AllergyWatch®

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

A Publication of The American College of Allergy, Asthma & Immunology

Volume 10, Number 3 May-June 2008

Sensitization Doesn't Occur In Utero

SEVERAL lines of evidence, including the presence of allergen-specific IgE in cord blood, suggest that atopic sensitization may occur in utero. This is the basis for current recommendations to avoid exposure to allergens during pregnancy, athough studies have found no effect on the risk of allergic sensitization in infants. This study evaluated the clinical relevance of allergen-specific IgE in the cord blood of infants born to mothers with asthma.

Cord blood samples were obtained from 243 children of mothers with verified asthma, drawn from a prospective birth cohort study. The presence of specific IgE to inhalant and food allergens was assessed in the cord blood samples. Specific IgE was also measured in infant blood samples obtained at 6 months, as well as from the parents. Cord blood IgA was measured to assess the possibility of contamination by the mother's blood.

Fourteen percent of the cord blood samples had allergen-specific IgE, mainly to inhalant allergens. However, none of the 6-month blood samples had specific IgE to the allergens found in cord blood. The specific IgE in cord blood was identical to that in maternal blood in terms of allergen specificity, specific IgE level, and total to specific IgE ratio. Specific IgE in cord blood was positively correlated with IgA in cord blood, suggesting contamination by maternal blood.

The presence of specific IgE in cord blood from infants of asthmatic mothers appears to reflect contamination of the cord blood with maternal blood, rather than transplacental transfer of specific IgE from mother to fetus. This is supported by the correlation between cord blood IgE and IgA, which does not cross the placental barrier. The findings challenge the theory that allergic sensitization occurs in utero, and do not support the recommendation for allergen avoidance during pregnancy.

COMMENT: *This study questions the concept of intrauterine IgE sensitization. Although 14% of* ➤➤

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The American College of Allergy, Asthma & Immunology expresses its appreciation to Schering-Plough for its unrestricted grant in support of the publication of *AllergyWatch*®.

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- 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
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cord blood samples had allergen specific IgE, this was not the case when the infants were 6 months old. Other evidence supporting the authors' conclusions includes matching of allergen sensitivity, total/specific IgE ratios, and the presence of IgA in cord blood. The practice of allergen avoidance during pregnancy should be revised if these findings can be confirmed.
S. M. F.
Bønnelykke K, Pipper CB, Bisgaard H: Sensitization does not develop in utero.
J Allergy Clin Immunol. 2008;121:646-651.

♦♦

High Rate of Skin Sensitization in Children Under 2

EARLY diagnosis of sensitization to aeroallergens has prognostic implications, including opportunities to prevent the development of asthma. Skin prick testing is the standard approach to assessing allergic sensitization, but skin reactivity is reduced in infants and young children. The rates and significance of skin sensitization to aeroallergens were assessed in a large clinical sample of infants and young children.

The study included 824 children under age 2 seen at a tertiary asthma clinic. All had clinical indications for skin prick testing, which was performed using a panel of aeroallergens and food allergens. Information on environmental exposure and family history of allergic disease was available for each patient.

The skin test results showed sensitization to one or more allergens in 40% of children. Sensitization to aeroallergens, most commonly dust mite, was demonstrated in 28% of children. Seventeen percent of children were sensitized to egg. Children with large wheals in response to histamine were more likely to have sensitization. Sleeping with soft toys was also a significant risk factor: odds ratio 1.45. When the definition included the size of the histamine-induced wheal, a history of eczema had a protective effect against skin sensitization to aeroallergens: odds ratio 0.66. Sensitization was unrelated to age or day care attendance.

Infants and young children with clinical indications for skin prick testing have a higher rate of sensitization to aeroallergens. Sleeping with soft toys is a risk factor for sensitization. More follow-up will be needed to determine whether early sensitization predicts the later risk of asthma.

COMMENT: *Few prior studies have provided skin test data for children under age 2. This large study does not represent a cross-section of the population since each of the children had been referred to a pulmonary clinic, but the results are intriguing. Nearly 30% of the children had positive skin testing to an aeroallergen, and nearly 20% had a positive egg skin test. Sensitization to an aeroallergen was associated with a reported history of sleeping with soft toys, a presumed marker of increased dust mite exposure.*
S. A. T.
de Bilderling G, Mathot M, Agustsson S, et al: Early skin sensitization to aeroallergens.
Clin Exp Allergy. 2007;38:643-648.

♦♦

FeNO Reflects Asthma Control in Everyday Clinical Practice

EXHALED nitric oxide (FeNO) monitoring has been shown to lead to improved asthma control. However, the patients selected for controlled trials may not reflect the full range of situations seen in clinical practice. This longitudinal study evaluated the use of FeNO to monitor asthma control in regular clinical practice.

The 3-year study included 341 unselected patients with persistent asthma seen at a tertiary asthma clinic. All were assessed at least once by FeNO measurement and by the Asthma Control Questionnaire. The ability of FeNO to predict improvement or worsening of asthma control was evaluated, overall and for patients in different treatment subgroups.

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Patients with a FeNO decrease of less than 40% were unlikely to have optimal asthma control--negative predictive value 79%. In contrast, those with a FeNO increase of less than 30% were unlikely to have deterioration in disease control--negative predictive value 82%. For patients receiving low-dose inhaled corticosteroids (ICS)--beclomethasone dipropionate (BDP) equivalent 500 µg or less--a FeNO decrease of greater than 40% was associated with optimal asthma control, positive predictive value 83%. Among ICS-naive patients, a FeNO value greater than 35 ppb was associated with improvement in disease control after starting ICS, positive predictive value 68%. Measuring FEV_1 did not provide useful information on asthma control for most patients.

In usual clinical practice, FeNO values are significantly associated with asthma control over time. The value of FeNO monitoring is lower in patients receiving medium- to high-dose ICS (BDP equivalent greater than 500 µg). Changes in individual FeNO values may be more useful than absolute cutoff points.

COMMENT: *This study is quite helpful in understanding the role of FeNO in tracking asthma control in a group of patients not receiving high-dose inhaled steroid. The responsiveness of FeNO to either increased or decreased asthma control in patients taking BDP less than 500 µg/d was significant. The lack of effect in patients taking high-dose inhaled steroids suggests that mechanisms other than eosinophilic airway inflammation are driving their lack of asthma control.*
B. E. C.
Michils A, Baldassarre S, Van Muylem A: Exhaled nitric oxide and asthma control: a longitudinal study in unselected patients.
Eur Respir J. 2008;31:539-546. ♦♦

Household Chemicals Increase Wheezing Risk in Nonatopic Children

HIGH exposure to household chemicals during pregnancy has been linked to an increased risk of persistent wheezing in offspring. The "hygiene hypothesis" provides one possible explanation: that homes with increased chemical exposure are cleaner, and thus have reduced exposure to environmental antigens. Atopy was evaluated as a potential modifier of the association between household chemical exposure and childhood wheezing.

The analysis included data on 7,162 children from a long-term follow-up study. Based on questionnaire responses, a composite household chemical exposure (CHCE) score was calculated for each mother. The children's wheezing phenotypes were assessed up to age 7; skin-prick testing was performed at age 7.5 and lung function testing at age 8.5. Regression models were used to assess associations among wheezing, lung function, and CHCE score and their interactions with atopy.

Higher CHCE scores were associated with higher rates of wheezing, and the associations were particularly strong for nonatopic children. For children without atopy at age 7.5 years, odds ratios per z-score of CHCE were 1.41 for onset of wheezing before 18 months of age, 1.43 for onset between 18 and 30 months, and 1.69 for onset after 30 months. Increased CHCE scores were also linked to lower levels of FEV_1 and forced expiratory flow from 25% to 75%.

High exposure to household chemicals during pregnancy is linked to increased rates of persistent wheezing in nonatopic offspring. The association between household chemicals and childhood wheezing does not appear to be explained by the hygiene hypothesis. Prenatal developmental effects or postnatal irritant effects on the developing airway are a more likely explanation.

COMMENT: *This study contributes to the increased awareness of prenatal exposure to irritants other than cigarette smoke and prediction of adverse outcomes related to wheezing and lower lung function in a nonatopic cohort. The data presented in this paper do not suggest that the mechanism supported by the hygiene hypothesis is operative in predicting the results.*
B. E. C.
Henderson J, Sherriff A, Farrow A, Ayres JG: Household chemicals, persistent wheezing and lung function: effect modification by atopy?
Eur Respir J. 2008;31:547-554. ♦♦

Delayed DPT Immunization May Reduce Asthma Risk

IT has been suggested that childhood vaccinations may promote the development of asthma, either by enhancing a Th2-type immune response or by decreasing microbial pressure. Studies evaluating the effects of diphtheria, pertussis, tetanus (DPT) immunization on childhood asthma or atopy risk have yielded mixed results, possibly because of differences in immunization schedule. The association between the timing of DPT immunization and childhood asthma was assessed.

Manitoba immunization records were used to identify 11,531 children born in 1995 who received at least four doses of DPT. Most children received whole-cell pertussis DPT. Health care records were used to assess the development of asthma by age 7 years. The relationship between the timing of DPT immunization and the development of childhood asthma was evaluated by multivariate logistic regression.

The percentage of children who developed asthma by age 7 was 13.8% for those who received their first dose of DPT by 62 days after birth compared to 10.3% for those immunized between 63 and 92 days after birth. On adjusted analysis, the odds ratio for asthma was 0.50 for children receiving their first dose of DPT more than 4 months after birth. For those with delays in all three doses, the odds ratio was 0.39. The protective effects of delayed DPT administration remained significant in sensitivity analyses.

Delays in DPT immunization appear to be associated with a reduced risk of childhood asthma. The protective effect is particularly strong among children with delays in all three doses. Further study is needed to determine the mechanism of the association, including whether there is a similar effect with acellular DPT combination vaccines. ➤➤

COMMENT: *The search continues for things that influence the development of asthma in children. This large retrospective study implies that there may be an adverse influence of giving the first DPT immunization earlier (at 2 months of age) than later (at 4 months or older). The "reduction" in asthma risk in those vaccinated about 2 months behind schedule was large, about 50%. These children had received the whole-cell pertussis version of the vaccine. The reasons for the delays in vaccination were unstudied, and may be relevant to the finding. This is an intriguing bit of data-mining, but needs a prospective study before changing the recommended vaccine regimen.*
R. J. M.

McDonald KL, Huq SI, Lix LM, et al: Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma.
J Allergy Clin Immunol. 2008;121:626-631. ♦♦

Daily Asthma Treatments Have Differing Effects on EIB

EXERCISE-induced bronchoconstriction (EIB) is a common problem with a major impact on the lives of asthmatic children. The effects of regular daily treatment for childhood asthma on EIB remain unclear. Four different patterns of daily antiasthmatic therapy were compared for protection against EIB.

The randomized, placebo-controlled trial included 100 children, aged 6 to 18 years, with atopic asthma and at least a 20% drop in FEV_1 after exercise. Children were assigned to receive budesonide 100 µg twice daily plus formoterol 4.5 µg twice daily; budesonide plus montelukast, 5 or 10 mg once daily; montelukast alone; budesonide alone; or placebo. The children performed a treadmill exercise test before and after 4 weeks of treatment. Exercise-induced bronchoconstriction was assessed in terms of the area under the time-response curve from 0 to 20 minutes and the maximum percentage decrease in FEV_1 after exercise.

All four active treatments were associated with significant reductions in EIB, compared to placebo. Montelukast, with or without budesonide, had a greater protective effect than budesonide, alone or with formoterol. The protective effect of montelukast was about 50%, with a mean posttreatment fall of around 12%.

Different daily treatments for childhood asthma have differing effects on EIB. Of the four active-treatment options tested, those including montelukast have the greater protective effect. Although low-dose steroid is effective, adding montelukast might further reduce EIB.

COMMENT: *There are several treatment strategies for inhibiting exercise-induced asthma in children. This study compared three medications, all of them controllers: an inhaled steroid, a long-acting beta agonist, and montelukast, alone or in combination. The simplest commonly used strategy--intermittent pre-exercise use of a short-acting beta agonist--was not included in this study. The results clearly favored montelukast; adding the inhaled steroid offered no additional benefit. The study would have been improved if the authors had included albuterol as one of the treatment options.*
R. J. M.

Stelmach I, Grzelewski T, Majak P, et al: Effect of different antiasthmatic treatments on exercise-induced bronchoconstriction in children with asthma.
J Allergy Clin Immunol. 2008;121:383-389. ♦♦

Exhaled NO Identifies Subgroups of Young Children with Wheezing

UP to 30% of young children experience cough and wheezing, mainly associated with lower respiratory viral infections. Objective measures are needed to help predict which children with lower respiratory symptoms will develop asthma later in childhood. This study sought to determine whether exhaled nitric oxide (FeNO), as a measure of airway inflammation, can distinguish between young children with wheezing vs nonwheezing respiratory symptoms.

The prospective cohort study included 391 children under age 4 who were being evaluated for respiratory symptoms. All underwent FeNO measurement. Based on their symptoms and history, the children were separated into three diagnostic groups. Children in group 1 had recurrent cough with no history of wheezing, group 2 children had early recurrent wheezing and met a "loose" index for the prediction of asthma by school age, and group 3 children had frequent recurrent wheezing with a "stringent" index for prediction of childhood asthma.

Median FeNO level was 6.5 ppb in group 1 and 6.4 ppb in group 2, compared with 11.7 in group 3. On regression analysis, phenotype as represented by the diagnostic group assignment was the only factor significantly associated with FeNO--demographic, clinical, and treatment variables were unrelated to FeNO. On separate analysis of children in group 3, FeNO levels were higher in those with allergic sensitization, whether or not they had been treated with inhaled corticosteroids.

Young children with frequent recurrent wheezing who meet a stringent index for prediction of asthma by school age have elevated FeNO, compared to those with other patterns of respiratory symptoms. Exhaled NO measurement may help to differentiate between subgroups of children with wheezy and nonwheezy respiratory symptoms. Follow-up studies are needed to determine the value of FeNO in predicting subsequent asthma risk.

COMMENT: *It seems to me that pediatricians' indication for giving a prescription for home-nebulized bronchodilators these days is basically a child who coughs enough to keep the parents awake at night. Bronchodilators are the new "cough syrup." Deciding which of these coughing children have or will develop asthma is a challenge, one that parents (and pediatricians) anxiously await help with. This study suggests that FeNO levels might help with that determination. Unfortunately, the clinical utility for any individual child is compromised by the substantial overlap among study-defined categories of coughing kids. Perhaps we could use FeNO as an indicator for anticipatory* ➤➤

prescribing of inhaled corticosteroids. Such a study needs to be done.
R. J. M.
Moeller A, Diefenbacher C, Lehmann A, et al: Exhaled nitric oxide distinguishes between subgroups of preschool children with respiratory symptoms.
J Allergy Clin Immunol. 2008;121:705-709. ♦♦

Inhaled Steroid Potentiates the Effects of β_2-Agonists

IN asthmatic patients, long-term glucocorticoid therapy may improve the response of airway smooth muscle and blood vessels to inhaled β_2-agonists. The mechanism of these effects is unclear. This study evaluated the effects of a single dose of inhaled glucocorticoid on β_2-adrenergic airway and airway smooth muscle responses in asthma.

The study included 10 patients with mild intermittent asthma and 10 healthy controls. On eight separate visits, the subjects underwent inhalation of fluticasone or placebo, followed by inhalation of racemic albuterol, 0.6 or 1.25 mg; or (R)-albuterol, 0.3 or 0.6 mg. Airway blood flow and FEV_1 were measured before and after fluticasone/placebo inhalation, and again after β_2-agonist inhalation.

After both fluticasone and placebo inhalation, the controls showed similar increases in airway blood flow after treatment with both forms of albuterol. For asthmatic subjects, placebo pretreatment was associated with a significant reduction in the blood flow response to racemic albuterol and (R)-albuterol. The airway smooth muscle and vascular responses were restored after fluticasone pretreatment. The FEV_1 response to racemic albuterol 0.6 mg (but not the other albuterol treatments) was increased by fluticasone pretreatment.

In mild intermittent asthma, a single dose of inhaled fluticasone acutely restores the blunted bronchodilator and airway vascular responses to albuterol. The results add in vivo evidence that inhaled glucocorticoids potentiate the effects of inhaled β_2-agonists in asthmatic patients.

COMMENT: *Glucocorticoid-naive mild asthmatics had an impressive response when inhaled corticosteroids were used in conjunction with β-agonists. This suggests that there may be a benefit to using inhaled steroids with rapid-acting β-agonist in the treatment of acute exacerbations of asthma.*
S. M. F.
Mendes ES, Horvath G, Campos M, Wanner A: Rapid corticosteroid effect on β_2-adrenergic airway and airway vascular reactivity in patients with mild asthma.
J Allergy Clin Immunol. 2008;121:700-704. ♦♦

Asthma Characteristics Linked to Aeroallergen Sensitization

ALLERGENS are an important trigger for asthma attacks. Various factors are known to influence rates of allergic sensitization, but there are few data on the relationship between sensitization to aeroallergens and asthma characteristics. Skin test results were used to assess the correlation between aeroallergen sensitization and disease characteristics in a large group of patients with asthma.

The study included 1,338 patients with an objective diagnosis of asthma, drawn from 11 Asthma Clinical Research Network studies. Epicutaneous skin tests for 14 aeroallergens were performed using a standardized technique, with quality assurance measures to ensure uniform test procedures across study centers. The investigators hypothesized that most patients would be sensitized to at least one aeroallergen, and that sensitization would be correlated with airway inflammatory markers and pulmonary function measures.

At least one positive skin test was recorded for 95% of patients: 14% reacted to one or two allergens, while 81% had positive results for three or more allergens. Sixty-seven percent of patients reacted to both seasonal and perennial allergens, 2% to seasonal allergens only, and 26% to perennial allergens only. Patients with higher IgE and exhaled nitric oxide levels, those with lower PC_{20} values, and minority patients had more positive skin test responses. Sensitization rates were lower among patients with late-onset asthma. However, aeroallergen sensitization was present in 89% of patients over age 60. Correlations between sensitization and asthma symptoms could not be assessed.

The vast majority of patients with mild to moderate asthma have positive skin tests for sensitization to aeroallergens. Patterns of sensitization vary by ethnicity as well as geographic location; sensitization rates remain high among asthmatic older adults. Aeroallergen sensitization is correlated with IgE levels, exhaled nitric oxide, and PC_{20} measurement. The findings highlight the clinical importance of aeroallergens as asthma triggers.

COMMENT: *Once again, aeroallergens are found to be important triggers for both mild and moderate asthma and correlated with lung function and inflammatory markers. Although there are regional differences in allergen sensitivity, there is minimal decline in allergic sensitivity even in the elderly. Patients with persistent asthma should have allergy skin testing to determine triggers.*
S. M. F.
Craig TJ, King TS, Lemanske RF, et al: Aeroallergen sensitization correlates with PC_{20} and exhaled nitric oxide in subjects with mild-to-moderate asthma.
J Allergy Clin Immunol. 2008;121:671-677. ♦♦

Protocol Induces Tolerance in Severe Milk Allergy

IN children with very severe allergy to cow's milk protein (CMP), severe reactions can occur even with exposure to trace amounts of antigen. Standard management includes strict allergen avoidance, which has a major impact on the child and family's lives. A specific oral tolerance induction (SOTI) protocol for children with severe milk allergy was evaluated. ➤➤

The study included 97 children, age 5 or older, with severe reactions to milk or dairy products and very high levels of CMP-specific IgE. On double-blind, placebo-controlled food challenge, 60 eligible children had severe reactions to very small amounts of cow's milk. Thirty of these children were immediately started on a new SOTI protocol, with a 10-day in-hospital rush phase followed by an at-home phase with gradually increasing exposure to milk--1 mL every other day. Control children remained on strict allergen avoidance for 1 year.

At the end of the study year, 30% of children assigned to SOTI were completely tolerant of cow's milk in doses of 150 mL or more. Some of these children achieved a completely unrestricted diet. Another 54% percent achieved partial tolerance of cow's milk (5 to 150 mL). Ten percent had to discontinue the SOTI protocol because of persistent respiratory or abdominal symptoms. In the control group, the response to milk challenge remained positive after 1 year.

The SOTI protocol achieves at least partial milk tolerance in 90% of children with severe allergy to CMP. The authors highlight the need to attempt this procedure only in highly controlled settings. Larger trials with longer follow-up are needed.

COMMENT: *These researchers were able to show an impressive induction of tolerance in most children with severe milk allergy. Although 54% of children could only tolerate limited amounts of milk, the authors make a strong case for this risky procedure. They suggest that since there is likelihood that children may accidentally ingest the offending food, a controlled exposure is preferable to anaphylaxis. They also suggest continued limited intake to maintain the tolerant state.*
S. M. F.

Longo G, Barbi E, Berti I, et al: Specific oral tolerance induction in children with very severe cow's milk-induced reactions.
J Allergy Clin Immunol. 2008;121:343-347. ♦♦

Cost-sharing Reduces Use of Asthma Medications by Children

CHILDREN with asthma may need different types of medications to achieve optimal disease control. Even for insured patients, various types of cost-sharing may act as barriers to use of prescribed medications. Insurance data were used to assess the impact of cost-sharing on medication use by children with asthma.

The investigators analyzed claims data on 17,046 asthmatic children in Ontario who were covered by private direct-pay drug plans. (Most children in Ontario receive drug benefits through private insurance.) Information on out-of-pocket expenses and reimbursement for prescription drugs was used to classify each patient as having no cost-sharing, low cost-sharing (less than 20%), or high cost-sharing (20% or higher). The impact of cost-sharing on use of various classes of asthma medications was assessed.

Overall asthma management was good, with 83% of children receiving some type of controller medication. However, children with high cost-sharing made fewer claims for asthma medications: 6.6 per year, compared to 7.0 for those with zero cost-sharing and 7.2 for those with low cost-sharing. High cost-sharing was associated with reductions in the purchase of bronchodilators, inhaled corticosteroids, and leukotriene receptor antagonists, odds ratio 0.76. For dual-agent inhalers, the odds ratio was 0.70, compared with the low cost-sharing group.

High cost-sharing may be associated with reduced use of medications by children with asthma. Use of asthma controller medications may be particularly affected. Prescription drug benefits for children with asthma should be integrated with family asthma education and disease management programs, the authors suggest.

COMMENT: *These Canadian researchers show that shifting the cost of medications to patients reduces prescription fill rates for both controller and rescue asthma medicines. The implications are particularly disconcerting for the U.S. population, since the current trend in health insurance encourages high-deductible plans and more cost-sharing by patients. The potential for even more barriers to appropriate asthma therapy in children is a real concern.*
S. M. F.

Unger WJ, Kozyrskyj A, Paterson M, Ahmad F, et al: Effect of cost-sharing on use of asthma medication in children.
Arch Pediatr Adolesc Med. 2008;162:104-110. ♦♦

Meta-analysis Supports SLIT for Allergic Asthma in Children

SUBLINGUAL immunotherapy (SLIT) has gained acceptance as an alternative to traditional subcutaneous immunotherapy for allergic rhinitis. However, its value as a treatment for asthma has yet to be established. This meta-analysis evaluated the evidence for the use of SLIT in children and adolescents with allergic asthma.

A literature review was performed to identify randomized, double-blind, placebo controlled trials of SLIT for the treatment of asthma in patients aged 3 to 18 years. Meta-analysis focused on the primary outcomes of symptom scores and rescue medication use. The final analysis included 441 patients from nine trials: 232 received SLIT and 209 received placebo.

The studies varied considerably in terms of the scoring systems used, resulting in significant heterogeneity. The meta-analysis suggested that children undergoing SLIT had significant reductions in asthma symptoms, standard mean difference (SMD) -1.14; and rescue medication use, SMD -1.63. On subgroup analysis, the effects of SLIT appeared greater in patients with mite allergy compared to pollen allergy. There were no lethal or severe systemic reactions.

Despite the limitations of the available data, meta-analysis supports the efficacy of SLIT for children with allergic asthma. Clinical trials are needed to determine the most effective SLIT dose and regimen for pediatric asthma. This should include studies of pollen aller- ➤➤

gy and of the possible preventive effects of SLIT in children less than 3 years old.

COMMENT: *Sublingual immunotherapy is the hot topic of our time. This is the first meta-analysis demonstrating the efficacy of SLIT in pediatric asthma. Only 9 studies were included, the largest of which included 47 treated subjects. The meta-analysis included small studies, with inconsistent outcome measurements involving subjects of variable treatments and severities. Nevertheless, there is ample justification for larger definitive studies with proscribed outcomes. Also see the accompanying editorial by Dr. Townley (Chest. 2008;133:589-590).*
S. F. W.
Penagos M, Passalacqua G, Compalati E, et al: Metaanalysis of the efficacy of sublingual immunotherapy in the treatment of allergic asthma in pediatric patients, 3 to 18 years of age.
Chest. 2008; 133:599-609. ♦♦

Thinking Pertussis? Maybe It's Bocavirus

IN clinical practice, viral respiratory infections in young children commonly go undiagnosed. Using newer molecular diagnostic techniques, it is possible to identify the causative pathogen in close to 90% of acute respiratory infections. A new polymerase chain reaction (PCR) assay was evaluated for its ability to diagnose respiratory infections caused by adenovirus, bocavirus, and metapneumovirus in children.

Over a 21-month period, approximately 1,500 nasal swab specimens were collected from patients at a children's hospital. The PCR assay led to the detection of adenoviruses in 5.9% of children, human bocavirus in 5.6%, and human metapneumovirus in 5.2%. The combination of PCR and antigen detection led to a viral diagnosis in up to 62% of swabs.

Sixty-three percent of children infected with metapneumovirus had lower respiratory disease, compared to 45% of those with adenovirus. In 59 cases, PCR detected adenovirus after negative results on antigen detection testing. In 19% of the children with bocavirus, paroxysmal coughing led to clinical suspicion of pertussis.

A PCR assay finds substantial rates of infection with bocavirus, metapneumovirus, and adenovirus among patients at a children's hospital. Clinically, children with bocavirus and metapneumovirus appear more likely to have lower respiratory involvement, while bocavirus infection may mimic pertussis. Antigen detection tests may miss some cases of adenovirus infection.

COMMENT: *While respiratory syncytial virus continues to be a major respiratory pathogen in infants and toddlers, novel viruses have been identified in recent years as causes of respiratory infections and asthma exacerbations in young children. This study shows the utility of PCR in detecting novel viral pathogens such as bocavirus and metapneumovirus. It also shows the superiority of PCR in detecting adenovirus, compared with more commonly used methods. In a number of patients in whom bocavirus was detected, treatment with macrolides had been given for presumed pertussis; infection with bocavirus can cause paroxysmal coughing. Rather than having to tell anxious parents their child "has a virus" when commonly used assays are negative, someday we may be better able to tell them which virus.*
K. R. M.
Arnold JC, Singh KK, Spector SA, Sawyer MH: Undiagnosed respiratory viruses in children.
Pediatrics. 2008;121:e631-e637. ♦♦

Reducing Hospital-Related Pediatric Asthma Costs

THE format in which evidence-based guidelines are presented can affect their implementation in daily practice. Integrated care pathways (ICPs) are structured documents that incorporate guideline recommendations, with the aim of limiting clinical variations. This study evaluated the effects of an ICP on the care of children seen in the emergency department (ED) for acute asthma and wheezing.

The cluster randomized trial included 298 children, aged 2 to 16 years, seen at a children's hospital ED for acute asthma/wheeze. In 7-day blocks, the children were assigned to standard care or care delivered using an ICP. The main outcome of interest was length of stay in the hospital, from ED arrival to hospital discharge.

One hundred eighteen children were discharged home from the ED. Of those treated on the ICP, 81% received prednisolone, compared to 63% in the standard care group. Children in the ICP group were also more likely to be referred for primary care evaluation: 72% versus 33%. The remaining 180 children were hospitalized; group assignment had no effect on the rate of recovery from acute asthma. However, mean length of stay was 37.6 hours in the ICP group, compared with 40.7 hours in the standard care group. For children assigned to the ICP who had a discharge checklist completed, length of stay decreased to 34.3 hours.

Use of the ICP was also associated with a 30% reduction in prescribing errors. A 48-hour discharge plan was provided to 89% of children in the ICP group versus 41% in the standard care group. Children assigned to the ICP had more clinical contacts, including medical and nursing staff.

This trial documents some benefits of using an ICP to guide care for children with acute asthma and wheezing. A modest reduction in length of stay is accompanied by improved education and fewer prescribing errors. Recovery time is unaffected. Additional studies will be needed to see how the ICP affects staff workload.

Cunningham S, Logan C, Lockerbie L, et al: Effect of an integrated care pathway on acute asthma/wheeze in children attending hospital: cluster randomized trial.
J Pediat. 2008;152:315-320. ♦♦

PATIENT and caregiver education is a key component of current guidelines for pediatric asthma care. Many different types of childhood asthma education programs have been developed and evaluated, with mixed results. A meta-analysis was performed to evaluate the effects of asthma education on use of acute care services among children with asthma.

The investigators performed a literature review to identify studies evaluating the effects of pediatric asthma education on the outcomes of hospitalization, emergency department (ED) visits, and urgent physician visits. The meta-analysis included pooled data from 37 studies: 27 comparing educational interventions to usual care and 10 comparing different educational interventions.

Compared to usual care, asthma education was associated with significant reductions in hospitalizations and ED visits, with a trend toward reduced odds of ED visits. There was no significant effect on the odds of hospitalization or on mean number of physician visits. Studies comparing different types of educational approaches providing more sessions and more interactions between educators and patients/caregivers were more effective.

Pediatric asthma education programs reduce utilization of some types of acute care services, including hospitalizations and ED visits. The results support the development of asthma education programs and/or incentives for clinicians to provide education for pediatric asthma patients. More research is needed to identify the most important components of asthma education interventions.

COMMENT: *With increasing concerns regarding hospital-acquired infection and health care costs in the United States, the less total time our pediatric asthma patients are hospitalized, the better. The first study, from the United Kingdom, demonstrates that use (upon admission) of a protocol to integrate asthma care and teaching yields measurable improvement in length of stay, at the same time enhancing patient/caregiver education and reducing medical errors. We will likely see an increase in use of similar protocols, and concurrent studies to assess them, over time.*

In the second paper, meta-analysis of asthma education studies points to the importance of parent teaching in reducing ED visits and hospitalizations. And the method of teaching matters: more frequent and personalized teaching has a differential, positive effect. This is an area where our specialty should have a tremendous impact!

K. R. M.

Coffman JM, Cabana MD, Halpin A, Yelin EH: Effects of asthma education on children's use of acute care services: a meta-analysis.
Pediatrics. 2008;121:575-586. ♦♦

Is Smoking a Chronic Disease?

DESPITE the high preventable mortality associated with tobacco use, smoking is still viewed mainly as a "bad habit." This perspective piece outlines the argument for considering--and treating--tobacco dependence as a chronic disease.

Most smokers want to quit, and their chances of doing so can be increased through effective treatments such as behavioral counseling and medications, including nicotine replacement therapy. There are no data on the "optimal duration" of treatment for tobacco dependence. However, given the difficulty of smoking cessation, treatment may need to continue for a prolonged period.

The authors urge physicians to encourage long-term use of smoking cessation medications by their patients who smoke, and to encourage third-party payers to provide coverage for such treatment. Tobacco dependence has characteristics in common with recognized chronic diseases such as diabetes--these conditions can exacerbate other medical problems and have effective behavioral as well as pharmacologic treatments.

Nevertheless, whereas treatments for diseases like diabetes are covered by insurance, smoking cessation treatments are not. The authors conclude by recommending that tobacco dependence be treated like any other chronic disease--with treatment continued and covered as long as needed to achieve the best possible outcome.

COMMENT: *Tobacco smoke is an important exacerbating factor for asthma and sinusitis. Smoking cessation is an important component of asthma prevention and therapeutic intervention. This article discusses a case report, long-term use of cessation versus long-term smoking, and the need to consider treatment for tobacco dependence as similar to therapy of other chronic medical conditions, such as diabetes. The authors feel that tobacco dependence should share the status of other chronic illnesses, with effective treatments given as long as is necessary to achieve successful clinical outcomes*

M. F.

Steinberg MB, Schmelzer AC, Richardson DL: The case for treating tobacco dependence as a chronic disease.
Ann Intern Med. 2008;148:554-556. ♦♦

Can Rhinosinusitis Symptoms Predict Benefit of Antibiotics?

THE difficulty of distinguishing between bacterial and viral causes of acute rhinosinusitis can lead to unnecessary prescriptions for antibiotics. This meta-analysis sought to identify clinical factors useful in selecting patients with acute rhinosinusitis for antibiotic treatment.

A literature review was performed to identify randomized trials of antibiotic versus placebo treatment for adult patients with rhinosinusitis-like symptoms. The meta-analysis included individual patient data from 9 trials, including a total of 2,547 patients.

Analysis of overall effectiveness suggested that the number needed to treat (NNT) to cure 1 additional patient with rhinosinusitis-like symptoms was 15. Time to cure was longer for patients with purulent pha-➤➤

ryngeal discharge--in this group, the NNT was 8. Certain patient subgroups also had longer times to cure, including older patients and those with longer-lasting or more severe symptoms. However, even these groups were no more likely to benefit from antibiotics treatment.

The analysis identifies no common clinical findings associated with a greater likelihood of benefit from antibiotics in patients with rhinosinusitis. Antibiotic treatment is not justified even for patients with symptoms lasting 1 week or longer.

COMMENT: *Acute rhinosinusitis is a comorbid condition for asthma and a common condition seen by allergists-immunologists. These authors undertook a meta-analysis of randomized trials based on individual data from 2547 adults to assess whether common signs and symptoms can be used to identify a subgroup of patients who benefit from antibiotics. They found that common clinical signs and symptoms cannot identify patients with rhinosinusitis for whom treatment is clearly justified and watchful waiting is warranted. Antibiotics are not justified even if a patient reports symptoms for longer than 7 to 10 days.*
M. F.

Young J, De Sutter A, Merenstein D, et al: Antibiotics for adults with clinically diagnosed acute rhinosinusitis: a meta-analysis of individual patient data.
Lancet. 2008; 371:908-914. ♦♦

Does BCG Vaccine Reduce Allergic Disease Risk?

IN newborns as well as adults, the bacillus Calmette-Guèrin (BCG) vaccine induces a Th1 response. Epidemiologic studies of the relationship between BCG vaccination and subsequent risk of allergic disease have yielded conflicting results. Data from a large study of Japanese schoolchildren were used to assess the relationship of BCG vaccination and tuberculin reactivity with allergic disease risk.

The study included 5,717 children from public elementary and junior high schools in Okinawa. Allergic disease symptoms and diagnoses were assessed using International Study of Asthma and Allergies in Childhood criteria. History of BCG vaccination and the results of tuberculin tests were assessed from school records. A wide range of potential confounders were included in logistic regression analyses.

There was no association between BCG vaccination in infancy and the risk of allergic disorders. Overall, 5,567 of the children received BCG vaccine. Those with a positive tuberculin test (induration of at least 10 mm) in first grade had lower rates of some allergic disease outcomes--multivariate odds ratios were 0.80 for wheezing, 0.78 for asthma, and 0.77 for atopic asthma. The inverse association was more pronounced for children whose parents were free of allergic disease. The tuberculin tests results were unrelated to the risk of allergic rhinoconjunctivitis.

Bacillus Calmette-Guèrin vaccination and tuberculin reactivity are associated with lower rates of wheezing and asthma in Japanese schoolchildren. The association is more pronounced in children with a negative parental history of allergic disease. More study is needed to establish the protective effect of BCG vaccine, including further adjustment for environmental and genetic factors.

COMMENT: *This large cross-sectional study of BCG-vaccinated Japanese schoolchildren identified an inverse relationship between tuberculin reactivity and wheezing, asthma, and eczema. Although these results help clarify previous conflicting data and strengthen the hypothesis that BCG vaccination may prevent certain atopic diseases, establishing this causal link would require additional prospective study. Understanding the hygiene hypothesis has been a challenging undertaking, and as the accompanying editorial points out (Obihara et al: Clin Exp Allergy.2008;38:388), the task of convincingly relating epidemiologic findings to underlying pathophysiologic mechanisms is still incomplete.*
S. A. T.

Miyake Y, Arakawa M, Tanaka K, et al: Tuberculin reactivity and allergic disorders in schoolchildren, Okinawa, Japan.
Clin Exp Allergy. 2008;38:486-492. ♦♦

ACEIs Cause 30% of ED Cases of Angioedema

ANGIOEDEMA is a potentially life-threatening adverse effect of treatment with angiotensin-converting enzyme inhibitors (ACEIs). Despite the growing number of patients taking ACEIs, there are no recent data on the frequency of ACEI-induced angioedema or on current treatment and outcomes. The authors inquired into the clinical epidemiology of ACEI-induced angioedema seen in the emergency department (ED).

The Emergency Medicine Network was used to identify 175 patients with ACEI-induced angioedema seen at 5 U.S. EDs from 2003 to 2005. The cases accounted for 30% of all patients with angioedema, with no variation between years. Cases from previous years were included for a final sample of 220 patients with ACEI-induced angioedema. The mean age was 60 years, and 62% of patients were women. The indication for ACEI treatment was hypertension in 98% of patients; atopy was much less frequent than in the general population.

Overall, ACEI-induced angioedema was seen at a rate of 0.7 cases per 10,000 ED visits. The most common signs and symptoms were shortness of breath, swelling of the tongue and lips, and laryngeal edema; median time to presentation was between 4 and 6 hours. Most patients received corticosteroids and diphenhydramine, while 10% received epinephrine. Fifty-eight percent of patients were discharged home from the ED, 11% were admitted to the ICU, 12% were admitted as regular inpatients, and 18% were admitted for observation (less than 24 hours). Patients with pharyngeal swelling and respiratory distress were more likely to be hospitalized and had longer hospital stays.

Although ACEI-induced angioedema accounts for ➤➤

nearly one-third of ED cases of angioedema, it remains a rarely seen problem. Some patients with respiratory compromise and upper airway angioedema require hospitalization and ICU admission. More study is needed to define the mechanism of ACEI-induced angioedema and to explore new treatment options.

COMMENT: *It surprises me that the proportion of subjects with angioedema in the ED due to ACEIs has not changed in 10 years--still about 30%. This consistent result occurred even with greater awareness of this association and more options for blood pressure treatment. Keep the ACE inhibitor in mind whenever you encounter swelling.*
D. K. L.

Banerji A, Clark S, Blanda M, et al: Multicenter study of patients with angiotensin-converting enzyme inhibitor-induced angioedema who present to the emergency department.
Ann Allergy Asthma Immunol. 2008;100:327-332. ♦♦

Study Looks at Cellular Responses to SLIT

A growing body of evidence supports the clinical use of sublingual immunotherapy for treatment of allergic rhinitis. However, questions remain about the mechanisms of SLIT; few studies have examined the biologic changes in response to treatment. T-cell and cytokine responses to SLIT were investigated in patients with grass pollen allergy.

The open, observational study included 11 patients receiving SLIT for seasonal rhinitis and confirmed sensitization to grass pollen. All underwent a simplified 2-month SLIT protocol, without up-dosing. From February to April, patients used a monomeric allergoid derived from a 3-grass pollen extract. Peripheral blood mononuclear cells (PBMCs) were obtained to assess allergen-specific T-cell proliferation and production of interleukin-10 (IL-10) and transforming growth factor-β (TGF-β). Responses to tetanus toxoid were evaluated for comparison.

After SLIT, the patients' PBMCs showed decreased allergen-specific T-cell proliferation, but not tetanus toxoid-specific proliferation. Production of IL-10 by allergen-specific T cells was significantly increased; these two effects were correlated with each other. Although TGF-β transcription was increased, the difference was not significant.

For patients with grass pollen allergy, 2 months of preseason SLIT with a modified allergen leads to reduction in allergen-specific T-cell proliferation and upregulation of IL-10. These effects suggest that SLIT is associated with systemic downregulation of the Th2 allergen-specific immune response, with tolerance to allergen exposure. More comprehensive studies of the mechanisms of SLIT are needed.

COMMENT: *The literature on sublingual immunotherapy continues to grow. Most of the studies showing clinical benefit have not been able to demonstrate definitive immunologic changes. This short-term, unblinded pilot study does show an effect on T cell regulation with an in vitro proliferation assay. Regulation of IL-10 does seem to be an important cytokine response to subcutaneous immunotherapy; therefore this finding with sublingual treatment needs confirmation in a large study.*
D. K. L.

Burastero SE, Mistrello G, Falagiani P, et al: Effect of sublingual immunotherapy with grass monomeric allergoid on allergen-specific T-cell proliferation and interleukin 10 production.
Ann Allergy Asthma Immunol. 2008;100:343-350. ♦♦

Should We Use Spirometry to Screen for COPD?

CHRONIC obstructive pulmonary disease (COPD) is often not diagnosed until it has reached an advanced stage. Some commentators have suggested using spirometry to screen for early COPD in asymptomatic current or former smokers. This report summarizes the research evidence on the use of spirometric screening for COPD.

A literature review was performed to answer key questions regarding the benefits and harms of screening for COPD using spirometry. The findings suggested that airflow obstruction consistent with COPD is underdiagnosed in primary care. However, basing the diagnosis on symptoms alone would lead to overdiagnosis of COPD in patients without airflow obstruction. There was little evidence of adverse effects of spirometry, although some percentage of false-positive results would occur. Spirometry does not appear to be an effective motivational tool for smoking cessation, although studies of this issue have had limitations.

Drug treatments can reduce exacerbations in patients with severe symptomatic COPD. However, few studies have included patients with mild to moderate COPD, and none have included asymptomatic patients with airflow obstruction. Data analysis suggested that screening for COPD would mainly identify patients with mild to moderate airflow obstruction who would likely not derive additional health benefits from being labeled as having COPD. Treatment to reduce exacerbations might benefit the small number of patients identified as having severe airflow obstruction.

Current evidence does not support the use of spirometry to screen for COPD. Based on the available data, hundreds of patients would have to be screened to identify one patient with COPD, in whom the incremental health benefit would probably be avoidance of a first exacerbation.

COMMENT: *I utilize spirometry in patients who smoke to show them a visible reason why they should stop. I always thought it was appropriate to determine lung function in anyone with a condition that would potentially decrease lung function, including asthma. This evidence-based document does not recommend spirometry in someone without current symptoms. Although not focused on asthma, the findings may influence payers to question the use of spirometry for* ➤➤

screening at risk subjects, including those with a history of asthma.
D. K. L.
Lin K, Watkins B, Johnson T, et al: Screening for chronic obstructive pulmonary disease using spirometry: summary of evidence for the U.S. Preventive Services Task Force.
Ann Intern Med. 2008;148:535-543. ♦♦

High-Dose Inhaled Steroid Is Effective for Acute Asthma

SYSTEMIC corticosteroids are an important part of treatment for acute asthma exacerbations. However, several hours are probably required before improvement in airflow obstruction. Some reports have suggested that high-dose inhaled corticosteroids might be a faster-acting alternative. This study compared the kinetics of high-dose inhaled fluticasone with oral prednisone for patients with asthma exacerbations.

Of 45 adult patients seen in the emergency department for moderate asthma exacerbations, 39 were randomly assigned to inhaled fluticasone, 4,000 µg/d in 16 puffs; or oral prednisone, a single dose of 30 mg. Both groups received matching placebos. In addition to lung function tests, the two groups were compared for airway plasma protein exudation and markers of airway inflammation.

Both groups had significant improvement in symptoms by 24 hours. Both routes of administration were associated with progressive improvement in peak expiratory flow and FEV_1, with some decay after 24 hours. Both treatments were associated with improvement in sputum eosinophil count. This effect was more rapid in the inhaled fluticasone group, but the advantage was partially lost at 24 hours. The two groups had significant and similar decreases in sputum plasma proteins and blood eosinophil counts up to 24 hours. Eosinophil counts were unrelated to indices of plasmatic proteins.

For patients with moderate asthma exacerbations, high-dose inhaled fluticasone yields outcomes similar to those of standard oral prednisone. Responses are for the most part similar, although the effects of fluticasone on airway eosinophil counts suggest a local anti-inflammatory effect. Future studies should assess the effects of adding inhaled steroid to oral prednisone for treatment of asthma exacerbations.

COMMENT: *This study does show that very high doses of inhaled steroid can be used in the treatment of acute asthma. The results are similar to a single daily dose of oral corticosteroid. The topical actions of inhaled steroid were significant, and are probably the reason for the effect. The accompanying editorial (Eur Respir J. 2007;30:1035-1037) summarizes this and previous studies and is worth reading.*
B. E. C.
Belda J, Margarit G, Martínez C, et al: Anti-inflammatory effects of high-dose inhaled fluticasone versus oral prednisone in asthma exacerbations.
Eur Respir J. 2007;30:1143-1149. ♦♦

Pesticides Increase Atopic Asthma Risk in Farm Women

LITTLE is known about how pesticide exposure may contribute to the increased rates of asthma and other respiratory diseases among agricultural workers. The characteristics of farm women provide an opportunity to clarify the effects of agricultural exposures on respiratory outcomes, including both the protective effects of early farm exposure and the adverse effects of agricultural exposures. Pesticide exposure was evaluated as a risk factor for asthma among farm women.

The analysis included data on 25,814 farm women in two states. Each woman provided detailed information on exposure to specific pesticides. Cases of atopic and nonatopic asthma were identified on the basis of subject reports of physician-diagnosed asthma, with or without eczema or hay fever. Associations between farming exposures and asthma were assessed in polytomous logistic regression models.

A physician's diagnosis of asthma was reported by 2.7% of the women. Of the 702 cases, 282 were classified as atopic and 420 as nonatopic. Sixty-one percent of the women had grown up on a farm, and this was associated with a significant reduction in risk of atopic asthma: odds ratio (OR) 0.55. There was also a weaker protective effect against nonatopic asthma, OR 0.83.

Fifty-seven percent of the women had applied pesticides at some time in their lives. Pesticide exposure was related mainly to atopic asthma. Odds ratio for atopic asthma associated with any use of pesticides on the farm was 1.46, stronger for women who had grown up on farms. In contrast, women who had grown up on farms but did not apply pesticides were at lowest risk of atopic asthma: OR 0.41. Atopic asthma risk was associated with seven different insecticides, two herbicides, and one fungicide. The only exposure significantly related to nonatopic asthma was permethrin use on crops.

Exposure to pesticides appears to be an important risk factor for atopic asthma, but not nonatopic asthma, among farm women. The results support the protective effects of early-life farm exposure against asthma. However, they also suggest that pesticides, especially organophosphate insecticides, may be an significant asthma risk factor.

COMMENT: *Here is another study showing that patients with allergic disease who are exposed to persistent allergic stimuli have increasing symptoms with irritant fume exposure. This is another important epidemiologic observation regarding the occupational precautions of asthma.*
B. E. C.
Hoppin JA, Umbach DM, London SJ, et al: Pesticides and atopic and nonatopic asthma among farm women in the Agricultural Health Study.
Am J Respir Crit Care Med. 2008;177:11-18. ♦♦

REVIEWS OF NOTE

COMMENT: *This practice parameter provides a complete update on diagnostic testing, including IgE testing, both skin tests and in vitro tests, as well as cell-mediated testing and a review of allergens. This is a very useful resource.*
D. K. L.
Bernstein IL, Li JT, Bernstein DI, et al: Allergy diagnostic testing: an updated practice parameter.
Ann Allergy Asthma Immunol. 2008;100:S1-S141. ♦♦

COMMENT: *This is a well-written, succinct review of a complex topic. It provides more questions than answers, but such is the state of the art of chronic urticaria. The paper does provide a very nice, balanced discussion of autologous skin testing and the role of autoantibody in chronic urticaria.*
D. K. L.
Brodell L, Beck LA, Saini SS: Pathophysiology of chronic urticaria.
Ann Allergy Asthma Immunol. 2008;100:291-298. ♦♦

COMMENT: *This review focuses on defining the minimum threshold for clinical reactions to food allergens. The authors propose a food challenge protocol that begins with just a 3 µg dose and advances in semi-logarithmic increases every 20 minutes.*
S. A. T.
Crevel RWR, Ballmer-Weber BK, Tolzhauser T, et al: Thresholds for foods allergens and their value to different stakeholders.
Allergy. 2008;63:597-609. ♦♦

COMMENT: *Considering that non-allergic rhinitis is present in roughly one-third of patients referred to allergists for evaluation and treatment, surprisingly little research has focused on the mechanisms and treatment of this disorder. This excellent review focuses on mechanisms and mediators, calling for a more standardized approach to investigating the various nonallergic phenotypes.*
S. A. T.
Salib RJ, Harries PG, Nair SB, Howarth PH: Mechanisms and mediators of nasal symptoms in non-allergic rhinitis.
Clin Exp Allergy. 2008;38:393-404. ♦♦

COMMENT: *This review summarizes the utility of eNO measurements in children, including for helping establish correct diagnosis and for adjusting asthma management.*
S. A. T.
Pijnenburg MWH, De Jongste JC: Exhaled nitric oxide in childhood asthma: a review.
Clin Exp Allergy. 2008;38:246-259. ♦♦

COMMENT: *This review summarizes the attributes of rupatadine, a dual inhibitor of receptors for both histamine and platelet activating factor.*
S. A. T.
Mullol J, Bousquet J, Bachert C, et al: Rupatadine in allergic rhinitis and chronic urticaria.
Clin Exp Allergy. 2008;63(Suppl 87):5-28. ♦♦

COMMENT: *This excellent review ties together air pollution and the resultant oxidative stress the airway undergoes. Data are reviewed that support the possible mitigating role of oral dietary supplement strategies to decreases these effects.*
B. E. C.
Romieu I, Castro-Gilner F, Kunzil N, Sunyer J: Air pollution, oxidative stress and dietary supplementation: a review.
Eur Respir J. 2008;31:179-196. ♦♦

COMMENT: *Atopic dermatitis is one of the most vexing medical conditions. This very insightful article outlines an all-inclusive model of the pathogenesis of the disease, in which allergies may be only an epiphenomenon. In the model, genetic and environmental influences first create nonatopic dermatitis, which then invites allergic sensitization compounded by* S. aureus *infection, leading finally to autoimmune reactions against self proteins in the skin. It is a big mistake for patients to assume that only allergies are involved.*
R. J. M.
Bieber T: Atopic dermatitis.
N Engl J Med. 2008;358:1483-1494. ♦♦

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