AllergyWatch®

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

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Can Skin Prick Test Size Predict Systemic Reactions to Subcutaneous Immunotherapy?

SYSTEMIC reactions, sometimes severe, are a potential risk of subcutaneous allergen immunotherapy (SCIT). Although studies have identified risk factors for severe reactions to SCIT, this has not led to any reduction in the overall rate of systemic reactions. The current study sought to determine whether certain "highly allergic" patients--identified on the basis of prominent reactions to skin tests--are a high-risk group for systemic reactions to SCIT.

The researchers analyzed 16,735 SCIT injections administered from 2001 through 2007. A total of 46 systemic reactions occurring in 20 patients were identified: a rate of 0.28% per injection visit. Sixty-three percent of the patients had previous systemic reactions.

Cases with systemic reactions were matched for age, sex, and time of injection to controls without such reactions. A highly allergic pattern of previous skin test responses--specifically, 3+ to 4+ reactions to more than one-third of skin tests--was analyzed as a risk factor for systemic reactions.

All severe reactions occurred within 30 minutes after SCIT injection. Patients with the highly allergic pattern were at sharply increased risk of systemic reactions: odds ratio 5.83. For each additional 4+ skin test, the odds of systemic reaction increased by 17%.

Patients with a higher number of large responses to skin tests are a group at high risk of systemic reactions to SCIT injections. Patients with the "highly allergic" pattern described in this study may benefit from risk reduction measures when receiving SCIT. Most systemic reactions to SCIT occur in a small group of patients--all severe reactions observed in the study occurred within 30 minutes.

COMMENT: *This study looked at the frequency of systemic reactions during immunotherapy. The question of whether patients with larger skin prick reactions were more likely to have systemic reactions was investigated. "Highly allergic" patients were identified as* ➤➤

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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
- 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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having 3+ to 4+ reactions to inhalants on more than one-third of skin tests. The study reassures us that all severe reactions occurred within 30 minutes of the injection. Patients with larger reactions during skin testing had increased risk of systemic reactions during immunotherapy. This provides us with practical information to identify a subgroup of patients who may be more likely to have systemic reactions during treatment with immunotherapy.
V.H.T.
DaVeiga SP, Liu X, Caruso K, et al: Systemic reactions associated with subcutaneous allergen immunotherapy: timing and risk assessment.
Ann Allergy Asthma Immunol. 2011;106:533-537.

♦♦

Drug Provocation Tests--To Test or Not?

DRUG provocation tests (DPTs) are the gold standard for diagnosis of adverse drug reactions. Despite the high number of patients referred for evaluation of drug allergy, few studies have examined the results and safety of DPTs in clinical practice. The researchers analyzed the outcomes, including severe systemic reactions, in a large series of 500 patients undergoing DPT.

The retrospective study included 500 patients referred for evaluation of adverse drug reactions over a 4-year period. A total of 243 DPTs were performed in 198 patients. Local anesthetics were the most common drugs tested, followed by acetaminophen, benzydamine, cylo-oxygenase 2 inhibitors, antibiotics, and other drugs.

The results of DPT were positive in 4.1% of tests and inconclusive in 1.6% of cases. The positive results included 2 of 19 tests using antibiotics. There were two severe reactions: one case of anaphylactic shock in response to cephalexin and one anaphylactic reaction (without shock) to bupivacaine. Two percent of patients reacted to placebo before receiving the study drug.

This large experience documents the safety of DPTs in clinical practice, including a 4% rate of positive results. Drug provocation tests are essential to confirm the presence of drug allergies and to ensure appropriate management. However, they should be done with placebo control and under the supervision of an allergist.

COMMENT: *Patients labeled as "drug allergic" are common. On some days, I wonder which patient really has an allergy to medications. This article shows that most patients with a history of adverse drug reactions will tolerate a DPT--less than 5% of all tests were positive. Placebo reactions were seen in a small number of patients, and the authors recommend performing placebo-controlled DPT. This provides more evidence to the practicing allergist that DPTs are safe and necessary to properly diagnose patients with drug allergy. More important, DPTs remove the "drug allergy" label from patients who would tolerate the suspected drug.*
V.H.T.
Aun MV, Bisaccioni C, Garro LS, et al: Outcomes and safety of drug provocation tests.
Allergy Asthma Proc. 2011; 32:301-306.

♦♦

Asthma Control: More Art than Science

STUDIES suggest that adult asthma patients tend to overestimate their level of disease control. Adolescents may also overestimate asthma control, which may partly account for the high morbidity of asthma in this age group. Perceptions of asthma control were assessed in adolescent patients, including the effect of disease severity.

The study included 201 adolescent asthma patients, aged 12 to 22, receiving primary care at an urban teen clinic. Patients were asked to ➤➤

rate their level of asthma control over the past month. The patient perceptions were compared to impairment-related asthma control, based on self-reported medication use, symptoms, and activity limitations.

Just 8% of the adolescent asthma patients were rated as having good impairment-related asthma control. Asthma was not well-controlled in the remaining patients; this included a 46% rate of very poorly controlled asthma. Just 25% of patients accurately perceived their impairment-related control, while 74% overestimated their level of control. (The remaining 1% underestimated their asthma control.) Patient confidence was independently related to asthma control.

Nearly three-fourths of adolescent asthma patients rate themselves as having good control of their disease. In contrast, only 8% actually have good control of asthma symptoms, activity limitations, etc. The use of detailed, structured questionnaires may help to obtain a more comprehensive picture of asthma control in adolescent patients.

COMMENT: *It would be rather easy to implicate the adolescent population's questionable grasp of reality here. But sadly, these results do not differ much from studies of perceived asthma control in adults. These overconfident overestimators may not realize what is truly possible, with excellent control!*
K.R.M.
Britto MT, Byczowski TL, Hesse EA, et al: Overestimation of impairment-related asthma control by adolescents.
J Pediatr 2011;158:1028-1030. ♦♦

Pediatric Eosinophilic Esophagitis: 15-Year Outcomes

INCREASED recognition and the use of endoscopy have led to a rapid increase in the diagnosis of pediatric eosinophilic esophagitis (EoE). There are very few data on the natural history of this condition, particularly without treatment. Fifteen-year outcomes in a large number of patients with pediatric EoE are reported.

A review of 3,817 pediatric esophageal biopsy specimens from 1982 to 1999 led to retrospective recognition of 198 cases of pediatric EoE, as well as 468 patients with chronic esophagitis (CE). An average of 15 years after endoscopy, a validated set of health-related questionnaires were completed by 42 patients with EoE and 67 with CE, as well as 100 age-matched controls. Quality of life, upper gastrointestinal symptoms, and need for continued treatment were analyzed.

Both the EoE and CE patients had decreased quality of life at long-term follow-up, compared to controls. Dysphagia was reported by 49% of patients with EoE and 37% with CE, compared to 6% of controls. Rates of food impaction were 40%, 14%, and 3%, respectively. Patients with higher eosinophil counts at childhood endoscopy were more likely to have dysphagia at follow-up: odds ratio (OR) 1.6 per every 10 eosinophils/hpf. Other factors associated with dysphagia were food allergy, OR 2.7; allergic rhinitis, OR 3.5; and asthma, OR 2.1. Food allergy was also associated with food impaction at follow-up: OR 3.1.

As they enter adulthood, patients with a retrospective diagnosis of pediatric EoE have reduced quality of life and persistent dysphagia and other symptoms. Higher eosinophil counts at the time of endoscopy--including counts as low as 5 eosinophils/hpf--are associated with an increased risk of dysphagia in adulthood. Many patients diagnosed with GERD-related esophagitis in childhood may still have unrecognized EoE.

COMMENT: *This study looks at the natural history of pediatric EoE at about 15 years after original endoscopy. It is limited by the fact that it was a retrospective questionnaire study. But it concludes that symptoms of EoE often continue for 15 years (73% of patients), that the diagnostic criterion of 15 eosinophils/hpf should be lowered to 5, and that the occurrence of other atopic diseases (eczema, rhinitis, asthma, and food allergy) worsens the rate of long-term adverse outcomes. Notable is the finding that only 27% of the originally endoscoped group with eosinophilia were diagnosed with EoE; most cases were called GERD.*
R.J.M.
DeBrosse CW, Franciosi JP, King EC, et al: Long-term outcomes in pediatric-onset esophageal eosinophilia.
J Allergy Clin Immunol. 2011;128:132-138. ♦♦

Muffins--A New Treatment for Milk Allergy?

A RECENT study found that three-fourths of children with milk allergy can tolerate baked milk products--eg, muffins or waffles. This study evaluated the effects of incorporating baked milk products into the regular diet of children with cow's milk allergy (CMA).

In the study, 88 children with CMA underwent food challenge with a muffin to evaluate their ability to tolerate baked milk products. Of these, 65 were initially tolerant of baked milk. These patients were instructed to incorporate baked milk products into their daily diet. Children who reacted to baked milk were instructed to avoid all milk products.

After 6 months or longer, both groups underwent sequential food challenges, starting with a muffin, followed by baked cheese (pizza), and then unheated milk. Outcomes were compared with those of matched CMA children who did not undergo the initial muffin challenge.

Of the CMA-allergic children who initially tolerated baked milk, 60% were able to tolerate unheated milk at follow-up. Another 28% tolerated baked milk and baked cheese; the remaining 12% opted for strict milk avoidance. Among children who reacted to baked milk challenge, 9% tolerated unheated milk, 13% tolerated baked milk/baked cheese, and 78% practiced strict avoidance.

Children who initially tolerated baked milk were 28 times more likely to be able to tolerate unheated milk that those who initially reacted to baked milk. The ➤➤

baked milk-tolerant group were also 16 times more likely to tolerate unheated milk than children receiving standard care. Children who tolerated baked milk had a significant increase in casein IgG_4 level, but not in milk IgE level.

Cow's milk allergy is more likely to be a transient problem in children who can tolerate baked milk products. In this group, adding baked milk to the diet seems to hasten the ability to tolerate unheated milk. In contrast, children who can't tolerate baked milk are more likely to have persistent CMA.

COMMENT: *There seems to be a paradigm shift in the management of children with food allergies. In the 74% of children with CMA who initially tolerated a baked milk challenge with a muffin, 60% were able to have unheated milk challenge after frequent baked-milk ingestion over approximately a 3-year period. Interestingly, only 9% of children who didn't initially tolerate the muffin were able to tolerate the milk challenge at the end of the study. So it seems that most children with CMA will benefit from frequent baked milk ingestion. Unfortunately, the study doesn't suggest how to predict which children are more likely to tolerate the muffin challenge. However, the researchers do recommend considering a muffin challenge for all children with milk allergy.*
S.M.F.

Kim JS, Nowak-Węgrzym A, Sicherer SH, et al: Dietary baked milk accelerates the resolution of cow's milk allergy (CMA) in children.
J Allergy Clin Immunol. 2011;128:125-131. ♦♦

Breathmobile Improves Asthma Control in Inner-City Kids

POOR asthma control is a particular problem for children of low socioeconomic status in inner-city neighborhoods. The Breathmobile is a school-based asthma management program using specialist-staffed mobile clinics. A 10-year experience was analyzed to evaluate the effects of mobile asthma clinics on asthma control in inner-city children.

The researchers analyzed data on 7,822 pediatric asthma patients making a total of 34,339 visits to U.S. mobile asthma programs from 1998 to 2008. Baseline and follow-up data were analyzed to assess measures of disease control. All patients were enrolled in the program for at least 1 year.

Mobile asthma clinic care was associated with a mean 66% reduction in emergency department (ED) visits and an 84% reduction in hospitalizations. The percentage of children with 5 or more missed school days per year decreased by 78%. By the third visit, 80% of patients were considered to have well-controlled asthma. Good disease control was more likely to be achieved by non-African American children, those with less than 90 days between visits, and those who followed prescribed treatments.

The Breathmobile and similar mobile asthma care programs can achieve and maintain good asthma control in inner-city children. The experience underscores the importance of regularly scheduled, specialty-based preventive care for this group of high-risk pediatric asthma patients.

COMMENT: *Unfortunately, African American and Hispanic children with asthma living in inner-cities have had the highest asthma-related morbidity and mortality. These children present with particular challenges both in terms of access to and availability of appropriate care. This study reports the impressive results of the Breathmobile intervention program in 4 major cities over a five year period. Not only did the percentage of hospitalizations drop 84%, but ED visits fell by 66% and missed school days fell by 78%. This confirms that regularly scheduled specialty-based care for these difficult-to-treat patients can be helpful, particularly using community outreach interventions.*
S.M.F.

Scott L, Morphew T, Bollinger ME, et al: Achieving and maintaining asthma control in inner-city children.
J Allergy Clin Immunol. 2011;128:56-63. ♦♦

Daily Air Pollutant Levels Affect Exhaled NO in Children

EXPOSURE to ambient air pollution--even at levels below current regulatory standards--has documented adverse effects on respiratory health in children. The pathophysiology of these harmful effects may involve airway inflammation. The relationship between daily ambient air pollution levels and exhaled nitric oxide (eNO) were evaluated in a large sample of children.

The analysis included data on 2,240 Southern California children enrolled in the Children's Health Study. Associations between daily air pollutant levels and eNO were analyzed, with lag times up to 30 days.

Significant associations were noted for daily 24-hour cumulative lagged averages of particles with a 50% cutoff aerodynamic diameter of 2.5 µm ($PM_{2.5}$ over 1 to 8 days); particles with a 50% cutoff diameter of 10 µm (PM_{10} over 1 to 7 days); and 10:00- to 18:00-hour cumulative lagged average of O_3 over 1 to 23 days. These pollutant levels were associated with eNO increases of 17.42%, 9.25%, and 14.25%, respectively. All three factors showed a greater effect on eNO during warm temperatures. The adverse effects of airborne particles were unchanged by adjustment for O_3 and temperature and were unaffected by the presence of asthma or allergy.

Daily variations in particulate air pollutants and ozone are associated with airway inflammation in children. The associations are significant for children with or without allergy or asthma.

COMMENT: *This paper presents significant observation from a cohort of children that has added greatly to our knowledge of the association of airway inflammation with exposure to air pollution. The results extend our observations, allowing greater insight into the mechanism of airway injury and providing guidance for clinical trial design.* ➤➤

B.E.C.
Berhane K, Zhang Y, Linn WS, et al: The effect of ambient air pollution on exhaled nitric oxide in the Children's Health Study.
Eur Respir J. 2011;37:1029-1036. ♦♦

Omalizumab for Chronic Urticaria with IgE-anti-TPO

SOME patients with chronic urticaria have IgE autoantibodies against thyroperoxidase (TPO). Previous studies have suggested that this group of patients might benefit from anti-IgE therapy with omalizumab.

This issue was addressed in a multicenter, randomized trial. The study included 49 patients with CU and IgE-anti-TPO antibodies: 38 women and 11 men, mean age 39 to 42 years. All patients had persistent wheals, pruritus, and other symptoms while receiving standard antihistamine therapy.

One group received subcutaneous omalizumab, 75 to 375 mg every 2 or 4 weeks, based on approved asthma dosing tables. Controls received placebo; both treatments continued for 24 weeks. Patient diaries were used to assess the change from baseline in mean weekly urticaria activity score.

Forty-two patients completed the study. Mean reduction in weekly urticaria activity score was 17.8 with omalizumab versus 7.9 with placebo. Wheals were completely eliminated in 70% of patients receiving omalizumab, compared to 4.5% of the placebo group. Symptom-free rates at the end of treatment were 59% and 14%, respectively. Omalizumab was also associated with a substantial reduction in the need for other medications. Suspected drug-related adverse events were similar between groups.

Omalizumab is an effective treatment for patients with treatment-refractory chronic urticaria associated with IgE autoantibodies against TPO. Compared to placebo, 24 weeks of omalizumab leads to a significant reduction in disease activity, with complete symptom resolution in many patients. Treatment is safe and well-tolerated.

COMMENT: *This German study adds to a growing body of evidence that omalizumab can be used to treat chronic urticaria. Most of the previous studies haven't been randomized and controlled. This study specifically included 49 patients with elevated levels of IgE anti-TPO antibodies--the significance of that is unclear. The patients were refractory to conventional antihistamine doses. The improvements in symptom scores and quality-of-life measures with omalizumab were highly significant.*
R.J.M.
Maurer M, Altricher S, Bieber T, et al: Efficacy and safety of omalizumab in patients with urticaria who exhibit IgE against thyroperoxidase.
J Allergy Clin Immunol. 2011;128:202-209. ♦♦

Albuterol vs Placebo vs No Treatment for Asthma

PREVIOUS studies of asthma treatments have reported significant placebo effects, including measurable increases in expiratory airflow. However, it is difficult to separate these placebo responses from the natural physiologic changes occurring with no treatment. This randomized, crossover trial compared responses to active albuterol versus placebo, sham acupuncture, and no treatment in patients with asthma.

Forty-six patients with mild to moderate asthma received the four treatments in sequential visits made at 3- to 7-day intervals. Of these, 39 patients completed three blocks of visits, for a total of twelve visits. The FEV_1 response to each treatment was measured by spirometry; these objective measurements were compared with subjective ratings of symptom improvement.

Active albuterol was associated with a 20% increase in FEV_1. For the other three treatments--including the inactive interventions and no treatment--the change in FEV_1 was approximately 7%. In contrast, all three inactive treatments were associated with greater subjective improvement, compared to no treatment. Patient-reported improvement was 50% with albuterol, 45% with placebo inhaler, and 46% with sham acupuncture, compared to 21% with no treatment.

Albuterol and placebo or sham interventions produce similar subjective improvements in patients with asthma, compared to no treatment. In contrast, only albuterol leads to a significant reduction in objective FEV_1. The authors suggest that studies evaluating patient-reported outcomes should include assessment of untreated responses.

COMMENT: *It isn't news that placebos have a very positive effect on patient reports of treatment outcomes. But this study of asthmatics goes further, showing that the subjective reports of improvement on placebos (two different kinds were used) did not mirror the objective measure (FEV_1 response). The distinctive feature of this study is that the placebo "treatments" themselves were compared to a control group with no intervention. These findings have an important implication for clinical and research evaluations of asthma treatments: objective measurements must be made.*
R.J.M.
Wechsler ME, Kelley JM, Boyd IOE, et al: Active albuterol or placebo, sham acupuncture or no intervention in asthma.
N Engl J Med. 2011;365:119-126. ♦♦

FOCUS ON BIOMARKERS

Can Obesity Biomarkers Affect Inflammation in Asthma?

EXERCISE-induced bronchoconstriction (EIB) is common among children who are obese as well as those who have asthma. While childhood obesity and asthma are both increasing, associations between ➤➤

obesity and adipokine on asthmatic airway inflammation remain unclear.

The researchers measured the adipocyte-derived hormones leptin and adiponectin and assessed EIB in a group of 85 prepubertal children. The study included two groups of asthmatic children, 19 obese and 23 normal weight; and two groups of nonasthmatic children, 23 obese and 20 normal weight.

Levels of both leptin and adiponectin were significantly increased in obese children. In the asthmatic children, the peak decrease in FEV_1 and the severity of EIB over a 20-minute period after exercise were positively associated with leptin levels and negatively associated with adiponectin levels. As serum leptin levels increased, so did the odds of having EIB.

The adipokines leptin and adiponectin are significantly associated with EIB among children with asthma. More research will be needed to determine whether obesity-related increases in leptin and adiponectin show any causal association with EIB in children.

COMMENT: *This study looked at levels of serum leptin and adiponectin in children with a history of asthma. Obese children had elevated leptin and decreased adiponectin. These levels correlated with postexercise challenge decreases in lung function. The study provides insight into the possibility of using hormone levels to predict bronchial hyperresponsiveness in obese patients with asthma. This may provide yet another opportunity to encourage weight loss in our obese patients with asthma.*
V.H.T.
Baek, HS, Kim, YD, Shin JH, et al: Serum leptin and adiponectin levels correlate with exercise-induced bronchoconstriction in children with asthma.
Ann Allergy Asthma Immunol. 201;107:14-21. ♦♦

A New Biomarker for Asthma Severity and Persistence in Children?

IN animal models, the costimulatory molecule OX40 and its ligand, OX40L, appear to mediate eosinophilia and other important aspects of allergic airway inflammation. It remains unclear whether OX40 and OX40L play any important role in Th2-dominated childhood allergic asthma. Expression of OX40L was measured in childhood asthma across a wide range of disease activity and attack severity.

An enzyme-linked immunosorbent assay was used to measure serum OX40L in 50 children with atopic asthma and 40 healthy controls. In the asthma group, OX40L was measured between and during attacks. Median OX40L levels in asthmatic children were 731 pg/mL between attacks and 1,487 pg/mL during attacks, compared to 193 pg/mL in controls.

Asthmatic children with acute severe exacerbations had higher OX40L levels than those with mild or moderate exacerbations. The children with acute severe exacerbations also had higher OX40L levels between attacks. OX40L levels during exacerbations were positively correlated with levels during remission. Higher OX40L levels were associated with lower peak expiratory flow rates and higher absolute eosinophil counts.

The study provides evidence that OX40L is upregulated in children with atopic asthma, increasing with asthma severity. The results suggest that OX40L may be a useful biomarker for allergic inflammation, as well as a possible target for immune intervention.

COMMENT: *Parents often ask the allergist whether their children will outgrow their asthma. This study found that patients with acute severe exacerbations of asthma were more likely to have markedly elevated OX40L levels, as compared to patients with mild or moderate asthma, as well as healthy controls. The patients with severe exacerbations also had higher levels when the exacerbations resolved. This biomarker may be able to guide our treatment of children with asthma, and truly allow us to predict which cases are most severe.*
V.H.T.
Ezzat MHM, Imam SS, Shaheen KYA, Elbrhami EM: Serum OX40 ligand levels in asthmatic children: a potential biomarker of severity and persistence.
Allergy Asthma Proc. 2011;32:313-318. ♦♦

Can IL-10 Polymorphisms Predict Susceptibility to Asthma?

MANY cytokines affecting inflammatory processes have been shown to be associated with asthma, including pleiotropic effects of interleukin-10 (IL-10). Polymorphisms of the IL-10/IL-10R pathway affecting asthma susceptibility were sought in Egyptian children with and without asthma.

Genotyping of the IL-10 (-1082G/A), IL-10R1 (G330R), and signal transducer and activator of transcription 3 (STAT3) rs2293452 polymorphisms was performed in 110 children with atopic asthma, 110 nonatopic children with asthma, and 110 healthy children. The IL-10 polymorphism was significantly associated with asthma in both the atopic and nonatopic groups. Atopic asthma was also significantly associated with the STAT3 polymorphism. There was no evidence of interactions between genes.

Single-nucleotide polymorphisms of the IL-10/IL-10R pathway may be associated with childhood asthma. The IL-10 and STAT3 polymorphisms may be useful in DNA-based biomarker tests to identify high-risk children susceptible to asthma.

COMMENT: *This study looked at polymorphisms in genes of children with asthma. Patients with atopic and nonatopic forms of asthma had polymorphisms of IL-10. In patients with atopic asthma, the presence of STAT3 polymorphism and asthma susceptibility was seen. This reminds us of the importance biomarkers will play in the future for identifying patients at risk of developing asthma.*
V.H.T.
Hussein YM, Shalaby SM, Mohamed RH, Hassan TH: Association between genes encoding components of the IL-10/IL-10 receptor pathway and asthma in children.
Ann Allergy Asthma Immunol. 2011;106:474-480. ♦♦

CLINICAL TIDBITS

Should Epinephrine Be Prescribed for Patients with Angioedema in the ED?

MANY patients with angioedema receive treatment in the emergency department (ED). Although previous studies have looked at the use of self-injectable epinephrine in anaphylaxis, little is known about prescribing for patients with angioedema.

The investigators reviewed 63 patients with angioedema seen in their ED over a 2-year period. Patient presentation and management were analyzed. The analysis sought to identify factors associated with epinephrine administration, hospitalization, and prescription of self-injectable epinephrine.

Sixty-two percent of the patients were female; the median age was 49 years. Most patients had a known precipitating factor and a history of other allergic conditions. Treatment included antihistamines in 87% of patients, steroids in 81%, and epinephrine in 27%. Factors associated with epinephrine use included edema of the tongue, risk ratio (RR) 5.28; tightness or fullness of the throat, RR 3.31; and dyspnea or wheezing, RR 3.04. Dyspnea/wheezing was also associated with an increased risk of hospitalization, as was history of allergy.

Self-injectable epinephrine was prescribed to 22% of patients. Associated factors were younger age, median 26 vs 57.5 years; and throat tightness/fullness, RR 4.2.

The study lends insights into the ED management of patients with angioedema. More research is needed to identify patients most likely to benefit from treatment with epinephrine and prescription of self-injectable epinephrine.

COMMENT: *This study looked at the treatment of angioedema in the ED setting. Prescriptions for epinephrine were given more commonly in the presence of symptoms affecting the throat. In the presence of wheeze or tongue edema, epinephrine was administered in the emergency department. This study reminds us that only a minority of patients are discharged with self-injectable epinephrine or referred to an allergist. This remains an opportunity to collaborate with our emergency medicine colleagues to investigate the patients who would benefit from the use of epinephrine in the treatment of acute angioedema.*
V.H.T.

Manivannan V, Decker WW, Bellolio MF, et al: Prescriptions for self-injectable epinephrine in emergency department angioedema management.
Ann Allergy Asthma Immunol. 2011;106:489-493. ♦♦

Folic Acid Use in Pregnancy and Childhood Atopy

TAKING folic acid supplements during pregnancy reduces the risk of neural tube defects. Two recent studies suggested possible increases in childhood airway disease associated with folic acid supplementation. Data from a large birth cohort study were used to examine the association between folic acid use in pregnancy and the risk of childhood atopic diseases.

The analysis included data on eczema and wheezing from infancy to age 7 in 2,384 children from a Dutch birth cohort. In addition to reported use of folic acid and/or multivitamin supplements, the study included measurement of intracellular folic acid (ICF) levels obtained late in pregnancy.

Multivariate models showed no association between maternal use of folic acid and the risk of wheezing, reduced lung function, asthma, or other atopic outcomes in children. Higher maternal ICF levels in late pregnancy were related to reduced asthma risk at age 6 or 7 years.

The study does not support the suggested link between maternal folic acid use and asthma or other atopic outcomes in offspring. Higher maternal ICF levels in the third trimester may have a small protective effect against childhood asthma.

COMMENT: *Is folic acid supplementation--which is necessary for prevention of neural tube defects--a risk or benefit for the potential development of childhood atopy? Answers prior to this study were inconclusive. The current research adds prospective data, including late pregnancy intracellular folic acid levels. We can now reassure expectant mothers that folic acid supplementation does* not *seem to increase the risk of atopy.*
K.R.M.

Magdelijns FJH, Mommers M, Penders J: Folic acid use in pregnancy and the development of atopy, asthma, and lung function in childhood.
Pediatrics. 2011;128:e135. ♦♦

High Burden of Influenza Hospitalizations in Pediatric Asthma

ASTHMA is a known risk factor for influenza complications. Surveillance data were analyzed to assess the characteristics and course of asthmatic children hospitalized for influenza in recent years.

The study included data for the 2003 to 2009 influenza seasons, including the 2009 H1N1 influenza pandemic. Overall, 32% of children hospitalized for influenza (701 of 2,165) had asthma. This included 44% of children (733 of 1,660) hospitalized for 2009 pandemic H1N1 influenza. The median age was 7 years; in nearly three-fourths of cases, asthma was the only predisposing medical condition.

Compared to those hospitalized for seasonal influenza, children with 2009 pandemic influenza were more likely to need intensive care (16% vs 22%) and more likely to be diagnosed with pneumonia (40% vs 46%). There was no difference in the rates of respiratory failure and death: 5% vs 1%, respectively. Among asthmatic children, an asthma exacerbation was diagnosed in 51% of those with influenza A (seasonal or pandemic) vs 29% of those with influenza B.

About one-third of children hospitalized for influenza have asthma, usually with no other medical conditions. ➤➤

Many serious complications are more common in asthmatic children. The findings underscore the importance of influenza vaccination for children with asthma.

COMMENT: *A disproportionate number of influenza admissions over the past years--including admissions from the 2009 H1N1 pandemic--involved children with asthma and no other comorbidities. Consistently, less than 50% of these children have received an influenza vaccine in any of the study years. While not perfectly protective, immunization remains our best preventive option.*
K.R.M.
Dawood FS, Kamimoto L, D'Mello TA, et al: Children with asthma hospitalized with seasonal or pandemic influenza, 2003-2009.
Pediatrics. 2011;128:e27-e32. ♦♦

Obesity and Asthma Associated at Age 3!

LOW-income children are at increased risk of both obesity and asthma. Studies of early-life risk factors and potential sex differences may help to clarify the mechanisms of the relationship between these two conditions.

The association between asthma and obesity was examined in 1,815 children enrolled in a prospective birth cohort study of children in 20 large U.S. cities. Fifty-five percent of the children were African American. At age 36 months, a physician diagnosis of active asthma (within the past 12 months) was reported for 10% of children. At the same time, 19% of the children were overweight and 17% were obese.

In stratified analyses, the risk of asthma was significantly increased for obese girls, odds ratio (OR) 1.97; and obese boys, OR 2.55. The association was also significant for overweight boys, OR 1.69, but not overweight girls. The links between body weight and asthma were not explained by the social and physical environment of the children's homes.

In this sample of urban children, a significant association between obesity and asthma is already present at age 36 months. Although further study is needed, the association does not appear to be related to factors in the home environment.

COMMENT: *How early are the effects of obesity associated with increased asthma risk? Obese preschoolers can now be convincingly placed in a higher risk category for asthma, with overweight boys running a close second. It is not possible to assess causality from these associations--ie, whether obesity at age 3 increases asthma risk or asthma increases risk of obesity. Current evidence favors the former hypothesis.*
K.R.M.
Suglia SF, Chambers EC, Rosario A, Duarte CS: Asthma and obesity in three-year-old urban children: role of sex and home environment.
J Pediatr. 2011;159:14-20. ♦♦

Early Change in IgE Predicts Long-Term Response to Omalizumab

ANTI-IgE therapy with omalizumab is clinically effective in patients with severe, difficult-to-treat atopic asthma. Currently, there is no predictor of which patients will have a good response to long-term omalizumab therapy. Early changes in IgE levels were evaluated as a predictor of long-term responsiveness to omalizumab.

The study included 23 nonsmoking patients with severe asthma. All were sensitized to perennial allergens and had an inadequate response to high doses of conventional respiratory drugs. Plasma IgE response to omalizumab at 3 months was evaluated as a predictor of FEV_1, asthma symptoms, and other clinical outcomes at the end of 12 months of treatment.

Over 12 months, omalizumab treatment was associated with significant reductions in emergency visits, hospitalizations, and asthma exacerbations. There were also improvements in FEV_1 and asthma symptoms; the change in Asthma Control Test score did not peak until 3 months. On statistical modeling, an increase in IgE of 250 IU/mL or greater at 3 months was associated with a reduction in exacerbation rate at 1 year. Improvement in FEV_1 was independent of the early IgE response.

At a threshold value of 250 IU/mL, an early increase in plasma IgE in response to omalizumab predicts later clinical improvement in patients with severe atopic asthma. The ability to predict which patients will respond to anti-IgE therapy will help to target those likely to benefit from long-term treatment with omalizumab.

COMMENT: *Currently there is no reliable indicator for assessment of clinical response to anti-IgE therapy in terms of pulmonary function and clinical outcomes. In this exciting study, the authors demonstrate that an absolute increase in total IgE of at least 250 IU/mL from baseline by end of 3 months of anti-IgE therapy is predictive of future exacerbations in difficult-to-treat atopic asthmatics. The results are synchronous with improvement in asthma control but not in FEV_1, which is independent. These results, if confirmed in larger prospective studies, would be momentous. Using a measurable increase in total IgE by 3 months of anti-IgE therapy to predict future clinical responsiveness would allow us to minimize the economic burden of anti-IgE therapy in clinical practice.*
C.C.R.
Dalnegro R, Guerriero M, Micheletto C, et al: Changes in total IgE plasma concentration measured in the third month during anti-IgE treatment predict future exacerbation rates in difficult-to-treat atopic asthma: a pilot study.
J Asthma. 2011;48:437-441. ♦♦

School-Based Program Helps Urban Teens Self-Manage Asthma

Low-income minority youth are at increased risk of asthma complications, related to low adherence to preventive medications. A school-based intervention was developed to enhance delivery of preventive treatments for urban adolescents with persistent asthma.

The pilot study included 28 patients, aged 12 to 15 years, with persistent asthma. For 6 to 8 weeks, at the beginning of the school year, the teens visited the school nurse every day for directly observed therapy with asthma preventive medications. The intervention also included three counseling sessions, with motivational interviewing techniques to support transition to independent use of preventive medications.

Follow-up visits were completed by 89% of enrolled teens. The intervention was associated with fewer days with asthma symptoms, less activity limitation, less rescue medication use, and lower exhaled nitric oxide levels. The teens reported being more motivated to take their daily medications and better able to manage asthma on their own.

This school-based intervention shows promise in enhancing self-management by urban adolescents with persistent asthma. Initial data suggest improved adherence and confidence in asthma self-management, leading to meaningful clinical improvements.

COMMENT: *In an exciting pilot study, the authors demonstrate that low-income minority teens can be motivated in a school-based counseling program to be adherent with asthma therapy plans. The program--which included phone and in-home counseling, with direct observation of medication taking by the school nurse--led to improved asthma outcomes. There was a cumulative increase in symptom-free days with a decline in symptoms, less rescue medication and activity limitation, and improvement in exhaled nitric oxide. Ninety-three percent of teens said they would participate in the program again, and were motivated to take their medications. This significant study demonstrates that school-based asthma interventions can incentivize more autonomous asthma management and improve asthma outcomes in high-risk urban adolescents with asthma.*

C.C.R.

Halterman JS, Riekert K, Bayer A, et al: A pilot study to enhance preventive asthma care among urban adolescents with asthma.

J Asthma. 2011;48:523-530. ♦♦

Inhaled Montelukast Plus Mometasone for Chronic Asthma

STUDIES have shown that oral montelukast is an effective adjunct for patients whose asthma symptoms are not adequately controlled by inhaled corticosteroids alone. A recent phase I study showed significant bronchodilation in chronic asthma in response to a single dose of inhaled montelukast.

In this trial, 134 patients with chronic asthma received crossover treatment with inhaled montelukast 1 mg plus inhaled mometasone 220 µg; and inhaled placebo plus mometasone. Patients received each treatment for 2 weeks, with a 1-week washout period in between.

Change from baseline in FEV_1, the main outcome of interest, was significantly greater with inhaled montelukast plus inhaled mometasone: least squares mean 0.22, compared to 0.17 L with inhaled placebo plus mometasone. Secondary outcomes also favored inhaled montelukast plus mometasone, including daytime and nighttime symptom scores, percentage of days with asthma control, and blood eosinophil count. There was no significant difference in morning or evening peak expiratory flow or use of short-acting beta-agonists.

Adding inhaled montelukast to inhaled mometasone improves lung function and disease control in patients with chronic asthma. The combination of inhaled montelukast and mometasone is well tolerated.

COMMENT: *Oral montelukast is known to be effective when added to inhaled steroid in asthma uncontrolled with inhaled steroid alone, while inhaled montelukast has been demonstrated to produce significant bronchodilation compared to placebo. In this striking multicenter randomized, placebo-controlled crossover study, inhaled montelukast added to inhaled mometasone was significantly more effective than placebo plus mometasone. The combination of inhaled mometasone with inhaled montelukast improved FEV_1, symptoms, asthma control, and blood eosinophil count to a greater extent than mometasone with placebo. These provocative results suggest that a future combination mometasone/montelukast inhaled product may provide more effective asthma therapy in asthma uncontrolled with inhaled steroids alone.*

C.C.R.

Philip G, Villarán C. Shah SR, et al: The efficacy and tolerability of inhaled montelukast plus inhaled mometasone compared with mometasone alone in patients with chronic asthma.

J Asthma. 2011;48:495-502. ♦♦

'Atopic March' Continues into Adulthood

THE "atopic march" describes the progression from childhood eczema, to allergic rhinitis, to asthma. However, it remains unclear whether this progression continues into adulthood, and if it is associated with any specific asthma phenotype.

These questions were addressed using very long-term follow-up data on Tasmanian birth cohort. Children were recruited in 1968 at age 6 to 7, then followed up at age 44. Childhood eczema and rhinitis were analyzed as risk factors for new-onset or persistent asthma in middle age.

Childhood eczema or rhinitis was unrelated to nontoxic asthma in adulthood. However, the combination of childhood eczema and rhinitis predicted new-onset asthma in middle age; adjusted multinomial odds ratio ➤➤

(aMOR) 6.3; as well as atopic asthma persisting from childhood to adulthood, aMOR 11.7. Childhood eczema alone increased the risk of new-onset atopic asthma, aMOR 4.1; while rhinitis alone increased the risk of persistent atopic asthma, aMOR 2.7. Childhood eczema and rhinitis appeared to account for 29.7% of cases of persistent atopic asthma and 18.1% of new-onset adult atopic asthma.

Eczema and rhinitis in childhood are strong risk factors for atopic asthma in adulthood. The findings may have important implications for public health programs to prevent the progression of allergic diseases.

COMMENT: *When a report uses data from a prospective cohort of almost all 8,500 children born in Tasmania in 1961 and reports findings 44 years later, we should take notice. Using a clinical subset of patients with known allergic sensitization status, these authors show that although there was an increased risk of adult atopic asthma in children with eczema, this risk significantly increased when the children had both rhinitis and eczema. The study provides further proof that the "atopic march," beginning in childhood, continues for at least 40 years.*
S.M.F.

Martin PE, Matheson MC, Gurrin L, et al: Childhood eczema and rhinitis predict atopic but not nonatopic adult asthma: a prospective cohort study over 4 decades.
J Allergy Clin Immunol. 2011;127:1473-1479. ♦♦

In Different Types of Skin Cells, Vitamin D3 Induces Different Types of Tregs

VITAMIN D and its metabolites have potent immunosuppressive effects. The mechanisms of these effects are unclear, although regulatory T cells (Tregs) may play a role. There are questions about the phenotype of these vitamin D-derived Tregs, as well as the dendritic cell-derived molecules leading to their induction.

In an experimental study, dermal Langerhans cells (LCs) and dermal dendritic cells (DDCs) were primed with vitamin D and cultured with allogeneic native T cells. After priming with vitamin D, both subtypes of skin dendritic cells induced T cells with regulatory activities.

However, they generated two different types of Tregs. The LCs developed into classical inducible Tregs, which were $CD25^{hi}CD127^{lo}$ forkhead box protein 3(Foxp3)-positive cells. In contrast, the DDCs led to the developing of Foxp3-negative T_R1 cells that expressed interleukin-10 (IL-10). Whereas DDC-derived IL-10 played an important role in induction of the IL-10-positive T_R1 cells, the development of Foxp3-positive Treg cells depended on LC-derived TGF-β.

When primed with vitamin D3, skin LC and DDC subsets develop into two distinct types of Treg cells. The findings lend new insights into the varied properties of vitamin D3, and may lead to new approaches to specific immunotherapy and other treatments for immune diseases.

COMMENT: *Vitamin D3 has anti-inflammatory and immunosuppressive properties that may be due, at least in part, to its effect on Treg cells. These researchers used well-designed in vitro models to demonstrate that vitamin D3 targets both epidermal LCs and DDCs, but in two distinct mechanisms. Vitamin D-treated LCs generated functional FOXP3+ Treg cells via TGF-β, which may help maintain skin homeostasis; whereas DDCs treated with vitamin D generated IL-10-positive FOXP3-Tr_R1 cells, which can help reduce excessive immune responses. Therefore vitamin D3 is able to induce subset-specific induction of a variety of functional Treg cells, which may help explain its diverse immunosuppressive effects.*
S.M.F.

van der Aar, Sibiryak DS, Bakdash G, et al: Vitamin D3 targets epidermal and dermal dendritic cells for induction of distinct regulatory T cells.
J Allergy Clin Immunol. 2011;127:1532-1540. ♦♦

Most Children with Acute Asthma Have HRV Group C

HUMAN rhinovirus (HRV) infection is an important cause of asthma exacerbations in children. Recent studies have described a distinct, potentially more pathogenic group of HRV strains: group C (HRVC). This study used advanced techniques to assess the prevalence of HRVC among children with acute asthma.

The study included 128 children with acute asthma seen in an Australian emergency department. Nasal secretion specimens were tested using direct fluorescent antibody testing with virus-specific monoclonal sera. The presence of HRVC and its association with asthma severity were assessed.

Eighty-five percent of the children had moderate to severe asthma, and 99% were hospitalized. The overall rate of HRV detection was 87.5%. Of the 14.8% of children with other respiratory viruses, 14.8% also had HRV. Tests showed HRVC in 59.4% of all children with acute asthma. Asthma severity scores were higher in the children with HRVC than in those with other strains or no HRV. Of 19 children with a non-HRV virus, 13 also had HRV. Seven of these had HRVC.

In this emergency department sample, most children with acute asthma have HRVC. The presence of HRVC is associated with more severe asthma attacks than other HRV groups. Further study of pathogenicity and host susceptibility to various HRV strains is needed.

COMMENT: *This study expands our knowledge regarding the role of HRVC in acute asthma. The association with asthma severity is a new finding that will add to our understanding and affect the conduct of future studies.*
B.E.C.

Bizzintino J, Lee W-M, Laing IA: Association between human rhinovirus C and severity of acute asthma in children.
Eur Respir J. 2011;37:1037-1042. ♦♦

Trauma and PTSD Linked to Airflow Limitation

PREVIOUS reports have linked traumatic experiences and post-traumatic stress disorder (PTSD) to pulmonary diseases, including asthma. These studies have had several important limitations, however. The association between trauma and PTSD and objective measures of lung function was assessed in a general population study.

The study included a population sample of 1,772 adults. Based on a PTSD interview, participants were classified as having no history of traumatic exposure, trauma but not PTSD, or trauma with PTSD. A medical history was obtained and spirometry performed in each subject.

Twenty-eight participants were classified as having PTSD. In adjusted analyses, subjects with PTSD were at higher risk of asthma: odds ratios for most asthma symptoms ranged from 3.2 to 3.8. The PTSD group also had lower pulmonary function measures: mean ratio of FEV_1 to forced vital capacity (FVC) was 83.2%, compared to 84.4% in the group with trauma but no PTSD and 85.4% in the group with no trauma. History of trauma was associated with both FEV_1 and FEV_1/FVC. The presence of PTSD was also independently associated with an increased risk of airflow limitation: odds ratio 4.2 to 7.8.

The study is the first to link history of trauma and PTSD to objectively measured airflow limitation. This association could be mediated by inflammatory processes. From a clinical standpoint, the possibility of obstructive pulmonary diseases should be considered in patients with a history of traumatic exposure.

COMMENT: *This is the first study to link PTSD and traumatic events to objective measurements of airflow limitation. The data help us refine our understanding of the factors that add to the burden of asthma.*
B.E.C.

Sptizer C, Koch B, Grabe HJ, et al: Association of airflow limitation with trauma exposure and post-traumatic stress disorder.
Eur Respir J. 2011;37:1068-1075. ♦♦

Dynamic CT Shows VCD in Difficult-to-Treat Asthma

MANY reports have discussed vocal cord dysfunction (VCD) masquerading as difficult-to-treat asthma. However, the potential etiologic role of VCD has received little attention. An advanced computed tomography (CT) technique was used to evaluate laryngeal behavior in asthma patients.

Dynamic 320-slice CT was performed to quantify vocal cord movement in a group of healthy volunteers. The findings were used to develop and validate an algorithm for defining normal function. That technique was then used to assess vocal cord function in a group of 46 patients with difficult-to-treat asthma.

The results showed abnormal vocal cord movement with excessive narrowing in 50% of patients with difficult-to-treat asthma. Nineteen percent of patients had severe vocal cord dysfunction, with abnormal motion through more than half of inspiration or expiration time. The abnormal dynamic CT findings included laryngeal dysfunction in addition to vocal cord dysfunction.

Dynamic 320-slice CT noninvasively detects abnormal vocal cord movement and narrowing in many patients with difficult-to-treat asthma. This technique may prove useful in detecting coexisting upper airway dysfunction in asthma patients, with important implications for disease control and treatment.

COMMENT: *There is an expanding body of evidence regarding the effect of abnormal laryngeal movement on respiratory symptoms. This technique is not widely available, but may be a less arduous approach to confirming the clinical impression. The extremely high number of asymptomatic patients with VCD is surprising. See the accompanying editorial by Ayres and Mansur (Am J Respir Crit Care Med. 2011;184:2-3) for enhanced understanding.*
B.E.C.

Low K, Lau KK, Holmes P, et al: Abnormal vocal cord function in difficult-to-treat asthma.
Am J Respir Crit Care Med. 2011;184:50-56. ♦♦

Epinephrine plus Dexamethasone Improve Outcomes in Children with Bronchiolitis

THE treatment approach to children with bronchiolitis varies considerably. One report has suggested possible interactive effects of steroids and bronchodilators. A meta-analysis was performed to evaluate these two treatments--alone and in combination--for acute management of bronchiolitis.

Randomized controlled trials of any bronchodilator or steroid, alone or combined, for an initial diagnosis of bronchiolitis with wheezing in children younger than 2 years were identified in a systematic review of the literature. Data on 4,897 children from 48 trials were pooled for meta-analysis. The main outcomes of interest were hospitalization rate for children initially seen as outpatients and hospital length of stay for those treated as inpatients.

In outpatients, the only treatment associated with a reduced risk of hospitalization on day 1 was epinephrine: pooled risk ratio 0.67 compared to placebo, with a number needed to treat of 15. One large trial reported a reduced risk of hospitalization on day 7 for children treated with epinephrine plus dexamethasone: risk ratio 0.65, number needed to treat 11. In a mixed-treatment comparison, epinephrine alone or with steroids had the highest probability of being the best treatment for outpatients with bronchiolitis: 45% for epinephrine alone and 39% for epinephrine combined with steroids. Reported harms were similar for the various treatments, none of which was clearly effective in shortening hospital stay.

Review and analysis of the available data suggest that epinephrine reduces the risk of hospitalization for ➤➤

infants with bronchiolitis. The evidence includes one large trial supporting the efficacy of epinephrine plus dexamethasone. More research is needed to establish the benefits of this combination for outpatients with bronchiolitis, and to identify the most effective treatment for inpatients.

COMMENT: *Children with bronchiolitis and "early wheezers" have similar presentations. This meta-analysis only investigates first- time wheezers with presumed bronchiolitis. On analysis of treatment for this condition, epinephrine and dexamethasone conjointly appeared to have better outcomes. The authors postulate beta=agonist/steroid synergy as well as alpha-adrenergic effects of epinephrine as potential reasons for their finding. Nevertheless, they admit that many studies have a high degree of bias. Final conclusions await the results of definitive clinical trials.*
S.F.W.
Hartling L, Fernandes RM, Bialy L, et al: Steroids and bronchodilators for acute bronchiolitis in the first two years of life: systematic review and meta-analysis.
BMJ. 2011;342:d1714. ♦♦

Age-Related Differences in Food Anaphylaxis Presentation

THERE are several challenges to the diagnosis of anaphylaxis. In younger children, inability to communicate symptoms may lead to delayed diagnosis, increasing the risk of poor outcomes. This study looked for differences in the clinical presentation of anaphylaxis in children of different ages.

From a larger sample of children seen in two hospital emergency departments for food-related acute allergic reactions over a 6-year period, the researchers identified 657 children who met criteria for anaphylaxis. The largest age cohort, about 29%, was children less than 2 years old. Younger patients were more likely to be male, although girls accounted for about half of adolescent anaphylaxis cases.

Peanuts and milk were frequent triggering foods in infants, while adolescents were more likely to react to tree nuts and fruits/vegetables. Hives and vomiting were common presenting signs in infants, whereas preschoolers were more likely to present with wheezing and stridor and adolescents with trouble swallowing and difficulty breathing. Hypotension was documented in 3% of children in all groups, but infants were less likely to undergo blood pressure measurement. The discharge diagnosis included anaphylaxis in 14% of patients overall, but only 6% of infants.

Food-induced anaphylaxis occurs in all pediatric age groups, including infants. The study highlights some age-related differences in clinical presentation, which may help to increase recognition of anaphylaxis in infants.

COMMENT: *Are infants statistically less likely to present with food-induced anaphylaxis, or are their symptoms more subtle and difficult to interpret, making this a less common diagnosis? Infants might very well suffer from food anaphylaxis at rates similar to other pediatric age groups. But an infant cannot relate nausea, the sensation of respiratory difficulty, dizziness, or other symptoms as readily as an older child or adolescent. Perhaps a proportion of cases are misidentified.*
K.R.M.
Rudders SA, Banerji A, Clark S, Camargo CA Jr: Age-related differences in the clinical presentation of food-induced anaphylaxis.
J Pediatr. 2011;156:326-328. ♦♦

REVIEWS OF NOTE

COMMENT: *This review nicely summarizes existing pediatric asthma study data (CAMP, START, etc) while discussing the best approach to treating the common asthma phenotypes seen in childhood. A modified Asthma Predictive Index is also included.*
K.R.M.
Chipps BE, Bacharier LB, Harder JM: Phenotypic expressions of childhood wheezing and asthma: implications for therapy.
J Pediatr. 2011;158:878-884. ♦♦

COMMENT: *Why are antibiotics prescribed so frequently with acute asthma treatment in children? And what risk does the earliest antibiotic use confer on those who later may develop asthma? These are important questions; in the youngest children, answers to the latter question are complicated by potential reverse causality.*

The studies by De Boeck and Paul indicate that coprescription of antibiotics with acute asthma treatment commonly occurs. Granted, allergists prescribe antibiotics when treating concurrent sinusitis triggering asthma, an appropriate indication. But in these studies, prescribing patterns were not sufficiently explained by any rationale, as a number of antibiotic prescriptions were given despite lack of evidence of concurrent bacterial infection.

Considering the routine prescription of antibiotics in patients with asthma in those studies, is it any wonder that the systematic review by Murk et al finds slightly increased odds of asthma with early antibiotic use? Reverse causality is almost certainly playing a role here.
K.R.M.
De Boeck K, Vermeulen F, Meyts I, et al: Coprescription of antibiotics and asthma drugs in children.
Pediatrics. 2011;127:1022-1026.
Paul IM, Maselli JH, Hersh AL, et al: Antibiotic prescribing during pediatric ambulatory care visits for asthma.
Pediatrics. 2011;127:1014-1021.
Murk W, Risnes KR, Bracken MB: Prenatal or early-life exposure to antibiotics and risk of childhood asthma: a systematic review.
Pediatrics. 2011;127:1125-1138. ♦♦