.
Weatherall M, Ioannides S, Braithwaite I, Beasley R: The association between paracetamol use and asthma: causation or coincidence.
Clin Exp Allergy. 2015;108-113. ♦♦