AllergyWatch®

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

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"Egg-citing" News on Egg Oral Immunotherapy

EGG avoidance is currently the only approved therapy for egg allergy. But total avoidance is difficult to achieve; it also has a significant impact on quality of life for the family, while the risk of unintentional ingestion persists. Recent studies, mainly uncontrolled, have reported promising results with oral desensitization to food allergens. A randomized, double-blind trial of oral immunotherapy for egg-allergic children is reported.

The study included 55 children, median age 7 years, with a clinical history of egg allergy and elevated egg-specific IgE. Forty children were assigned a three-phase oral immunotherapy protocol, with a target of up to 2 g/d of egg white powder during the maintenance phase. The remaining 10 children served as placebo controls. Both groups underwent oral challenge with egg-white powder at 10 and 22 months.

Children who passed the 22-month challenge stopped oral immunotherapy and avoided egg for 4 to 6 weeks. They then performed oral challenges with egg-white powder and cooked egg at 24 months. Patients who passed this challenge were considered to have "sustained unresponsiveness"; they were instructed to add egg to their diet and re-evaluated at 30 and 36 months.

Thirty-five children passed the 10-month oral challenge and were considered desensitized, compared to none in the placebo group. Of 34 children who continued oral immunotherapy, 30 passed the 22-month challenge. Of 29 patients who underwent the 24-month challenge, including whole cooked egg, 11 passed the challenge. All children with sustained unresponsiveness at 24 months were still consuming egg at 20 and 36 months. Sustained unresponsiveness was more likely to be achieved by children who had small wheal reactions to skin-prick testing and increases in egg-specific IgG4 antibody.

In this trial, oral immunotherapy for pediatric egg allergy results in desensitization for 75% of children and sustained unresponsiveness to egg ingestion in 28%. Treatment is "relatively safe," with mainly mild reactions to oral egg dosing. Further studies are needed ➤➤

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

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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to elucidate the risks, optimal dosing regimen, patient selection, and post-desensitization strategies.

COMMENT: *Finally, a solution for some of our patients with persistent egg allergy! In this landmark multicenter study, oral egg immunotherapy given for 22 months to egg-allergic children between 5 and 18 years of age produced sustained unresponsiveness in a significant proportion (28%) of children. "Sustained unresponsiveness" was defined as the ability--after the course of immunotherapy and a month of egg avoidance--to consume 10 g of egg-white powder and a whole cooked egg without clinically significant symptoms. The approach was found to be relatively safe with largely mild reactions, although there was enough concern to deter completion of the study in approximately 15% of children. Notably, no one in the placebo group developed sustained unresponsiveness.*
C.D.
Burks AW, Jones SM, Wood RA, et al: Oral immunotherapy for treatment of egg allergy in children.
N Engl J Med. 2012;367:233-243. ♦♦

Thymic Stromal Lymphoprotein Is Upregulated in Asthma

INTERACTIONS between mast cells and the airway smooth muscle (ASM) play an important role in the development of airway physiologic disorders. Previous studies have suggested that thymic stromal lymphoprotein (TSLP), expressed by airway structural cells, may play an important role in mast cell-ASN interactions. This experimental study evaluated expression of TSLP in bronchial tissue from asthma patients, and assessed the expression and function of primary ASM and mast cells.

The researchers assessed TSLP expression in bronchial tissue from 18 patients with mild to moderate asthma, 12 patients with severe asthma, and 9 healthy controls. The results showed increased expression of TSLP in the ASM bundle in mild to moderate asthma, and in the epithelium in both asthma groups. Further studies showed expression and function of both TSLP and its receptor in mast cells and ASN. Activation of mast cells by TSLP led to increased production of various chemokines and cytokines, with no apparent effect on mast cell or ASM proliferation, survival, or contraction. Differences in the intensity of TSLP expression suggested an association with epithelial damage.

Asthma is associated with upregulated expression of TSLP by the bronchial epithelium and ASM. The study supports a role of TSLP in promoting mast cell synthesis of chemokines and cytokines, but not in other functional effects of crosstalk between mast cells and ASM. Studies of specific TSLP therapy in humans are underway.

COMMENT: *Mast cell infiltration ASM has been documented for 10 years. Recently, TSLP--a product of ASM and airway epithelium--has been implicated in activation of airway mast cells and production of Th2 cytokines. Similar to asthma phenotypes that may respond to anti-IL13 or anti-IL5, there may be phenotypes that respond to anti-TSLP, as proposed by the authors. We await development of targeted therapy for asthma. (Also see the accompanying editorial:* **Chest**. 2012;142:11-13.)
S.F.W.
Kaur D, Doe C, Woodman L, et al: Mast cell-airway smooth muscle crosstalk: the role of thymic stromal lymphopoietin.
Chest. 2012;142:76-85. ♦♦

Breastfeeding and Childhood Asthma Risk, Revisited

THERE are conflicting data on the protective effect of breast-feeding against childhood asthma, especially after early childhood. An additional important question is how breastfeeding affects asthma risk in children with atopy or a family history of allergy. A previous birth cohort study of breastfeeding and asthma risk in early childhood was updated with follow-up to age 6.

The analysis included 1,105 infants enrolled in the New Zealand Asthma and Allergy Cohort Study. Detailed information on parental questionnaires from birth to age 15 months was used to determine the duration of exclusive and any breastfeeding. In logistic regression models, breastfeeding was analyzed for associations with wheezing and current asthma at age 2 through 6 years. The analysis included adjustment for potential confounders and the potential modifying effect of atopy, based on skin prick testing.

On adjustment for confounders other than parental history of allergic disease, longer durations of exclusive breastfeeding were associated with a lower rate of current asthma at follow-up. For each additional month of exclusive breastfeeding, the risk of current asthma decreased by 17% at age 2, 12% at age 3, 11% at age 4, 12% at age 5, and 9% at age 6. Longer durations of any breastfeeding also reduced the risk of current asthma at age 2 through 5.

The protective effects of exclusive breastfeeding were greater in children with atopy: reductions in current asthma risk were 62% at age 4, 55% at age 5, and 59% at age 6. Breastfeeding was also linked to lower rates of current wheezing at age 2 and 3, but not at older ages.

Continued follow-up in this birth cohort supports the protective effect of breastfeeding--especially exclusive breastfeeding--against current asthma up to age 6. The association is modified by atopy, with atopic children deriving greater benefit after age 3. Breastfeeding does not appear to reduce the rate of viral wheezing in early childhood.

COMMENT: *This report of breastfeeding reducing early childhood asthma is at odds with other data showing equivocal results or possibly increased (later childhood) risk of asthma or food allergy. Data regarding breastfeeding's impact on allergic disease continue to be conflicting, but are likely to show temporary benefit.*
K.R.M.

Silvers KM, Frampton CM, Wickens K, et al: Breastfeeding protects against current asthma up to 6 years of age.
J Pediatr. 2012;160: 991-996. ♦♦

Do Allergic Patients Follow Environmental Control Measures?

ENVIRONMENTAL control measures are a standard part of management for patients with persistent allergic asthma. However, previous studies suggest that most patients don't follow these recommendations. Patients with indoor allergen sensitivities were surveyed regarding what environment control measures they would be willing to follow, and what changes they actually make.

The two-part study included patients with asthma and known sensitization to perennial aeroallergens. In telephone interviews, 60 patients rated their willingness to make specific environmental changes on a 1-to-5 Likert scale. Items with a mean score of 3 or higher were then used to form a practical set of recommendations, which was given to a separate group of 36 patients. Two months later, the second group of patients were surveyed regarding what environmental changes they had made.

The first group of patients rated 14 out of 18 proposed environmental control measures acceptable: unacceptable measures related to replacing upholstered furniture, eliminating pets, and installing a whole-house filtration system. In the second survey, 80.6% of patients said they had implemented at least one of the recommended measures. The most commonly followed measures were washing bedding in hot water, reducing home humidity, and encasing pillows and mattresses. Homeowners were more likely to make changes than renters.

The surveys lend insights into what environmental control measures patients with indoor sensitizations are willing to follow. Further studies should focus on ways of increasing adherence to recommendations. The authors suggest that in-person counseling would help to highlight the importance of environmental control measures and the consequences of not following them.

COMMENT: *Previous studies have shown that, for a variety of reasons, allergy patients do not perform environmental control interventions. This survey of asthmatic patients with perennial allergies investigated what environmental interventions they are willing to institute. As one would expect, patients who were homeowners were more likely to make environmental changes than renters. Many patients sensitized to animal dander preferred not to follow the recommendations related to pets. Since this was a phone survey, the authors suggest that taking the time to counsel patients may allow for discussion of possible consequences of continued exposure to allergens. This study reminds us about the importance of using practical recommendations that patients are willing to adhere to.*
V.H.-T.

Shatz M, Zeiger RS: Telephone-based environmental control interventions in asthmatic patients: what are patients willing to do?
Ann Allergy Asthma Immunol. 2012;109: 99-102. ♦♦

What Risk Factors Lead to Hospital Admission for Anaphylaxis?

AT a time of rising anaphylaxis rates, there are no consensus guidelines on when hospitalization is needed for patients with anaphylaxis. This study examined factors associated with admission among anaphylaxis patients seen at a community hospital. ➤➤

The 5-year chart review included 58 patients with anaphylaxis seen in the emergency department (ED) of one community-based hospital. Fifty-five percent were adults and 53% male; 59% of the reactions were from ingested and non-insect sting allergens. The hospitalization rate was 34%. Independent predictors of hospital admission were analyzed.

On univariate analysis, hospitalization risk increased with number of organ systems involved: 26% with two systems, 55% with three systems, and 75% with four systems. Risk was also increased for patients with gastrointestinal symptoms, 59% versus 24%; non-sting allergens as the cause of anaphylaxis, 50% versus 12.5%; and previous ED visits for anaphylaxis, 67% versus 30%. On logistic regression analysis, independent predictors of hospitalization were non-sting allergens and increasing number of organ systems.

Characteristics associated with a greater likelihood of hospitalization for anaphylaxis include multiple organ system involvement, especially the gastrointestinal system; history of previous ED visits for anaphylaxis; and reactions to foods and other non-sting allergens. The authors recommend a "low threshold for admission" in patients with these characteristics.

COMMENT: *While anaphylaxis is increasing, we need guidelines describing when patients should be hospitalized. This study in a community-based hospital found that approximately one-third of patients with anaphylaxis presenting to the ED were hospitalized. The presence of gastrointestinal symptoms, prior ED visit for anaphylaxis, anaphylaxis caused by an allergen other than insect stings, and involvement of two or more systems were risk factors for hospitalization. As physicians responsible for the care of these patients, allergists must be able to identify the patients who will be at risk for hospitalization, so that we can educate not only our patients but emergency room personnel as well.*
V.H.-T.

Steele R, Camacho-Halili M, Rosenthal B, et al: Anaphylaxis in the community setting: determining risk factors for admission.
Ann Allergy Asthma Immunol. 2012;109:133-136. ♦♦

Infant Wheezing Linked to Maternal Intestinal Flora

A growing body of evidence suggests that the intestinal flora in early life can affect the development of allergy and immune responses to infection. The maternal intestinal flora is known to affect the infant's flora, but no previous studies have evaluated its effects on allergic disease outcomes. Maternal intestinal flora was evaluated for associations with wheezing and eczema in infants.

Stool samples were collected from 60 pregnant women between 24 weeks' gestation and delivery for quantitative culture of the intestinal flora. The women also provided information on their health, and on the infant's health at 2 and 6 months of age. The maternal flora was analyzed as a predictor of infant wheeze and eczema by age 6 months. Atopic wheezing--a combination of these two outcomes--was analyzed as a secondary outcome.

There were significant associations between maternal flora and infant wheezing, after adjustment for breastfeeding, day care attendance, and maternal atopy. For total aerobes in maternal stool, the odds ratio for wheezing was 2.32 per 1 log increase. For enterococci, the odds ratio was 1.57 per 1 log increase. Maternal flora was unrelated to eczema or atopic wheezing.

The maternal flora during pregnancy appears to affect some allergic disease outcomes in infants. Higher maternal total aerobes and enterococci are related to a higher risk of wheezing, but not eczema, in infants. Further studies are needed to identify possible protective bacteria, as well as the effects of probiotic foods or supplements.

COMMENT: *The effect of intestinal bacterial flora on the incidence of allergic disease and asthma is a hot area. Prior studies in infants have focused on either maternal vaginal flora or colonization of the infant's gastrointestinal tract. The authors examined stool samples of pregnant women in their third trimester, showing a significant correlation between infant wheezing and maternal colonization with aerobic bacteria and enterococci. It remains to be determined whether altering maternal gut flora--using probiotics, for example--will help reduce wheezing incidence.*
S.A.T.

Lange NE, Celedon JC, Forno E, et al: Maternal intestinal flora and wheeze in early childhood.
Clin Exp Allergy. 2012;42:901-908. ♦♦

Ragweed Pollen Near Highways Is More Allergenic

POLLUTION may contribute to rising allergic disease rates. Although pollutants may act directly on the individual, they might also act indirectly via effects on pollen and pollen allergens. This field-based experiment compared the allergenicity of ragweed growing in areas close to and distant from traffic-related air pollution.

The investigators collected samples of pollen from ragweed growing alongside heavy-traffic and low-traffic roads in Italy, as well as from plants in vegetated areas in the Po river plain. Light microscopy and image analysis were performed to assess the percentage of subpollen particle-releasing grains (SPPGs). Whole allergenicity and allergen patterns were evaluated using immunochemistry and LC-MS/MS.

There were no significant differences in the percentage of SPPGs in pollen samples from roadside and vegetated areas. In all groups, after hydration, the mean percentage of SPPGs was less than 4%. In contrast, samples from high-traffic roads had greater whole allergenicity compared to samples from low-traffic roads and vegetated areas. For the latter two groups of samples, allergenicity was similar to that of commercial ragweed pollen (Allergon). The increased allergenicity of ➤➤

pollen sampled from busy roads was apparent on both quantitative and qualitative analyses.

The results show increased allergenicity of pollen from ragweed plants growing near heavily trafficked roads. Traffic-related increases in pollen allergenicity may contribute to the rising prevalence of ragweed sensitization and allergy. The authors discuss possible mechanisms by which traffic pollutants could be associated with increased allergenicity.

COMMENT: *It is generally accepted that there is an association between air pollution and pollen allergy, and most previous data point toward pollution as an adjuvant that may increase the incidence of allergic disease. This study shows that the allergenicity of ragweed pollen collected near highways is distinctly different than that of pollen collected in vegetated areas, away from highways. Perhaps air pollution's direct effect on pollen is more important that its direct effects on the human airway.*
S.A.T.
Ghiani A, Aina R, Asero R, et al: Ragweed pollen collected along high-traffic roads shows a higher allergenicity than pollen sampled in vegetated areas.
Allergy. 2012;67:887-894. ♦♦

Exhaled NO Doesn't Predict Response to Treatment for Asthma Exacerbations

THERE is continued debate over the role and importance of exhaled nitric oxide (eNO) monitoring in patients with asthma. This study compared responses to oral corticosteroid treatment for asthma exacerbations in patients with increased versus normal eNO levels.

The study included two groups of adults with moderate to severe asthma experiencing clinical exacerbations: 17 patients with abnormal eNO and 11 with normal eNO. All exacerbations required 8 to 10 days of tapering oral corticosteroid therapy. The patients were nonsmokers receiving moderate-dose inhaled corticosteroid and long-acting β_2-agonist, but not maintenance oral corticosteroid. Exacerbations occurred in the outpatient setting, associated with normal chest x-rays and white blood cell counts.

Responses to treatment for exacerbations were compared, including eNO, postnebulized albuterol/ipratropium spirometry, and the Asthma Control Test (ACT). The study included a total of 18 exacerbations in the high eNO group and 15 in the normal eNO group.

In baseline studies, the high and normal eNO groups were similar in terms of IgE, eosinophil count, body mass index, and ACT. The two groups had similar and significant decreases in FEV_1 during their exacerbations, followed by similar increases during recovery. Clinical and spirometric responses to oral corticosteroid were robust regardless of eNO values, including large central airway NO flux and peripheral small airway/alveolar NO concentration.

The results suggest that measuring eNO during asthma exacerbations does not predict the response to oral prednisone therapy. Good clinical responses, with return to baseline spirometric and clinical values, are obtained in patients with increased or normal eNO values.

COMMENT: *The use of eNO is gaining popularity, particularly for monitoring control in patients with persistent asthma. These authors describe a technique of measuring eNO at various flow-rates to determine the fraction from central and peripheral small airways. Surprisingly, although eNO has previously been reported to potentially predict eosinophilic inflammation, increased versus normal eNO during exacerbations could not forecast a patient's response to systemic corticosteroids in this study. Time and experience will help determine the role for eNO in monitoring our patients with persistent asthma and potentially predicting their response to treatment.*
S.M.F.
Geilb AF, Moridzadeh R, Singh D, et al: In moderate-to-severe asthma patients monitoring exhaled nitric oxide during exacerbation is not a good predictor of spirometric response to oral corticosteroid.
J Allergy Clin Immunol. 2012;129:1491-1498. ♦♦

Different Farm Factors Affect Different Allergic Disease Risks

PREVIOUS results from the GABRIEL Surveys have suggested that farm environments may protect against the development of childhood asthma and atopy. However, not all farms have the same effect--specific characteristics may be more important than the farm environment in general. Data from the GABRIEL Advanced Studies were used in an attempt to identify distinct farm characteristics responsible from the protective effect.

From nearly 80,000 school-aged children in rural Austria, Germany, and Switzerland responding to a recruiting questionnaire, a random sample of 8,419 children responded to a questionnaire providing detailed information on farm exposures. The analysis included blood samples and specific IgE measurements for 7,682 children. Associations between specific farm characteristics and asthma (broadly defined as symptoms, diagnosis, or any history of treatment) and other allergic/atopic disease outcomes were analyzed.

Rates of asthma and other allergic disease outcomes were significantly reduced for children living on a farm. Adjusted odds ratio were 0.68 for asthma, 0.43 for hay fever, 0.90 for atopic dermatitis, and 0.54 for atopic sensitization, compared to nonfarm children. Specific farm exposures responsible for the protective effect against asthma included cows, straw, and farm milk. Atopic dermatitis risk was decreased for children exposed to fodder storage rooms and manure. The factors included in the questionnaire, or the diversity of exposures, could not explain the protective effect of farms on hay fever or sensitization.

The new GABRIEL findings suggest that a "traditional farming" environment, with cows and cultivation, protects against the development of asthma, hay fever, and atopic sensitization. Early-life exposure to cows ➤➤

and straw and consumption of farm milk may explain the reduction in asthma risk, but not in hay fever or atopy. The protective effect of farms against atopic dermatitis is comparatively small.

COMMENT: *Supporters of the hygiene hypothesis have used the European farm environment as a model for early childhood exposure to the farming lifestyle to explain the protective effect of farms on the development of allergies and asthma. These researchers determined that specific types of farms and farm exposures could be important factors in the development of allergy in farm children. Interestingly, consumption of farm milk showed a strong inverse correlation with asthma, hay fever and atopy development, whereas exposure to straw or animals impacted asthma but not hay fever or atopy. The large numbers and the availability of blood samples documenting sensitization in this study help to overcome the limitation of questionnaire data collection. The type of farm does seem to impact the development of atopy.*
S.M.F.
Illi S, Depner M, Genuneit J, et al: Protection from childhood asthma and allergy in Alpine farm environments--the GABRIEL Advanced Studies.
J Allergy Clin Immunol. 2012;129:1370-1377. ♦♦

What's the Impact of Omalizumab for Uncontrolled Asthma?

SOME asthma patients do not achieve adequate disease control even with high-dose inhaled corticosteroids (ICS) and long-acting β_2-agonists (LABAs). The recombinant humanized anti-IgE antibody omalizumab is indicated as add-on therapy in this situation. The new study sought to clarify the clinical effects of omalizumab on important clinical outcomes for patients receiving maximal treatment for uncontrolled asthma.

A health insurance claims database was analyzed to identify 655 patients with uncontrolled asthma at baseline with at least 8 weeks of high-dose ICS and LABA use. All had available data for 12 months before and 12 months after initiation of treatment with omalizumab. Outcomes of interest were emergency department (ED) visits, hospitalizations, and corticosteroid use.

All three outcomes showed significant reductions after the start of omalizumab therapy. The percentage of patients with at least one asthma-related ED visit decreased from 21.4% in the baseline year to 11.0% with omalizumab. The percentage with asthma-related hospitalizations decreased from 25.0% to 14.8%. Dispensings of ICS decreased from 7.8 to 6.5, with 41.9% of patients achieving reductions. Dispensings of oral corticosteroids decreased from 5.0 to 3.6, with reductions for 53.3% of patients.

For patients whose asthma is uncontrolled by high-dose ICS and LABAs, omalizumab therapy has clinical benefits. In the year after starting omalizumab, these patients have nearly a 50% reduction in ED visits, about a 40% reduction in asthma hospitalizations, and reductions in corticosteroid use. The study provides "real world" confirmation of the benefits of omalizumab for this group of difficult-to-manage patients.

COMMENT: *This study links omalizumab to significant decreases in emergency department visits, hospitalizations, and use of corticosteroids--inhaled and oral--in patients with uncontrolled asthma using high-dose ICS and LABAs. Omalizumab is an effective therapeutic adjunct for this group of patients, providing distinct immunomodulatory activity not provided by conventional therapy. The pharmacoeconomics may therefore justify the expense of omalizumab for the benefits derived in terms of enhanced quality of life and impact on health care costs.*
C.C.R.
Lafeuille MH, Dean J, Zhang J, et al: Impact of omalizumab on emergency-department visits, hospitalizations, and corticosteroid use among patients with uncontrolled asthma.
Ann Allergy Asthma Immunol. 2012;109:59-64. ♦♦

Asthma Phenotypes--New Findings

THERE is increasing attention to the role of systemic inflammation in asthma, including its potential causes and its contribution to the clinical asthma phenotype. This study assessed systemic inflammation in patients with different airway inflammatory phenotypes of asthma.

The study included 152 adults with stable asthma and 83 healthy controls. Based on analysis of adequate sputum samples from 132 patients, asthma was classified as neutrophilic in 26 patients and nonneutrophilic in 106. The neutrophilic asthma group had evidence of increased systemic inflammation, compared to the nonneutrophilic asthma group and healthy controls. Median C-reactive protein (CRP) level was 5.0 mg/L in the patients with neutrophilic asthma, compared to 1.8 in both the nonneutrophilic asthma and control groups. Interleukin-6 (IL-6) levels were 2.1, 1.4, and 1.1 pg/mL, respectively. The neutrophilic asthma group also had a higher proportion of subjects with elevated CRP and IL-6.

Neutrophilic asthma was also associated with higher sputum levels of IL-8 and neutrophil elastase protein and increased expression of IL-8 receptors α and β. On multivariate analysis, sex, body mass index, statin use, and percent sputum neutrophils were independent predictors of $\log_{10}$ CRP. Predictors of $\log_{10}$ IL-6 were sex, body mass index, and $\%FEV_1$.

The results suggest increased systemic inflammation in asthma patients with neutrophilic airway inflammation. Plasma IL-6 levels are associated with worse clinical outcomes. While the causes and consequences are still unclear, the researchers conclude, "[I]t is likely that increased systemic inflammation is contributing to the pathophysiology of neutrophilic asthma."

THERE are continued questions regarding the clinical effects of bronchial remodeling in asthma, as well as how the remodeling process affects lung function. This study evaluated the characteristics of airway remodeling in asthma patients and its effects on short-term steroid responsiveness. ➤➤

The study included 63 consecutive patients with severe asthma and chronic airflow impairment, with postbronchodilator FEV_1 of less than 80% predicted. All underwent endobronchial biopsy including measurement of reticular basement membrane (RBM) thickness as a marker of airway remodeling. This and other characteristics were evaluated as predictors of the response to 10 days of treatment with intravenous methylprednisone, 1 mg/kg/d.

Thirty-eight percent of patients responded to steroid treatment, with more than a 15% improvement in FEV_1. Values for RBM thickness were 5.78 μm in the steroid-responsive group versus 7.60 μm for steroid-refractory patients. Along with lack of long-term oral steroid treatment, increased RBM thickness was the best predictor of steroid nonresponse. At a threshold of 7 μm, RBM thickness predicted steroid responsiveness with an area under the receiver operating characteristic curve of 0.747.

Among patients with severe asthma, a measure of airway remodeling predicts the short-term response to steroid treatment. The study identifies a severe asthma phenotype including chronic airflow obstruction, low steroid reversibility, and increased RBM thickness.

COMMENT: *Phenotyping and endotyping asthma may ultimately point us to appropriate treatment strategies. The phenotype of neutrophilic asthma appears to be associated with evidence of systemic inflammation, possibly mediated by IL-6. Patients with severe asthma--;with no predilection for characterization by cell types on bronchoalveolar lavage--;are less responsive to anti-inflammatory (steroid) treatment and have evidence of increased airway remodeling. Recognizing the systemic nature of asthma inflammation as well as understanding that treatments for this condition may not yield optimum results are the challenges we face with patients with these asthma phenotypes and endotypes. Further characterization and targeted therapy will probably be available, but not in the immediate future.*

S.F.W.

Wood LG, Baines KJ, Fu J, et al: The neutrophilic inflammatory phenotype is associated with systemic inflammation in asthma. **Chest**. 2012;142:86-93.

Bourdin A, Kleis S, Chakra S, et al: Limited short-term steroid responsiveness is associated with thickening of bronchial basement membrane in severe asthma. **Chest**. 2012;141:1504-1511. ♦♦

Interaction between Asthma and Lung Function Growth in Early Life

BY early school age, children with asthma already have reduced lung function. It's unclear whether this reduction in lung function is a cause or a consequence of asthma; the distinction may have important implications for understanding the origin of asthma and developing effective preventive measures. Data from a birth cohort study were used to analyze the longitudinal direction of the association between childhood asthma and decreased lung function.

The analysis included 411 children with a maternal history of asthma, drawn from the Copenhagen Prospective Studies on Asthma in Childhood. Spirometric data were available at birth for 98% of children and at age 7 in 77%. Methacholine bronchial responsiveness was assessed using forced flow-volume measurements with the children under sedation. The diagnosis of asthma was made using daily diary cards and regular clinic visits.

Fourteen percent of the children had asthma by age 7. In this group, significant airflow deficits were already present at neonatal evaluation--at 1 month of age, forced expiratory flow at 50% of vital capacity was reduced by 0.34 *z* score. The deficit progressed further during early childhood, with a 0.82 *z* score reduction in forced expiratory flow at 0.5 seconds at age 7.

Thus about 40% of the airflow reduction was already present at birth, with the rest developing during the clinical course of disease. Exposure to environmental tobacco smoke was linked to reduced airflow growth, but allergic sensitization was not. Methacholine responsiveness in the neonatal period was associated with later development of asthma.

Children with asthma at age 7 already show reduced lung function and increased bronchial responsiveness as newborns. The progressive nature of the lung function deficit raises the possibility of early clinical intervention. "Prenatal programming" should be considered in evaluating the origins and prevention of pediatric asthma, the researchers suggest.

COMMENT: *This very interesting study suggests that significant aberrations in lung function and bronchial hyperresponsiveness occur immediately after birth. The findings reinforce the role of the intrauterine environment as a predisposing factor for the development of asthma. This may improve understanding of the determinants of persistent asthma and lead to therapeutic interventions.*

B.E,C.

Bisgaard H, Jensen SM, Bønnelyke K: Interaction between asthma and lung function growth in early life. **Am J Respir Crit Care Med**. 2012;185:1183-1189. ♦♦

Intranasal Steroids Do Improve Conjunctival Symptoms--More Proof!

CONJUNCTIVAL symptoms are present in as many as 70% of patients with allergic rhinitis. However, ocular symptoms are often not addressed by treatment, even though patients rate such symptoms highly bothersome. Nasal corticosteroid treatment may help to reduce conjunctival symptoms, possibly through a naso-ocular reflex. This study evaluated the effects of nasal corticosteroid on conjunctival symptoms and neuro-inflammatory mediators in patients with allergic rhinoconjunctivitis.

The double-blind, placebo-controlled study included 26 patients with grass pollen allergy and symptoms of rhinoconjunctivitis. All underwent selective nasal grass pollen provocation (GPP) during grass pollen season; the challenges were performed after 2 weeks of ➤➤

treatment with nasal fluticasone furoate or placebo. Patients provided visual analog scale ratings of nasal and conjunctival symptoms. In addition, samples of tear fluid were collected for enzyme-linked immunosorbent assay measurement of neuroinflammatory mediators, including substance P and histamine.

During pollen season, fluticasone treatment was associated with a significant reduction in conjunctival symptom scores: -1.75, compared to no change with placebo. In addition, fluticasone was associated with no significant change (0.05) in conjunctival symptoms after GPP, compared to a 2.05-point increase with placebo. One hour after GPP, the values were -0.45 versus 0.05, respectively.

Levels of substance P in tear fluid after fluticasone were 44.11 pg/mg of protein, compared to 65.26 pg/mg with placebo. After GPP, histamine levels increased significantly in the placebo group, from 5.71 to 7.26 ng/mg protein. This compared to no significant change in the fluticasone group: 5.24 versus 6.77 ng/mg.

The findings add to the evidence that nasal corticosteroid therapy improves conjunctival symptoms during pollen season in patients with allergic rhinoconjunctivitis. The observed reduction in substance P levels in tear fluid supports the theory of a naso-ocular interaction. Substance P may play a significant role in allergic rhinoconjunctivitis.

COMMENT: *Although rhinoconjunctivitis affects many patients, ocular symptoms may not be treated as often as rhinitis symptoms. This study found that the use of intranasal steroids decreased symptoms both during the pollen season and after nasal grass provocation. In addition, the levels of substance P in tears were decreased after treatment with intranasal steroid. These findings remind us about the importance of anti-inflammatory medications in the treatment of patients with rhinoconjunctivitis, as decreasing the mediators at the level of nasal tissue decreases the opportunity for entry into the systemic circulation. We can further reassure our patients that treating the nasal symptoms will improve the ocular symptoms they frequently complain about.*
V.H.-T.

Callebaut I, Vandewalle E, Hox V, et al: Nasal corticosteroid treatment reduces substance P levels in tear fluid in allergic rhinoconjunctivitis.
Ann Allergy Asthma Immunol. 2012;109:141-146. ♦♦

H1N1 Infection Is More Frequent and Severe in Asthmatic Children

THE 2009 H1N1 influenza pandemic was associated with a sharp increase in hospital admissions among children with asthma, compared to previous data on hospitalizations associated with seasonal influenza. It is still unclear whether patients with asthma are more likely to be infected with H1N1 and whether the illness is more severe than in nonasthmatic patients. The authors compared H1N1 infection rates and illness severity in children with and without asthma.

The study included 180 children, aged 4 to 12 years, participating in a prospective study of the relationship between illness symptoms and viral infectivity. Patients were to provide eight consecutive weekly nasal mucus samples from September 5 through October 24, 2009. The study coincided with the H1N1 pandemic, providing an opportunity to study the impact of H1N1 infection and illness. The pandemic peaked between October 24 and 31, 2009.

The analysis included data on 161 children--95 with asthma and 66 without--who provided at least six nasal samples. Infection with H1N1 was documented in 41% of asthmatic children, compared to 24% of those without asthma: odds ratio 4.0. In contrast, the rate of human rhinovirus infection was 90% in both groups. Rates of other viral infections were similar as well: 47% and 41%, respectively.

H1N1 infection in asthmatic children was associated with a nonsignificant trend toward loss of asthma control: 28%, compared to 21% for human rhinovirus infection. Nearly one-fourth of episodes of loss of asthma control were associated with H1N1 infection.

The study documents nearly a twofold increase in the rate of H1N1 infection among children with asthma, compared to other viruses. This increased infection rate is also associated with increased symptom severity. The researchers underscore the need for annual influenza vaccination for children with asthma. They also call for further research into the mechanisms underlying the asthma-related increase in susceptibility to influenza infection.

COMMENT: *Previous studies have shown that H1N1 illness is quite severe in asthma. The study extends these observations to show that children with asthma have increased susceptibility to H1N1 infections. The findings are not only important from a mechanistic perspective, but also reinforce the need for flu vaccine in this age group.*
B.E.C.

Kloepfer KM, Olenec JP, Lee WM, et al: Increased H1N1 infection rate in children with asthma.
Am J Respir Crit Care Med. 2012;185:1275-1279. ♦♦

CLINICAL TIDBITS

SLIT Appears Safe in Pregnancy

DESPITE some reservations about safety, it is considered appropriate to continue subcutaneous immunotherapy during pregnancy. No previous studies have reported on the safety of sublingual immunotherapy (SLIT) in pregnant women.

This prospective study evaluated safety outcomes in 155 Indian women receiving SLIT during a total of 185 pregnancies. Adverse event rates were compared with two groups of controls not receiving immunotherapy: 85 women receiving budesonide 400 µg twice daily and 40 receiving rescue salbutamol. The women were allowed to select their preferred treatment; avoidance measures were recommended for all groups. ➤➤

At 6 years, the overall rate of pregnancy complications--including abortion, premature birth, and toxemia--was lower for women taking SLIT compared to the control groups. There were no complications, and no reactions to SLIT, among 24 women prescribed SLIT for the first time during pregnancy.

This initial study supports the safety of SLIT during pregnancy, plus appropriate avoidance, when indicated. Pregnancy complications may be even lower with SLIT than in pregnant women not receiving immunotherapy,

COMMENT: *In this study from India, 155 patients during 185 pregnancies received SLIT with either house dust mite or a mixture of up to five allergens: grass and tree pollen, insects (mosquito, cockroach and house fly), and dust mite. The indication for prescribing SLIT was the presence of nasobronchial symptoms with positive skin prick test to aeroallergens. Two control groups received budesonide or rescue salbutamol. The incidence of complications such as abortion, perinatal mortality, prematurity, toxemia, and congenital malformations was less with SLIT than in the control groups. It is to be noted that although this was a prospective study, patients were allowed to choose the mode of treatment. Also, some of the allergens used in the study may not be pertinent to the U.S. population.*
C.D.
Shaikh WA, Shaikh SW: A prospective study on the safety of sublingual immunotherapy in pregnancy.
Allergy. 2012;67:741-743. ♦♦

Prospective Study of Early Childhood Food-Allergic Reactions

THERE are few data on the rates, severity, characteristics, and response to allergic reactions to foods in young children with known food allergies. This issue was addressed in a prospective cohort study of infants and preschoolers allergic to milk and/or egg.

The study included 512 infants, aged 3 to 15 months, with "documented or likely" allergies to milk or egg. Over a median follow-up of 36 months, reactions occurred at an annualized rate of 0.81 per year; more than half of children (52.5%) experienced multiple reactions. Milk caused 42.3% of reactions, egg 21.0%, and peanut 7.9%. Causes of exposure included accidental ingestions, misread labels, and cross-contact. In about half of cases, people other than parents provided the foods.

In 11% of reactions to milk, egg, or peanut, the exposure was purposeful. Risk of reactions was higher for children with more food allergies and those with higher food-specific IgE. Epinephrine was used in only 30% of 134 severe reactions.

The findings help to clarify the causes and characteristics of allergic reactions in young children with diagnosed food allergies. Failure to use epinephrine in severe reactions is a major problem. The authors recommend improved education in this and other specific areas.

COMMENT: *Infants and young children are particularly vulnerable to accidental food allergy reactions, being neither able to discern ingredients nor adequately communicate symptoms to others. While our practices and professional and lay organizations have been working diligently over time to educate parents and the public about food-allergic reactions, this study underscores the distance yet to go. Educational materials used in this study are available at www.cofargroup.org*
K.R.M.
Fleischer DM, Perry TT, Atkins D, et al: Allergic reactions to foods in preschool-aged children in a prospective food allergy study.
Pediatrics. 2012;130:e25-e32. ♦♦

Hypertonic Saline and Viral-induced Wheezing

RHINOVIRUS is the main cause of acute episodes of wheezing in preschool children. Because of airway surface liquid dehydration and other factors, rhinovirus is associated with decreased mucus clearance. This randomized trial evaluated inhaled hypertonic saline as a treatment for acute wheezing in preschoolers.

The study included 41 children, mean age 32 months, seen in the emergency department for wheezing. Children received one inhalation of albuterol, followed by 4 mL of inhaled hypertonic saline 5% or normal saline. Both treatments were given with 0.5 mL albuterol: twice every 20 minutes in the ED then 4 times daily if the child was hospitalized.

Median length of stay was 2 days in the hypertonic saline group versus 3 days in the normal saline group. Hospital admission rates were 62% versus 92%, respectively. The two groups had similar and significant improvements in clinical severity scores.

Inhaled hypertonic saline can improve outcomes in preschool-aged children with acute wheezing. The authors discuss the several possible mechanisms by which this simple airway surface liquid hydration therapy may be beneficial.

COMMENT: *Lower respiratory symptoms caused by viral infection can be relatively resistant to typical asthma treatments of bronchodilators and corticosteroids, especially in children with symptoms severe enough to require hospitalization. Therapeutic measures that could enhance medication efficacy or improve the clinical course are much needed. That one option might be as straightforward as hypertonic saline via nebulizer is welcome news indeed!*
K.R,M.
Ater D, Shai H, Bar B-E, et al: Hypertonic saline and acute wheezing in preschool children.
Pediatrics. 2012;129:e1397-e1403. ♦♦

Predictive Value of AMP Challenge in Small Children

ADENOSINE 5'-monophosphate (AMP) provides a useful challenge test for asthma diagnosis. In children too young to perform spirometry, auscultation can be used to detect bronchial response to challenge, assessed as the "provocative concentration causing wheeze" (PCW). The AMP-PCW challenge in preschoolers was evaluated as a predictor of asthma diagnosis at 5 years' follow-up.

The study included 139 preschool-aged children undergoing AMP challenge in 2003-04. Of these, 82 had a positive response to AMP. In telephone interviews performed 5 years later, a physician diagnosis of asthma was reported for 55 of these children, for a positive predictive value of 67%.

Of 57 children with a negative preschool AMP challenge, 51 did not have asthma 5 years later, for a negative predictive value of 90%. Predictive value was greater for children undergoing AMP challenge at older ages, increasing from 50% at age 2 or 3 years to 83% at 6 or 7 years.

Performing AMP-PCW challenge in preschoolers has good predictive value for the presence of asthma 5 years later. The authors suggest that the test has sensitivity and specificity of 90% for the diagnosis of preschool asthma.

COMMENT: *Bronchial challenge with AMP can be performed in children too young for pulmonary function testing, with results interpreted by auscultation. In challenging pediatric cases, AMP-PCW testing could provide an additional tool to assess the likelihood of persistent asthma, beyond traditional clinical indicators.*
K.R.M.

Cohen S, Avital A, Hevroni A, et al: Predictive value of adenosine 5'-monophosphate challenge in preschool children for diagnosis of asthma 5 years later.
J Pediatrics. 2012;161:156-159. ♦♦

CXCR2 Antagonist Shows Promise in Neutrophilic Asthma

SEVERE asthma is associated with increased numbers of airway neutrophils, the clinical significance of which is unclear. A new selective CXCR2 receptor, SCH 527123, was evaluated for efficacy in reducing airway neutrophils in patients with severe asthma.

The randomized trial included 34 patients with severe asthma, associated with a sputum total cell count less than 10 x 10^6/g and neutrophils greater than 40%. Patients received 4 weeks of treatment with oral SCH 527123, 30 mg/d, or placebo. Sputum neutrophil percentage decreased by a mean of 36.3% with SCH 527123, compared to a 6.7% increase with placebo. There was also a 14% reduction in blood neutrophil count, although this recovered promptly after the end of treatment.

Adverse events were similar between groups. The CXCR2 antagonist was associated with fewer mild exacerbations, 1.3 versus 2.25, with a trend toward improvement in Asthma Control Questionnaire score. There were no significant effects on FEV_1, sputum myeloperoxidase, IL-8, or elastase.

CXCR2 antagonist therapy may have benefits in severe asthma, including a reduction in sputum neutrophils. Treatment is safe and well-tolerated, with possible improvements in asthma control.

COMMENT: *CXCR2 chemokines such as IL-8 are important for attracting and activating neutrophils, and therefore inhibiting the CXCR2 receptor is an attractive strategy for treating neutrophilic asthma. This study's main objective was to assess safety of an oral CXCR2 antagonist called SCH 527123. This once-daily treatment was generally well-tolerated and resulted in dramatic decreases in sputum and blood neutrophils. Further studies powered to assess its effect on asthma control are needed.*
S.A.T.

Nair P, Gaga M, Zervas E, et al: Safety and efficacy of a CXCR2 antagonist in patients with severe asthma and sputum neutrophils: a randomized, placebo-controlled clinical trial.
Clin Exp Allergy. 2012;42:1097-1103. ♦♦

Low Serum Adiponectin Predicts Future Asthma Risk in Women

CROSS-SECTIONAL data have suggested an inverse association between serum adiponectin levels and asthma in women. Data from a long-term follow-up study were used to examine the direction of the longitudinal association between serum adiponectin and incident asthma.

The researchers analyzed 10-, 15-, and 20-year follow-up data on 1,450 women, mainly premenopausal, from the Coronary Artery Risk Development in Young Adults (CARDIA) study. Two separate analyses were performed to examine associations of serum adiponectin at year 15 with incident asthma at year 20; and prevalent asthma at year 10 with serum adiponectin at year 15.

On multivariate analysis, women in the lowest tertile of serum adiponectin (less than 7 mg/L) at year 15 were at double the risk of incident asthma at year 20: odds ratio 2.07. This association was especially strong among current smokers. As a predictor of incident asthma, serum adiponectin was even stronger than body weight. Prevalent asthma in year 10 did not predict serum adiponectin level in year 15.

Women with low serum adiponectin are at increased risk of developing future asthma. The results raise the possibility that interventions to increase adiponectin levels might help to prevent asthma in women, especially smokers.

COMMENT: *This very interesting study suggests that low adiponectin levels, independent of weight, predict an increased incidence of asthma. Adiponectin is a protein that inhibits proinflammatory cytokines. This may be an explanation for the refractory asthmatic par-* ➤➤

adigm seen in adult female asthma patients who are obese, and may provide a future target for therapeutic intervention.
B.E.C.
Sood A, Qualls C, Schuyler M, et al: Low serum adiponectin predicts future risk for asthma in women.
Am J Respir Crit Care Med. 2012;186:41-47. ♦♦

What Diet Is Best for Children with EoE?

EOSINOPHILIC esophagitis (EoE) is chronic, immune-mediated gastrointestinal inflammatory disorder that appears increasingly common. Food-elimination diets produce a clinical response, supporting the role of allergic sensitization to foods. This study compared the outcomes of three different diet therapies for pediatric EoE.

The retrospective analysis included 98 children with EoE seen at a specialized center for eosinophilic disorders. Fifty percent received an amino acid-based elemental diet, 27% received a six-food elimination diet (SFED), and 23% received a directed elimination diet based on the results of skin prick testing (SPT). The children had no response to proton pump inhibitors and were not treated with glucocorticoids; all had 2 consecutive endoscopic biopsy specimens to monitor the response to dietary therapy.

Clinical remission was achieved in 96% of children with the elemental diet, 81% with the SFED, and 65% with the SPT-directed elimination diet. Odds ratios for postdiet remission with the elimination diet were 5.6 versus the SFED and 12.5 versus the SPT-directed elimination diet; the latter two diets were not significantly different from each other. Based on 116 single-food reintroductions, negative predictive values of SPT for remission were 40% for milk, 56% for egg, 64% for soy, and 67% for wheat.

Although all 3 diets are effective for pediatric EoE, the elemental diet appears to have the highest response rate. The results of SPT are not useful as the sole basis for recommending dietary therapy; an SPT-directed diet is no more effective than an empiric SFED.

COMMENT: *Current recommendations for treatment of EoE include food elimination based on allergy prick and/or patch tests. In a retrospective analysis of 98 patients, these Cincinnati researchers found no significant difference in therapeutic efficacy for skin test-directed diets compared to an empiric SFED. Interestingly, they also found that neither of these diets was as helpful as an elemental diet. However, patient selection could have been a factor, since the data were collected retrospectively. We are still challenged by EoE which appears to be increasing, particularly in children--for whom food allergen triggers may play an important role in pathogenesis.*
S.M.F.
Henderson CJ, Abonia JP, King EC, et al: Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis.
J Allergy Clin Immunol. 2012;129:1570-1578. ♦♦

Add-on Montelukast for Elderly Asthma Patients

ELDERLY patients with asthma have decreased adherence to treatment, increased risk of drug adverse events, and increased fear of using corticosteroid therapy. This study explored the effects of add-on montelukast therapy in elderly patients with asthma.

The 2-year study included 512 severe asthma patients over 60 years old. Asthma was considered well-controlled in 13.9% of patients, partly controlled in 41.2%, and uncontrolled in 44.9%. In the first year, patients were treated with inhaled corticosteroids (ICS) and long-acting beta-agonists (LABAs). In the second year, two-thirds of patients received add-on therapy with montelukast; the remaining one-third remained on ICS and LABAs alone.

In the first year, median percentage of asthma-free days increased from 50.1% to 61.2%, while days with short-acting beta-agonist use decreased from 52.2% to 46.8%. In the second year, for patients receiving add-on montelukast, asthma-free days further increased to 78.4% while days without short-acting beta-agonists decreased to 39.5%. At 2 years, the median number of asthma exacerbations decreased from 1.6 to 1.2 per year with the addition of montelukast.

In older adults with severe asthma, adding montelukast to ICS/LABA therapy has clinical benefits, including improved asthma control. However, add-on montelukast does not resolve severe asthma control problems in this group of patients.

COMMENT: *Asthma in the elderly is underdiagnosed and undertreated. Comorbid conditions, lack of coordination, and visual and cognitive problems may contribute to poor adherence with inhaled steroids therapy. This study shows that adding montelukast to inhaled steroids in elderly asthma patients leads to enhanced control. Montelukast is associated with a decline in asthma exacerbations and increases in asthma-free days and medication adherence, but does not prevent severe asthma.*
C.C.R.
Bozek A, Warkocka-Szoltysek B, Filipowska-Gronska A, Jarzab J: Montelukast as add-on therapy to inhaled corticosteroids in the treatment of severe asthma in elderly patients.
J Asthma. 2012;49:530-534. ♦♦

Is Bronchial Thermoplasty a Critical Success?

BRONCHIAL thermoplasty (BT) provides a new alternative for treatment of severe persistent asthma. The authors report the indications for and outcomes of BT in a patient with debilitating asthma.

The patient was a 42-year-old woman with a long history of severe persistent asthma, with shortness of breath on mild exertion and difficult performing everyday activities. Despite good compliance with treatment, she had poor asthma control, decreased lung function, and frequent exacerbations. The patient underwent ➤➤

3 BT treatments, each of which was followed by worsening shortness of breath and other symptoms. Hospitalization was required because of partial lung collapse after the second treatment. After the third treatment, medical ICU admission was needed because of dyspnea and wheezing.

However, at 6 months' follow-up, the patient's respiratory condition was significantly improved. She reported increased activity and less shortness of breath and was also able to begin pulmonary rehab. Pulmonary function testing actually showed a small decrease in FEV_1 after BT: from 1.06 to 0.96 L (36% to 32% predicted).

This case report shows the clinical benefits of BT in a patient with severe persistent asthma. Although the potential benefits are "dramatic and unmistakeable," posttreatment exacerbations are possible. Close monitoring, with possible hospitalization, is essential.

COMMENT: *The authors provide a case report to illustrate the success of BT as a "minimally invasive" technique in severe intractable asthma. Bronchial thermoplasty is accomplished by bronchoscopy with fulguration of the airway smooth muscle and requires monitoring in the hospital. Patients often require several admissions, including ICU care for worsening respiratory symptoms. Limited prospective studies show no difference in FEV_1 or airway responsiveness. However, there are significant improvements in morning peak expiratory flow, asthma control and quality of life, percentage of symptom = free days, exacerbations, rescue medication use, and functional capacity. Thus BT may have a place in the treatment of severe intractable asthma that is uncontrolled by conventional therapy.*
C.C.R.
Mahajan AK, Hogarth DK: Bronchial thermoplasty: therapeutic success in severe asthma associated with persistent airflow obstruction.
J Asthma. 2012;49:527-529. ♦♦

REVIEWS OF NOTE

COMMENT: *This is a thorough, up-to-date, international asthma guideline focused exclusively on pediatrics. It clearly points out areas requiring more research.*
S.A.T.
Papadopoulos NG, Arakawa H, Carlsen K-H, et al: International consensus on (ICON) pediatric asthma.
Allergy. 2012;67:976-997. ♦♦

COMMENT: *Hypersensitivity pneumonitis is poorly defined. However, we should not miss its characteristic presentations: exposure to a known offending antigen, symptoms 4 to 8 hours after exposure, positive precipitating antibodies, inspiratory crackles, recurrent episodes of symptoms, and weight loss. This review summarizes the utility of imaging, antigen testing and bronchoalveolar lavage, as well as what's not known about this condition that presents with dyspnea. We shouldn't miss this condition when a patient comes to us with it.*
S.F.W.
Lacasse Y, Girard M, Cormier Y: Recent advances in hypersensitivity pneumonitis.
Chest. 2012;142:208-217. ♦♦

COMMENT: *This well-written case-based review highlights the approach to differential diagnosis of rash in a 50-year-old woman on multiple medications. Drug-related rash is a common clinical problem, and this article succinctly summarizes evidence-based evaluation and diagnosis. It also presents a critical appraisal of the features of selected severe cutaneous reactions that make up 90% of those reactions (DRESS, SJS-TEN and AGEP). The color pictures and helpful tables make this a handy bedside reference.*
C.D.
Stern RS: Exanthematous drug eruptions.
N Engl J Med. 2012;366:2942-2501. ♦♦

COMMENT: *This is an excellent update of recently published literature regarding asthma.*
B.E.C.
Kazani S, Israel E: Update in asthma 2011.
Am J Respir Crit Care. 2012;186:35-40. ♦♦