AllergyWatch®

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

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Does B16 Genotype Affect the Response to LABA/ICS Therapy?

REPORTS have suggested possible genetic differences in the clinical response to long-acting β_2-agonists (LABAs). In particular, the response to LABA plus inhaled corticosteroid (ICS) may be less favorable in patients homozygous for arginine at the 16th amino acid position of the β_2-adrenergic receptor (B16 Arg/Arg), compared to those homozygous for glycine (B16 Gly/Gly). This multicenter randomized trial evaluated the effect of B16 genotype on the response to LABA/ICS therapy for asthma.

Adults with moderate asthma were enrolled in matched pairs, based on B16 Arg/Arg (42 patients) or B16 Gly/Gly genotype. Members of each pair received double-blind treatment with salmeterol, 50 µg twice daily, or placebo in random order for two 18-week treatment periods. Throughout the study, all patients received open-label treatment with beclomethasone, 240 µg twice daily.

At the end of 18 weeks, the two genotype groups had similar improvement in mean morning peak expiratory flow on salmeterol, compared to placebo: mean difference 21.4 L/min in Arg/Arg patients and 21.5 L/min in Gly/Gly patients. Salmeterol was associated with a significant 2.4-fold increase in methacholine PC_{20} in Gly/Gly patients, compared to no significant change in Arg/Arg patients. For this secondary outcome, there was a significant 1.32-doubling dose difference between the two genotype groups.

Asthma exacerbations occurred during the study in 7 Arg/Arg patients and 6 Gly/Gly patients. There were 5 serious adverse events, none related to asthma or to study participation.

The results suggest that, with the B16 Arg/Arg or Gly/Gly genotype, the addition of salmeterol to ICS therapy improves airway function compared to ICS alone. Thus B16 genotype should not affect decisions regarding combined LABA/ICS therapy for asthma. Questions remain as to the genotype difference in methacholine responsiveness, as well as a possible lack of benefit from salmeterol in African Americans with the Gly/Gly genotype. ➤➤

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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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COMMENT: *Long-acting β_2-agonist monotherapy is not guideline- recommended for treatment of asthma. This may be related to differing genotypic responses to LABA. Combination therapy with ICS and LABA is recommended for moderate persistent asthma. This study did not show genotypic differences in lung function when LABA was added to ICS. These results are similar to pivotal registration trials of ICS/LABA combinations. S.F.W.*

Wechsler ME, Kunselman SJ, Chinchilli VM, et al: Effect of β_2-adrenergic receptor polymorphism on response to longacting β_2 agonist in asthma (LARGE trial): a genotype-stratified, randomised, placebo-controlled, crossover trial.
Lancet. 2009;374:1754-1764. ♦♦

Quradupled Dose of Inhaled Steroid May Be Effective for Worsening Asthma

THE written self-management plan is an important part of asthma management, but it is unclear what patients should be advised to do if their asthma control deteriorates. Previous studies have found no benefit of temporarily doubling the inhaled corticosteroid dose. This trial evaluated the effectiveness of quadrupling the inhaled corticosteroid dose in response to worsening asthma control.

Four hundred three adult asthma patients were randomly assigned to use an active or placebo inhaler in case of deteriorating asthma control (a 15% decrease in peak expiratory flow on 2 consecutive days, or a 30% drop on 1 day). The active inhaler quadrupled the patients' inhaled corticosteroid dose; the study inhalers were used in addition to the patients' usual asthma treatment. The two groups were compared for percentage of patients developing an asthma exacerbation requiring oral steroid treatment.

Nine percent of patients in the quadrupled-dose group had exacerbations requiring treatment, compared to 14% in the placebo group. The risk ratio for this outcome was 0.64, although the difference was not significant. Of 94 patients who started using their assigned inhaler, the rate of oral corticosteroid treatment was 21% in the intervention group versus 50% in the placebo group: risk ratio 0.43, a significant difference.

Advice to quadruple the inhaled corticosteroid dose in case of deteriorating asthma control may help to reduce exacerbations requiring oral steroid treatment. A larger multicenter trial will be needed to confirm the effectiveness of this approach to home asthma management.

COMMENT: *This excellent study continues to raise appropriate questions regarding the at-home treatment of asthma exacerbations, even though the primary outcome did not reach statistical significance. There was a significant protective effect regarding advancement to oral corticosteroid. A previous study in children* (N Engl J Med. 2009;360:339-353) *suggested that high dose of inhaled steroid may provide significant benefit. B.E.C.*

Oborne J, Mortimer K, Hubbard RB, et al: Quadrupling the dose of inhaled corticosteroid to prevent asthma exacerbations: a randomized, double-blind, placebo-controlled, parallel-group clinical trial.
Am J Respir Crit Care Med. 2009;180:598-602. ♦♦

Early Daycare Doesn't Reduce Childhood Asthma

BASED on the so-called Hygiene Hypothesis, it has suggested that children who attend daycare may be at lower risk of developing asthma. However, there is no convincing evidence of such an association, while ➤➤

some studies have found an increased risk of asthma in children with early childhood infections. Data from a prospective birth cohort study were used to analyze the effect of daycare on later rates of asthma and allergic sensitization.

The analysis included 8-year follow-up data on children enrolled in the Prevention and Incidence of Asthma and Mite Allergy study. Children were classified as attending daycare early, age 0 to 2 years; late, age 2 to 4 years; or no daycare before age 4. Daycare attendance and/or older siblings were analyzed as predictors of sensitization to airborne allergens, airway responsiveness, and asthma symptoms.

Early daycare was associated with an increased rate of wheezing in the first year of life, adjusted odds ratio 1.89. From age 4 to 8, the early daycare group had less wheezing and less steroid use. At age 8, there was no significant association between early daycare and asthma symptoms, allergic sensitization, or airway hyperresponsiveness. The daycare-related reduction in airway symptoms from age 4 to 8 was apparent only in children who did not have older siblings.

Children attending daycare in the first 2 years of life appear to have increased airway symptoms up to age 4, but fewer symptoms from age 4 to 8. Daycare appears unrelated to the risk of asthma symptoms, hyperresponsiveness, or allergic sensitization at age 8. The authors conclude that early daycare may shift childhood respiratory morbidity to earlier ages, when it may be "more troublesome."

COMMENT: *This study is very important as it is another nail in the coffin for the "Hygiene Hypothesis." Of greatest interest is the fact that these children have a high burden of illness early in life, with no protective effect going forward. There was also no significant increase in the prevalence of asthma associated with the development of an allergic state.*
B.E.C.

Caudri D, Wijga A, Scholtens S, et al: Early daycare is associated with an increase in airway symptoms in early childhood but is no protection against asthma or atopy at 8 years.
Am J Respir Crit Care Med. 2009;180:491-498. ♦♦

Reflux Isn't Related to Asthma Severity

MANY patients with asthma have asymptomatic, or "silent," gastroesophageal reflux (GER). Based on a suggested link to worse asthma control and asthma symptoms, treatment for GER is recommended in patients with difficult-to-control asthma, whether or not they have heartburn or other symptoms. This study assessed the relationship between GER and asthma severity and symptoms among patients with poorly controlled asthma.

Twenty-four-hour esophageal pH probe monitoring was performed in 304 adults with inadequately controlled asthma, drawn from a trial of esomeprazole therapy. Reflux was found in 53% of patients overall. In a subgroup of 242 patients undergoing proximal esophageal pH monitoring, 38% had proximal reflux.

Use of short-acting bronchodilators, nighttime awakenings, inhaled corticosteroid dose, long-acting beta-agonist use, pulmonary function, and methacholine reactivity were not significantly different for patients with and without proximal or distal GER. The presence of GER was associated with increased use of oral corticosteroids and decreased asthma quality of life, compared to no GER. Proximal GER was associated with worse asthma quality of life and health-related quality of life.

In patients with inadequately controlled asthma, the presence of objective GER is unrelated to asthma symptoms or pulmonary function. Despite the lack of these physiologic and clinical differences, proximal reflux may be associated with decreases in quality of life. The study confirms the high prevalence of silent GER in patients with asthma but does not support the routine use of ambulatory pH monitoring in patients with poorly controlled asthma and no reflux symptoms, unless indicated for other diagnostic reasons.

COMMENT: *This study continues to reinforce the lack of association between asthma control and reflux. It is important to note that proximal GER occurred in 38% of these patients. There was a discordance between negative distal and positive proximal pH probe results. How did it get there?*
B.E.C.

DiMango E, Holbrook JT, Simpson E, et al: Effects of asymptomatic proximal and distal gastroesophageal reflux on asthma severity.
Am Respir Crit Care Med. 2009;180:809-816. ♦♦

Asthma Varies with Hormone Levels During Menstrual Cycle

STUDIES have reported variations in asthma and atopy during different stages of the menstrual cycle. The mechanisms and clinical relevance of these effects are unknown. Changes in asthma characteristics during the menstrual cycle were related to changes in estrogen and progesterone levels, including the effects of oral contraceptive (OC) use.

The study included 17 women with physician-diagnosed asthma and regular menstrual cycles, 8 of whom were taking OC. Asthma symptoms, exhaled nitric oxide (eNO), spirometry, 17β-estradiol, and progesterone levels were measured daily during one menstrual cycle, plus allergen skin-prick tests performed every other day. The analysis included data from 526 daily visits.

Mean eNO levels were 48.2 ppb in women not using OC, compared to 27.0 ppb in OC users. For non-OC users, a 10 pmol/L increase in 17β-estradiol was associated with a 15.2 ppm decrease in exhaled NO, while a 0.5 nmol/L increase in progesterone was associated with a 10.0 ppb increase in eNO. Changes in both of these hormone levels were also significantly associated with the skin-prick test results. In contrast, for women taking OC, none of the asthma characteristics studied varied with hormone levels. ➤➤

Changes in estrogen and progesterone levels during natural menstrual cycles are associated with changes in asthma characteristics. The findings raise the possibility of addressing the proinflammatory effects of progesterone by increasing the dosage of asthma controller drugs during the luteal phase of the menstrual cycle. Oral contraceptives may also have a role to play in asthma management in women.

COMMENT: *This study examined the relationship between female sex hormones and asthma to shed light on menstrual associated asthma exacerbations. Exhaled nitric oxide was used as a marker of asthma inflammation which correlated with progesterone levels and inversely with 17ß-estradiol levels. Interestingly, there was greater than 18% variation of eNO throughout the menstrual cycle. With possible prospective use of eNO in asthma management, variations during menstrual cycles should be taken into account.*
S.F.W.
Mandhane PJ, Hanna SE, Inman MD, et al: Changes in exhaled nitric oxide related to estrogen and progesterone during the menstrual cycle.
Chest. 2009;136;1301-1307. ♦♦

Cats and Dogs and Atopy Risk

SEVERAL studies have concluded that early life exposure to animals, including pet cats and dogs, is associated with a lower risk of allergic diseases. One possible explanation would be selective avoidance of pets by families with a history of allergy. Pet ownership in childhood and young adulthood was evaluated as a predictor of atopy in adulthood.

The study included a population-based birth cohort of 1,037 subjects born in Dunedin, New Zealand, in 1972-73. Questionnaires were used to assess cat and dog ownership from birth to age 9 and from age 18 to 32. Skin prick testing was performed at age 13 and 32. Childhood cat or dog ownership was evaluated for association with the development of atopy.

Only about 12% of cohort members had no cat or dog ownership between birth and age 9. Parental history of atopy had no effect on childhood pet ownership. There were significant interactions between cat and dog ownership and atopy risk in childhood and adulthood. Ownership of both a cat and a dog during childhood was associated with a reduced rate of atopy at age 13: adjusted odds ratio 0.70. There was no protective effect of owning one type of animal but not the other.

For subjects who did not have atopy by age 13, ownership of both a cat and dog during adulthood was associated with a reduced risk of new-onset atopy by age 32: odds ratio 0.33 for those with a parental history of atopy. The associations remained significant after adjustment for potential confounders.

These prospective data suggest a synergistic interaction between cat and dog ownership and the risk of developing atopy. The protective effects of owning both types of pets are significant in both childhood and adulthood. In contrast, owning either a dog or a cat does not appear to affect atopy risk.

COMMENT: *The Dunedin birth-cohort has been monitoring patients for 32 years. The authors report data that confirm the Hygiene Hypothesis, concluding that children and adults in homes with both cats and dogs had a lower risk of atopy. The confounder is that over 87% of the homes in this survey report owning a pet. This is much higher than in most other countries. Therefore one should not recommend pet ownership to prevent allergies at this time.*
S.M.F.
Mandhane PJ, Sears MR, Poulton R, et al: Cats and dogs and the risk of atopy in childhood and adulthood.
J Allergy Clin Immunol. 2009;124:745-750. ♦♦

Score May Help Predict Later Asthma in Wheezing Preschoolers

IT can be difficult to tell which preschool-age children with asthma-like symptoms actually have asthma. Although some factors associated with early-onset asthma have been reported, few studies have focused on predicting asthma at the age when symptoms occur. Prospective follow-up data were used to develop a clinical prediction score for use in preschool-age children who have asthma-like symptoms for the first time.

The study included 8-year follow-up data on 3,963 children enrolled in the Prevalence and Incidence of Asthma and Mite Allergy birth cohort. Of these, 55% experienced asthma-like symptoms--wheezing and/or coughing at night without a cold--before age 5. Potential predictors of asthma were evaluated at the age when initial respiratory symptoms occurred. The presence of asthma, defined in terms of wheezing, prescription for inhaled steroids, or a physician's diagnosis, was assessed at age 7 and 8.

Just 11% of children who had asthma-like symptoms before age 5 had asthma at age 7 to 8. Eight factors were independent predictors of the development of asthma: male sex, postterm delivery, lower parental education, parental use of inhaled medications, frequency of wheezing, wheezing/dyspnea without a cold, respiratory infections, and eczema.

A model incorporating these variables correctly distinguished between children with and without asthma in 72% of cases. Based on a clinical risk score of 0 to 55, asthma risk at age 7 to 8 was 3% for children with a score of less than 10 versus 42% for those with a score of 30 or higher.

Several factors identified at the time of initial asthma-like symptoms in preschool-aged children are independent predictors of later development of asthma. A risk score based on these factors appears useful in assessing asthma risk. This clinical prediction score could be useful in primary care assessment of preschoolers with symptoms suggestive of asthma.

COMMENT: *These Dutch researchers validated the use of eight prognostic parameters in a cohort of preschool children with respiratory symptoms to predict persistent asthma at 7 to 8 years old. The authors suggest that their parameters have the same specificity with improved sensitivity, compared to the previ-*➤➤

ously used Asthma Predictive Index. Any of these predicative indices should be used with caution, since the precise definition of asthma in this age group is still variable and the questionnaires may not be applicable in every population.
S.M.F.
Caudri D, Wijga A, Schipper MA, et al: Predicting the long-term prognosis of children with symptoms suggestive of asthma at preschool age.
J Allergy Clin Immunol. 2009;124:903-910. ♦♦

In Mice, Maternal Peanut Feeding Reduces Allergy Risk in Offspring

MATERNAL allergy is a likely risk factor for peanut allergy in children, although there is no direct evidence of maternal transmission of susceptibility to peanut allergy. It is also unknown whether maternal peanut consumption during pregnancy has any effect on the risk of peanut allergy in offspring.

Five-week-old mice with peanut-allergic mothers underwent intragastric peanut challenge for assessment of reactions. These initial peanut exposures produced anaphylactic reactions, which were associated with peanut-specific IgG_1 levels and prevented by a platelet activation factor antagonist.

During pregnancy and lactation, some peanut-allergic animals were fed a low dose of peanut, while others were not. When offspring underwent peanut challenge at 5 weeks, those whose mothers were fed low-dose peanut had reduced first-exposure reactions. These offspring showed increased IgG_2 and reduced mitogen-stimulated splenocyte cytokine production, compared to mice whose mothers did not receive low-dose peanut. The offspring of peanut-fed mothers also had lower levels of peanut-specific IgE in response to an active sensitization protocol.

In this mouse model, susceptibility to peanut allergy is transmitted from mothers to their offspring. Offspring of peanut-allergic mothers fed low-dose peanut during pregnancy have reduced first-exposure reactions to peanut and are less likely to be sensitized. If a similar phenomenon occurs in humans, it may have implications for prevention of allergy in children of peanut-allergic mothers.

COMMENT: *Pregnant women often ask us how they can prevent food allergies in their children. In short, we don't know. (In one prior study in the United Kingdom, avoidance of peanut by mothers during pregnancy and lactation, and by children until 3 years of age, resulted in a high rate of peanut allergy in the children.) This study in mice showed that peanut allergy in the offspring of peanut-allergic mothers was inhibited by feeding low-dose peanut to the mothers during gestation and lactation. This needs confirmation in humans, but suggests a promising approach to the prevention of food allergies.*
R.J.M.
López-Expósito I, Song Y, Järvinen KM, et al: Maternal peanut exposure during pregnancy and lactation reduces peanut allergy risk in offspring.
J Allergy Clin Immunol. 2009;124:1039-1046. ♦♦

C1-INH Shows Promise for Acute HAE Attacks

HEREDITARY angioedema (HAE) can be caused by deficiency of C1 esterase inhibitor (C1-INH), a control protein that regulates vascular permeability for the complement system. Berinert is a highly purified, virus-inactivated C1-INH concentrate that is approved for treatment of acute HAE attacks in some countries; in the United States, orphan drug approval is being sought. A placebo-controlled study was performed to assess the safety, efficacy, and effective dose of C1-INH for treatment of acute HAE attacks.

The randomized phase II/III study included 125 patients with type I or II HAE, recruited from 36 centers around the world. Patients were randomly assigned to receive C1-INH concentrate at a dose of 10 or 20 U/kg or placebo for treatment of a single acute abdominal or facial attack of HAE. Time from the start of treatment to the onset of symptom relief was compared between groups, along with secondary outcomes.

Median time to onset of symptom relief was 0.5 hr at the 20 U/kg dose of C1-INH, compared to 1.2 hr at the 10 U/kg dose and 1.5 hr with placebo. Within 1 hour after treatment, symptoms had started to decrease in 75% of patients receiving C1-INH 20 U/kg, compared to 40% of the placebo group. The difference between C1-INH 20 U/kg and placebo was most pronounced with severe attacks: 0.5 vs 13.5 hr, respectively. The C1-INH concentrate was safe and well-tolerated, with no cases of seroconversion of bloodborne viruses (HIV, hepatitis viruses, or human B19 virus).

The study supports the safety and efficacy of human C1-INH concentrate, at a dose of 20 U/kg IV, for treatment of acute facial or abdominal attacks of HAE. Treatment provides a prompt onset of symptom relief compare to placebo. Treatment with C1-INH appears safe, with minimal risk of viral transmission.

COMMENT: *Most HAE results from a deficiency or dysfunction of C1 esterase inhibitor. Acute attacks in this disorder do not respond to standard treatments for histamine-mediated/allergic angioedema, including epinephrine. Bradykinin is probably the ultimate effector molecule, and some new bradykinin inhibitors show promise in the treatment of attacks. Replacement therapy with C1-INH concentrate has been used on other continents for 30 years with anecdotal success. This is the first double-blind placebo-controlled variable-dose study of the concentrate, and the results are impressive.*
R.J.M.
Craig TJ, Levy RJ, Wasserman RL, et al: Efficacy of human C1 esterase inhibitor concentrate compared with placebo in acute hereditary angioedema attacks.
J Allergy Clin Immunol. 2009;124:801-808. ♦♦

Local Reactions Don't Predict Subsequent Reactions

LOCAL reactions are common in patients receiving subcutaneous immunotherapy. Previous studies have reported that patients with a local reaction are ➤➤

not at increased risk of a future systemic reaction. This study evaluated a local reaction to immunotherapy as a predictor of reactions to future injections.

The retrospective study included 360 patients receiving subcutaneous immunotherapy over a 1-year period at a single department, where dose was not adjusted after local reactions. Overall, 78.3% of patients had at least one local reaction. Large local reactions (LLRs), defined as larger than the patient's palm, occurred in 7.5% of patients. In a total of 9,678 injections, the overall local reaction rate was 16.7%. Small local reactions occurred after 16.3% of shots and LLRs after 0.4%.

When a local reaction was followed by another injection, the rate of local reactions was 27.2%. The first local reaction predicted the second reaction with a sensitivity of 26.2% and positive predictive value of 27.2%. By comparison, absence of an initial reaction predicted absence of a subsequent reaction with a specificity of 85.5%. Just 6.0% of initial LLRs were followed by another LLR at the next injection: sensitivity was 5.2%, positive predictive value 6.0%, and specificity 99.6%.

In patients receiving subcutaneous immunotherapy, the occurrence of a local reaction does not predict another local reaction at the next injection. This is so for large as well as small local reactions and without immunotherapy dose adjustments.

COMMENT: *One of the vexing daily problems in an allergy practice is reactions to immunotherapy. Prior studies have demonstrated that local reactions do not predict subsequent systemic reactions. This study goes one step further: it shows that local reactions do not predict subsequent local reactions. Without dose adjustment, even large local reactions (LLR), defined as greater than the size of the patient's palm(!), were followed by another LLR only 6% of the time. Two-thirds of these LLR patients had no local reaction at all upon the next injection of the same dose. The authors recommend no dose adjustments after local reactions, and suggest several patient comfort measures.*
R.J.M.

Calabria CW, Coop CA, Tankersley MS: The LOCAL study: local reactions do not prediction local reactions in allergen immunotherapy.
J Allergy Clin Immunol. 2009;124:739-744. ♦♦

Antioxidants and Allergy Prevention in Children: Is It B-Carotene?

CHANGES in lifestyle, environment, or both have likely contributed to the rising rate of allergic diseases. One possible factor is reduced intake of dietary antioxidants, related to lower consumption of fruits and vegetables.

The relationship between antioxidant intake and atopy was assessed in 861 children enrolled in a U.K. birth cohort study. When the children were 5 years old, consumption of foods high in antioxidant vitamins A, C, and E was assessed using a food frequency questionnaire. Serum IgE levels were also measured at age 5; skin prick testing and respiratory symptom assessment were performed at age 5 and 8.

Mean intake of β-carotene was similar to recommended levels; vitamin C intake was several times higher than recommended levels, but vitamin E intake was lower than recommended. Children with higher β-carotene intake were at lower risk of allergic sensitization: odds ratio 0.80 at age 5 and 0.81 at age 8. Higher levels of β-carotene were also associated with lower total IgE levels. An association between vitamin E intake and allergic sensitization was significant only at age 5. Antioxidant intake was unrelated to symptoms of wheezing or eczema.

Higher consumption of β-carotene may be associated with a lower risk of allergic sensitization and lower IgE levels in young children. The study adds to the small body of evidence linking the increased prevalence of atopic sensitization to decreased consumption of foods high in vitamin C and β-carotene.

COMMENT: *Identifying the environmental influences responsible for the recent dramatic increase in atopy and asthma has been our specialty's Holy Grail for the past two decades. Among the many possible explanations, a diet deficient in antioxidants has been implicated by some investigators, although so far the results of dietary intervention studies have been unimpressive. This birth cohort study is one of the few to focus on early childhood, and there was a striking inverse correlation between dietary β-carotene and allergic sensitization at age 5 and 8. Maybe we should be feeding our babies more carrots and spinach?*
S.A.T.

Patel S, Murray CS, Woodcock A, et al: Dietary antioxidant intake, allergic sensitization and allergic diseases in young children.
Allergy. 2009;64:1766-1772. ♦♦

More Data Needed on SLIT for Dust Mite Allergy

META-analyses of randomized trial data have supported the safety and efficacy of sublingual immunotherapy (SLIT) for allergic rhinitis and allergic asthma. However, the conclusions on effectiveness for individual allergens are less clear. This updated meta-analysis focused on the SLIT's efficacy for treatment of allergy to house dust mites.

The literature through March, 2008, was searched to identify randomized, double-blind, placebo-controlled trials of SLIT for house dust mite sensitization. Meta-analysis was performed using data from 8 studies in patients with allergic rhinitis and 9 studies in patients with allergic asthma. Analysis of symptom scores included 194 allergic rhinitis patients and 243 allergic asthma patients receiving SLIT (and 188 and 209 patients receiving placebo, respectively).

The meta-analysis suggested that SLIT was effective in reducing symptoms: standard mean difference -0.95 for both diseases. Based on somewhat smaller numbers of patients, standardized mean differences for res-➤➤

cue medication use were -1.88 for allergic rhinitis and -1.48 for allergic asthma. There was evidence of significant heterogeneity between studies.

The best available data support the efficacy of SLIT using dust mite extract in patients with allergic rhinitis or allergic asthma. However, particularly for allergic asthma, further trials using objective outcome measures in larger patient populations are needed.

COMMENT: *This review focuses on the efficacy of SLIT for dust mite allergy. The results generally suggest that treatment is effective, compared to SLIT for pollen allergy. However, there are still questions whether published studies overestimate SLIT's effectiveness for dust mites. The authors state that larger-scale controlled studies would be helpful.*
S.A.T.
Compalati E, Passalacqua G, Bonini M, Canonica GW: The efficacy of sublingual immunotherapy for house dust mites respiratory allergy: results of a GA²LEN meta-analysis.
Allergy. 2009;64:1570-1579. ♦♦

Plasma VEGF May Be a Marker of Chronic Urticaria

ALTHOUGH chronic urticaria (CU) is regarded as an autoimmune disease, less than half of patients have detectable histamine-releasing autoantibodies on autologous serum skin testing. Vascular endothelial growth factor (VEGF) is an important mediator of vascular permeability. This study evaluated serum and skin expression of VEGF in patients with CU.

Enzyme immunoassays were used to measure VEGF and prothrombin fragment F_{1+2} in 80 consecutive adults with CU evaluated at two Italian allergy centers. The patients had a mean plasma VEGF concentration of 8.00 pmol/L, compared to 0.54 pmol/L in a group of 53 healthy controls. Patients with more severe CU had higher plasma VEGF concentrations, which were also associated with higher prothrombin fragment F_{1+2} levels. The results of autologous plasma skin testing were positive in 85.1% of CU patients, associated with higher VEGF levels.

Immunohistochemical studies were performed in wheal skin biopsy specimens from 6 patients. All showed stronger expression of VEGF, which colocalized with expression of eosinophil cationic protein.

Patients with CU have elevated plasma levels of VEGF, corresponding to disease severity. Eosinophils appear to be the main source of VEGF in CU skin specimens. The results suggest that overexpression of VEGF may contribute to the pathophysiology of CU.

COMMENT: *The concept of autoimmune urticaria, with confirmatory autologous skin tests or in vitro assays, has helped our ability to explain to patients why they have hives. However, a substantial proportion of CU patients have negative test results and are therefore still labeled "idiopathic." This provocative preliminary study establishes VEGF as a marker of CU. This marker may play an important role in the pathogenesis of CU and appears more sensitive than autologous skin testing.*
Tedeschi A, Asero R, Marzano AV, et al: Plasma levels and skin eosinophil-expression of vascular endothelial growth factor in patients with chronic urticaria.
Allergy. 2009;64:1616-1622. ♦♦

Have Candidate Gene Studies Missed the Boat?

PREVIOUS studies have identified many common polymorphisms as playing a possible causative role in asthma. A large international sample of children with asthma was used to evaluate candidate genes for association with wheezing and allergy.

Based on Phase 2 of the International Study of Asthma and Allergies in Childhood, the analysis included 1,105 wheezing and 3,137 nonwheezing children from 17 study centers in 13 countries. All children underwent DNA genotyping for 55 single nucleotide polymorphisms (SNPs) previously linked to asthma, all with a minor allele frequency of at least 20%. The goal was to assess genetic factors associated with wheezing and allergy in a sample from countries with wide variation in their rates of childhood asthma symptoms.

Just 4 of the 55 SNPs were significantly associated with wheezing in the past year: *IL4R*, *TLR4*, *MS4A2*, and *TLR9*. Odds ratios for these SNPs were generally less than 1.3 per allele. Associations with allergen-specific IgE were noted for *IL4R* and *TLR4* only. A *SPINK4* SNP was significantly associated with visible eczema but not IgE levels; an *IL13* SNP was associated with total IgE. There was little heterogeneity between different countries.

Analysis of a worldwide sample of children finds that, of the dozens of common gene variants previously linked to asthma, only a few are significantly associated with both wheezing and elevated IgE. Positional candidates *DPP10* and *PHF11*, previously reported to have no consistent associations with childhood asthma, are also not associated with wheezing. New genomewide studies may identify previously unknown genetic factors potentially affecting asthma risk.

COMMENT: *This worldwide case-control study compared candidate asthma genes in 8- to 12-year-old children in various parts of the world. The authors expected that previously identified gene polymorphisms would help explain the dramatic differences in asthma prevalence at various study sites. However, they found that only 4 of the 14 genes examined had associations between a SNP and wheezing. These unexpected results are a humbling testament to the complexity of human biology. The authors are hopeful that ongoing studies using "genomewide" technologies may capture what thousands of prior studies appear to have so far missed.*
S.A.T.
Genuneit J, Cantelmo JL, Weinmayr G, et al: A multicentre study of candidate genes for wheeze and allergy: the International Study of Asthma and Allergies in Childhood Phase 2.
Clin Exp Allergy. 2009;39:1875-1888. ♦♦

Size Matters: Low Birth Weight and Asthma Risk

STUDIES have consistently reported a link between asthma and low birth weight. However, the apparent association could reflect confounding by genetic or environmental factors. This issue was addressed using data from a Swedish twin registry.

A cohort analysis was performed in 19,918 twins, aged 9 to 12 years, including data on asthma, zygosity, birth weight and other birth characteristics, and a wide range of potential confounders. In addition, a case-control study was performed in 157 monozygotic and 289 dizygotic twin pairs in which one twin had asthma and the other did not.

Overall, 13.7% of twins had ever had asthma. The cohort analysis found a significant association between asthma and birth weight. The odds ratio for asthma was 1.57 for a 1,000 g decrease in birth weight and 1.10 per 1-week reduction in birth weight. In the co-twin control analysis, birth weight was not significantly associated with asthma in dizygotic same-sex twins. In monozygotic twins, the relationship was borderline significant; the results were similar for children born preterm versus at term.

The results support an association between fetal growth and childhood asthma, independent of gestational age and of genetic and environmental factors shared by twins. The study adds to the evidence suggesting that fetal growth restriction affects lung development. The authors call for more research into the early metabolic and physiologic processes affecting childhood asthma risk.

COMMENT: *An association between low birth weight and asthma risk has been noted throughout the literature on pediatric asthma. Implications regarding direct causation have been confounded by the possibility that other variables--such as familial or environmental factors--might be responsible for the observed association. This elegant twin study from Sweden bolsters the notion that low birth weight indeed increases the risk of asthma, independent of confounding variables. The evidence certainly "tips the scales" in favor of a causal relationship.*
K.R.M.
Örtqvist AK, Lundholm C, Carlström E, et al: Familial factors do not confound the association between birth weight and childhood asthma.
Pediatrics. 2009;124:e737-e743. ♦♦

Ongoing Burden of Secondhand Tobacco Smoke Exposure in Children

LAWS against smoking in public places have reduced exposure to secondhand smoke in the U.S. population, including children. However, many children are still exposed to smoking at home. Serum cotinine measurements were used to compare secondhand smoke exposure in children and adolescents with and without exposure to smoking at home.

The study included data on 5,518 children (aged 3 to 11 years) and nonsmoking adolescents (aged 12 to 19). Serum cotinine was measured as part of the 2003-2006 National Health and Nutrition Examination Survey. Associations of serum cotinine with self-reported home exposure to smoking and other factors were evaluated.

Children exposed to smoking at home had higher geometric mean serum cotinine levels: 1.05 ng/mL, compared to 0.05 ng/mL for nonexposed children. For the exposed group, cotinine levels were inversely associated with age, with no significant difference between black and white children. In contrast, among those without home exposure, cotinine levels were higher for black than for white children, unrelated to age. Exposure to secondhand smoke was lowest for Mexican American children.

About 1 in 5 U.S. children are exposed to smoking at home, leading to much higher exposure to secondhand smoke. For children exposed at home, serum cotinine levels have not changed significantly since the 1990s. The sociodemographic factors associated with cotinine levels differ for children with and without exposure to smoking at home.

NEARLY all of what is known about the health effects of exposure to secondhand smoke comes from studies in nonsmokers. A recent study reported that exposure to secondhand smoke at work had adverse health effects in adult smokers. The relationship between secondhand smoke exposure and respiratory symptoms was evaluated in adolescent smokers.

A questionnaire regarding respiratory symptoms, active smoking, and exposure to secondhand smoke was administered to a random sample of 32,506 Hong Kong secondary school students. Twenty-four percent had ever smoked, and 9% were current smokers. Among the current smokers, 51% were exposed to secondhand smoke at home and 85% outside the home.

Persistent respiratory symptoms--present for 3 consecutive months out of the last 12--were more likely to be reported by teenaged smokers who were exposed to secondhand smoke at home. Rates were 50% for those exposed for 1 to 4 days/wk and 77% for those exposed 5 to 7 days/wk. For exposure outside the home, rates of persistent respiratory symptoms were 41% and 85%, respectively. Exposure to secondhand smoke was also associated with respiratory symptoms in adolescent nonsmokers, but the relationship was not as strong.

Exposure to secondhand smoke is associated with persistent respiratory symptoms in adolescents who smoke, as previously reported for adult smokers. Exposure to secondhand smoke should be included in efforts to reduce the harms associated with smoking in adolescents.

COMMENT: *The Healthy People 2010 initiative (www.healthypeople.gov) has been promoting the goal of reducing adult cigarette smoking rates to 12% or less in the United States by this year. A concurrent goal involves reducing secondhand tobacco smoke exposure. Indeed, legislative measures to reduce exposure to secondhand tobacco smoke have been steadily enacted throughout the United States since this initiative was launched a decade ago.* ➤➤

So how have these efforts impacted pediatric tobacco smoke exposure? Progress has been made overall, reflected by declining serum cotinine levels in children. Sadly, however, those impacted in their own homes have shown no change in exposure in a decade. And secondhand smoke bothers the children/adolescents who are themselves smokers disproportionately. Even though there is much progress to be made, can we still envision a 22nd century where our population talks about an antiquated product--tobacco--and wonders why it was ever used?
K.R.M.
Marano C, Scholber SE, Brody DJ, Zhang C: Secondhand tobacco smoke exposure among children and adolescents: United States, 2003-2006.
Pediatrics. 2009;124:1299-1305.
Lai H-K, Ho S-Y, Wang M-P, Lam T-H: Secondhand smoke and respiratory symptoms among adolescent current smokers.
Pediatrics. 2009;124:1306-1310. ♦♦

Childhood Use of Chlorinated Swimming Pools: At What Risk to Airways?

ASTHMA and other respiratory problems in swimmers are thought to be related the chlorination products in swimming pool water. A growing body of evidence suggests that total exposure to chlorinated pools, whether indoor or outdoor, is a key risk factor. This study assessed the impact of total time spent in chlorinated pools on respiratory health in adolescents.

The study included 847 students, aged 13 to 18, with varying access to indoor or outdoor chlorinated swimming pools. Students from a school with an indoor pool sanitized by the copper-silver method served as a control group. Assessments included total and specific IgE measurement, respiratory symptoms, and asthma diagnosis or medications.

For adolescents with atopy (based on total serum IgE levels greater than 30 kIU/L or specific IgE), asthma symptoms and asthma diagnoses were significantly associated with lifetime number of hours spent in chlorinated pools. For those with more than 1,000 hours of exposure to chlorinated pools, odds ratios ranged as high as 7.1 to 14.9. Atopic teens with chlorinated pool attendance of more than 100 hours had odds ratios of 3.3 to 6.6 for hay fever and 2.2 to 3.3 for allergic rhinitis. No such associations were observed in nonatopic adolescents or in those attending the copper-silver pool. Exposure to chlorinated pools was estimated to account for 63.4% of asthma, 62.1% of hay fever, and 35.0% of allergic rhinitis in this population.

In adolescents, exposure to chlorinated swimming pools appears to interact with atopy to produce a substantial burden on respiratory health. The risks may increase along with hours of chlorinated pool attendance. Further research is needed, along with attention to the levels of chemicals present in chlorinated swimming pools.

COMMENT: *Previously, the finding of increased asthma among competitive swimmers was felt to be an artifact of reverse causation: children with asthma were thought more likely to become swimmers. In the last several years, studies have strongly suggested that reverse causation is* not *the explanation. Indoor chlorinated pools in particular are felt to be hazardous based on the presence of trichloramine, an irritant gas byproduct of pool chlorination that gives that particular "swimming pool odor." However, even that perspective--risk secondary to indoor chlorinated pools--must be reassessed, based on newer data suggesting that risks are equally high with outdoor chlorinated pools, where trichloramine would be effectively dissipated.*

This study adds assessments of rhinitis and atopy to the growing literature about asthma risk in this setting. Study weaknesses include the diagnosis of allergic disease based on serum total and specific IgEs, in the absence of directed medical history, physical examination, or allergy skin testing. Also, allergic rhinitis and "hay fever" are considered separate variables, are not further defined, and yield differing relative risks related to chlorinated pool attendance!
K.R.M.
Bernard A, Nickmilder M, Voisin C, Sardella A: Impact of chlorinated swimming pool attendance on the respiratory health of adolescents.
Pediatrics. 2009;124:1110-1118. ♦♦

Older Adults at Higher Risk of Death from H1N1

INITIAL reports of the 2009 influenza A(H1N1) pandemic suggested a relatively mild disease that disproportionately affected younger patients. Enhanced surveillance data from the first few months of the H1N1 pandemic in California were analyzed to identify factors associated with mortality.

The analysis included 1,008 cases of laboratory-confirmed influenza A(H1N1) infection associated with hospitalization or death in California from April to August, 2009. The median age was 27 years, with nearly one-third of patients being younger than age 18. More than two-thirds had risk factors for complications from seasonal influenza, such as chronic lung disease, cardiac disease, immunosuppression, or diabetes. When performed, chest radiographs showed pulmonary infiltrates in two-thirds of cases; ICU admission was required in about 30% of patients. Rapid antigen testing gave false-negative results in approximately one-third of tested cases. About 20% of patients did not receive antiviral therapy.

Infants had the highest hospitalization rate, but mortality was highest in patients over 50. Mortality was 11% overall, but 18% to 20% in adults over 50. Most deaths resulted from viral pneumonia and acute respiratory distress syndrome; median time from symptom onset to death was 12 days.

Despite its predilection for younger patients, pandemic 2009 influenza A(H1N1) is most likely to be fatal in adults aged 50 or older. Patients with risk factors for complications of seasonal influenza are at increased risk of hospitalization or death from H1N1. Obesity may be a significant risk factor. ➤➤

COMMENT: *As we move into the latter phases of the first year of this influenza pandemic, many questions remain. Many experts are surprised and relieved that the severity of the disease is not as intense as some had feared. Although older adults are not at as great a risk as children and young adults, the fact that mortality is increased for adults 50 years and older leads me to recommend vaccination of all adults now that the H1N1 vaccine is more readily available.*
D.K.L.

Louie JK, Acosta M, Winter K, et al: Factors associated with death or hospitalization due to pandemic 2009 influenza A (H1N1) infection in California.
JAMA. 2009;302:1896-1902. ♦♦

Breast-Feeding Linked to Egg Allergy in AD Infants

THERE is ongoing debate over the ability of breast-feeding to prevent childhood wheezing and atopic dermatitis (AD). Some studies have reported differences in the characteristics of allergic patients who were breast-fed versus formula-fed. This study assessed the relationship between type of feeding and evidence of food allergies in infants with AD.

The study included 143 infants with AD, all less than 6 months old. They were divided into three groups, based on feeding history: breast-fed, formula-fed, and mixed feeding. All underwent measurement of total IgE and specific IgE against food allergens; none of the infants had been fed egg or soy at the time of the study.

Breast-fed infants had a total IgE level of 107.68 kU/L, compared to 24.64 kU/L in the formula-fed group. The breast-fed infants also had a higher level of egg-specific IgE: 8.43 versus 0.09 kU/L, respectively. Forty percent of the breast-fed infants were sensitized to egg, compared to 6.2% of the formula-fed group. Rates of egg allergy were 36.9% versus 0%, respectively.

Among infants with AD, breast-feeding is associated with an increased risk of sensitization to egg. The results suggest that breast-feeding may not always be beneficial in terms of reducing allergy risk in high-risk infants, and that breast milk may play a role in sensitization to food allergens.

COMMENT: *Breast milk is the ideal food for infants but breast feeding does not seem to modify the development of allergic disease in infants and children. Maybe we should be introducing potentially important allergenic foods earlier in life when mechanisms of tolerance may be more active. The discussion continues, but clearly avoidance does not cut the mustard.*
D.K.L.

Han Y, Chung S-J, Kim J, Kim J, et al: High sensitization rate to food allergens in breastfed infants with atopic dermatitis.
Ann Allergy Asthma Immunol. 2009;103:332-336. ♦♦

Fluticasone Reduces Inflammation and Improves Outcomes in COPD

CURRENT guidelines call for inhaled corticosteroids (ICS) plus long-acting β_2-agonists (LABAs) in patients with moderate to severe chronic obstructive pulmonary disease (COPD). The benefits of ICS may be at least partially related to their anti-inflammatory effects. This study evaluated the effects of long-term ICS therapy on airway inflammation and other outcomes in COPD.

The study included 114 patients with COPD, none previously treated with steroids. They were randomly assigned to treatment with fluticasone, 500 µg twice daily, for 6 or 30 months; fluticasone plus salmeterol, 50 µg twice daily, for 30 months; or placebo twice daily. The primary outcome was inflammatory cell counts in bronchial biopsy and induced sputum specimens. Methacholine responsiveness and clinical outcomes were evaluated as well.

At 6 months, fluticasone decreased mucosal CD3+ cells by 55%, CD4+ cells by 78%, CD8+ cells by 57%, and mast cells by 38%, compared to placebo. Hyperresponsiveness was decreased as well; the effects were maintained through 30 months of treatment. Long-term fluticasone therapy was associated with reduced mast cell count, increased eosinophil count, and increased percentage of intact epithelium. Reductions in sputum neutrophil, macrophage, and lymphocyte counts were accompanied by improvements in FEV_1 decline, dyspnea, and quality of life.

Discontinuation of fluticasone at 6 months was followed by increases in CD3+ cells, mast cells, and plasma cells, with worse clinical outcomes. The addition of salmeterol was associated with improved FEV_1.

In steroid-naive patients with moderate to severe COPD, treatment with ICS reduces inflammation. Fluticasone is also associated with improvement of the decline in lung function, along with clinical benefits. Aside from lung function, these benefits are not increased by the addition of salmeterol.

COMMENT: *The effect of fluticasone on bronchial inflammation in COPD associated with smoking is not a great surprise. However, the reduction in the loss of lung function over 30 months in this group of current and prior smokers is surprising to me. The study suffers from small size and an inability to assess the primary outcome--airway inflammation--in 24% of recruited subjects. Nevertheless, these findings may strengthen the case for using inhaled corticosteroids earlier in the clinical course of COPD.*
D.K.L.

Lapperre TS, Snoeck-Stroband JB, Gosman MME, et al: Effect of fluticasone with and without salmeterol on pulmonary outcomes in chronic obstructive pulmonary disease.
Ann Intern Med. 2009;151:517-527. ♦♦

CLINICAL TIDBITS

Promising Results with Allergen Patch Therapy

NONINVASIVE alternatives to allergy shots might increase the use of specific allergen immunotherapy. Epicutaneous allergen administration using skin patches was evaluated in a randomized, double-blind trial.

The study included 37 adult patients with seasonal allergy to grass pollen. Patients received skin patches containing either allergen or placebo, used before and during pollen season. Follow-up evaluations were performed before and after the subsequent season.

Patients using allergen patches had significantly decreased scores on nasal provocation tests in both seasons. Those using placebo patches had decreased nasal provocation scores in the first season, but this effect was smaller in the follow-up year. Although the nasal provocation results were not significantly different between groups, patients receiving allergen patches rated their treatment success higher. The allergen patches were associated with eczema--an adverse effect that proved specific T-cell responses had occurred.

Epicutaneous allergen immunotherapy may provide a new approach to allergy treatment. The ability to self-treat at home while avoiding needles would encourage compliance.

COMMENT: *This is the first study to show clinical benefit for patients with seasonal allergic rhinitis using epicutaneous allergen patches applied before and during the grass pollen season. Most of the treated patients reported contact eczema from the patches. The advantage for this therapy is that the patients could apply the patch at home, with no shots.*
S.M.F.
Senti G, Graf N, Haug S, et al: Epicutaneous allergen administration as a novel method of allergen-specific immunotherapy.
J Allergy Clin Immunol. 2009;124:997-1002. ♦♦

Increased Airway NO Oxidation Products in Asthmatic Children

WHEN severe, childhood allergic asthma is associated with persistent airway inflammation and excessive nitric oxide oxidation. This study measured NO oxidation products in the epithelial lining fluid (ELF) of children with severe allergic asthma.

Bronchoalveolar lavage specimens were obtained from 30 children with severe allergic asthma, 15 children with mild to moderate asthma, and control groups of children and adults. Levels of the NO oxidation products nitrite, nitrate, and nitrotyrosine were measured in the proximal and distal ELF.

In the proximal ELF, all three NO oxidation products were significantly increased in both groups of asthmatic children, compared to controls. A similar pattern was observed in the distal ELF, although the levels were lower. On univariate analysis, the NO oxidation product levels were not significantly related to clinical characteristics. On multivariate analysis, exhaled NO levels were a significant predictor of NO oxidation.

Children with mild to moderate or severe asthma have elevated levels of NO oxidation products in the airway, despite inhaled corticosteroid therapy. More study is needed to understand the complex relationship between exhaled NO levels and airway nitrosative stress.

COMMENT: *Nitrosative stress is the inflammatory process that results in excess NO in respiratory airways. Collecting bronchoalveolar lavage samples in children with asthma, these researchers found consistent elevations of NO oxidation products in spite of ICS treatment. Interestingly, there was no direct correlation between lavage NO products and exhaled NO, suggesting that at least in children low exhaled NO values may not indicate reduced asthmatic inflammation.*
S.M.F.
Fitzpatrick AM, Brown LAS, Holguin F, et al: Levels of nitric oxide oxidation products are increased in the epithelial lining fluid of children with persistent asthma.
J Allergy Clin Immunol. 2009;124:990-996. ♦♦

Omalizumab Reduces Th2 Cytokine Responses

ANTI-IgE therapy with omalizumab reduces airway inflammation and asthma symptoms. A previous study reported that omalizumab causes dramatic but reversible loss of the cell-surface high-affinity IgE receptors (FcεRI). This study evaluated the consequences for FcεRI-mediated synthesis and release of cytokines and chemokines.

Peripheral blood basophils were isolated before, during, and after 12 weeks of omalizumab therapy in 15 asthma patients. Basal and anti-IgE-stimulated release of cytokines, chemokines and histamine by basophils were analyzed.

In response to anti-IgE, basophils synthesized and released the Th2 cytokines interleukin (IL)-4 and IL-13 and the chemokines IL-8 and RANTES. Anti-IgE-stimulated release of IL-4, IL-13 and IL-8 was significantly decreased during omalizumab therapy, returning to baseline after the end of treatment. There was no effect on basophil histamine levels or on basal and anti-IgE-stimulated histamine release.

The clinical benefit of omalizumab in asthma may result partly from reductions in FcεRI-mediated basophil production of Th2 cytokines and chemokines. The effect on cytokine production may be even greater in basophils stimulated by specific allergen, rather than anti-IgE.

COMMENT: *Omalizumab may reduce asthma symptoms by suppressing the FcεRI-mediated production by basophils of Th2 cytokines and selected chemokines. Oliver et al expanded studies to determine the effects of omalizumab on basophil cytokine and chemokine*➤➤

production. Based on their results, the authors felt that omalizumab may reduce asthma symptoms in part by suppressing the FcεRI-mediated production by basophils of Th2 cytokines and selected chemokines. Also, anti-IgE-stimulated basophil cytokine synthesis appears more sensitive than histamine release to the loss of FcεRI caused by omalizumab treatment.
M.F.
Oliver J M, Tarleton CA, Gilmartin L, et al: Reduced FcεRI-mediated release of asthma-promoting cytokines and chemokines from human basophils during omalizumab therapy.
Int Arch Allergy Immunol. 2010;151:275-284. ♦♦

Simple Screening Test for Chronic Sinusitis

THERE is a need for simple, validated tools to screen for sinusitis and rhinitis, which are associated with uncontrolled asthma. The authors report the development and evaluation of a brief questionnaire to screen for chronic sinonasal disease.

Based on the results of extensive evaluation in 57 patients, an expert panel used the Delphi method to reach a consensus regarding the presence (42 patients) or absence (17 patients) of chronic sinonasal disease. On evaluation of various tests, a 6-item questionnaire based on frequency of nasal symptoms provided the highest sensitivity, with minimal specificity of 90%.

Reproducibility testing was performed in a separate cohort of 63 patients with chronic sinonasal disease (41 with and 22 without asthma). A 5-item questionnaire had sensitivity of 90%, specificity of 94%, and area under the receiving operating characteristic curve of 97%. In contrast, sinus CT scans and nasal endoscopy were nonspecific for diagnostic purposes.

Five questions regarding the frequency of runny nose, postnasal drip, need to blow your noise, facial pain/pressure, and nasal obstruction perform well in screening for chronic sinonasal disease. Further validation is needed, including studies in asthma patients.

COMMENT: *The authors propose a 5-question sinonasal questionnaire to diagnose upper airway disease. The questions are commonly asked (or should be) in allergy practices and are highly sensitive and specific for diagnosis. Primary care practitioners should find this useful as an alternative to expensive and invasive CT scanning and endoscopy.*
S.F.W.
Dixon AE, Sugar EA, Zinreich SJ, et al: Criteria to screen for chronic sinonasal disease.
Chest. 2009;136;1324-1332. ♦♦

REVIEWS OF NOTE

COMMENT: *Although the influenza season is winding down, egg-containing influenza immunization is still a problem for our egg-allergic patients. The British Society for Allergy and Clinical Immunology guidelines were published for primary care. The recommended specialist evaluation and administration in the British guidelines differ from AAAAI guidelines, but both agree on specialist involvement.*
S.F.W.
Erlewyn-Lajeunesse M, Brathwaite N, Lucas JSA, Warner JO: Recommendations for the administration of influenza vaccine in children allergic to egg.
BMJ. 2009;339:b3680. ♦♦

COMMENT: *This is a succinct, practical and timely review of questions I regularly receive in clinic. I strongly recommend you read carefully.*
D.K.L.
Kelso JM, Li JT, Nicklas RA, et al: Adverse reactions to vaccines.
Ann Allergy Asthma Immunol.
2009;103(4 Suppl 2):S1-14. ♦♦

COMMENT: *Pharyngitis in young adults is most often viral, but the possibility of* Fusobacterium necrophorum *needs to be considered. The associated morbidity of 10% and mortality up to 4% or 5% underscores the need to be aggressive with antibiotics if this infection is suspected. Macrolides are ineffective and streptococcal screening will not detect the infection. Clindamycin would be the likely drug of choice in a subject with penicillin allergy. Keep this possibility in mind the next time you see a young adult with exudative tonsillitis.*
D.K.L.
Centor RM: Expand the pharyngitis paradigm for adolescents and young adults.
Ann Intern Med 2009;151:812-815. ♦♦

COMMENT: *This is an excellent review of medicines used in pediatric respiratory disease and is highly recommended for its scholarly evidence-based review.*
B.E.C.
Lenny W, Boner AL, Bont L, et al: Medicines used in respiratory diseases only seen in children.
Eur Respir J. 2009;34:531-551. ♦♦

COMMENT: *This is a good update of the new bronchodilators in development that may reach the U.S. market within the next several years.*
B.E.C.
Cazzola M, Matera MG: Emerging inhaled bronchodilators: an update.
Eur Respir J. 2009;34:757-769. ♦♦