AllergyWatch®

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

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Only First-Year Pet Exposure Affects Adult Sensitization

THE effects of keeping a pet at home on the risk of allergies in children remain unclear. Most studies of this issue have focused on early childhood allergic disease. This study used a life-course approach to evaluate the effects of lifetime dog and cat exposure on the risk of allergic sensitization to those animals at age 18.

The researchers contacted 18-year-old participants who were enrolled in the Detroit Childhood Allergy Study between 1987 and 1989. Annual interviews during childhood and follow-up interviews at age 18 were used to assess exposure to indoor dogs and cats--ie, animals that spent more than half their time indoors.

The analysis considered pet exposure in different time periods, including the first year, specific age ranges, and cumulative lifetime exposure. Allergic sensitization was defined as dog- or cat-specific IgE levels of 0.35 kU/L or greater.

Of 566 participants followed up at age 18, 17.8% were sensitized to dog and 20.5% were sensitized to cat. For male participants, exposure to an indoor dog during the first year of life reduced the risk of dog sensitization at age 18 by half: relative risk (RR) 0.50, compared to males without this exposure. This association was not significant for females overall. However, early dog exposure was associated with decreased risk for both males and females born by cesarean section: RR 0.33.

For both sexes, first-year exposure to an indoor cat was associated with a decreased risk of cat sensitization at age 18: RR 0.52. Neither type of sensitization was affected by exposure during subsequent age ranges, or by cumulative lifetime exposure. Household exposure to dogs or cats during the first year of life is associated with a reduced risk of sensitization to these pets at age 18. Exposure after age 1, including cumulative exposure throughout childhood and adolescence, has no effect on sensitization risk. The authors suggest further studies evaluating the effects of pet exposure during smaller time windows during the first year of life. ➤➤

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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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COMMENT: *The protective effect of cat or dog exposure in the first year of life is not a new concept. However, this study shows a significant reduction in risk of sensitization at age 18 in patients exposed to the pet in their first year of life. Cumulative exposure had no effect on later sensitization. The accompanying editorial by Erwin et al (*Clin Exp Allergy. *2011;41:920-922) nicely summarizes the literature, including the finding that it is difficult to "undo" the tolerance developed in the first year. When our (older than 12 months) patients' parents ask if obtaining a pet will prevent allergy to the pet, the answer is "No."*
S.A.T.

Wegienka G, Johnson CC, Havstad S, et al: Lifetime dog and cat exposure and dog- and cat-specific sensitization at age 18 years.
Clin Exp Allergy. 2011;41:979-986. ♦♦

'Star Wars' Treatment Approach Works for Dust Mite Rhinoconjunctivitis

ALLERGIC diseases are characterized by an "unbalanced" Th1/Th2 immune response to allergens, skewed toward Th2 cells. Approaches based on re-establishing a "balanced" response to allergen with a more Th1-like phenotype might provide a useful alternative to allergy treatment. Incorporating new knowledge on the role of Toll-like receptors (TLRs) and nanotechnology techniques, this study evaluated an allergen-free immune modulator for the treatment of perennial rhinoconjunctivitis.

The investigational treatment consisted of TLR9 agonist packed into virus-like nanoparticles (CYT003-QbG10). This approach was evaluated in a phase IIb randomized trial including 299 patients with perennial allergic rhinoconjunctivitis and allergy to house dust mite. Patients were randomly assigned to receive six weekly injections of CYT003-QbG10, 0.5 or 1.0 mg, or placebo. Ocular and nasal allergy symptoms and use of relief medications were assessed in double-blind fashion.

There were no serious adverse events; the main adverse effects were mild to moderate injection site reactions. Rhinoconjunctivitis symptoms were significantly reduced in patients receiving the 1.0 mg dose of CYT003-QbG10, compared to placebo: scores on a standardized average combined symptom and medication score were 0.31 versus 0.52, respectively. The higher dose of CYT003-QbG10 also led to improvement in quality of life, with scores of 0.71 versus 1.21 on the mini rhinoconjunctivitis quality of life questionnaire. On conjunctival provocation testing, allergen tolerance increased by a median of 10-fold in the high-dose CYT003-QbG10 group, compared to no change in the placebo group.

Treatment with nanoparticles loaded with TLR9 ligands effectively reduces symptoms of allergic rhinoconjunctivitis caused by dust mite allergy. This allergen-free immune modulator could open the way to a safe, fast-acting alternative to conventional desensitization for allergic diseases. Further study is needed to determine the exact mechanism of efficacy.

COMMENT: *Our understanding of the importance of the influence of innate immunity--particularly TLRs--on allergic responses has been an important advance in the past decade. Even more recently, nanotechnology has become a critical tool in both basic research and medical treatment. This study employs both advances by packaging a THR9 agonist into "virus-like" nanoparticles. In a phase IIa trial, weekly injectable treatment exhibited dose-dependent efficacy for dust mite allergy. This non-allergen-specific immunomodulatory treatment is somewhere between traditional immunotherapy and conventional medication treatment. Stay tuned.*
S.A.T.

Klimek L, Willers J, Hammann-Haeni A, et al: Assessment of clinical efficacy of CYT003-QbG10 in patients with allergic rhinoconjunctivitis: a phase IIb study.
Clin Exp Allergy. 2011;41:1305-1312. ♦♦

CRTH2 Antagonist Improves Asthma Control

CHEMOATTRACTANT receptor homologous molecule expressed on Th2 cells (CRTH2) is a G-protein-coupled receptor that mediates activation of Th2 lymphocytes, eosinophils, and basophils by prostaglandin D_2 (PGD_2). Previous studies have suggested that CRTH2 may contribute to asthmatic airway inflammation and hyperresponsiveness. The oral CRTH2 antagonist OC000459 selectively inhibits PGD_2. This trial assessed the clinical efficacy of OC000459 for treatment of moderate persistent asthma.

The randomized controlled trial included 132 steroid-free adult outpatients with moderate persistent asthma. Patients were randomly assigned to 28 days of treatment with oral OC000459, 200 mg twice daily, or placebo. Change in prebronchodilator FEV_1 was assessed, along with sputum eosinophil count.

On analysis of the full study population (including noncompliant patients), there was no significant difference in mean change in FEV_1: 7.1% in the OC000459 group and 4.3% in the placebo group. The difference became significant in a per-protocol analysis including 55 patients assigned to OC000459 and 52 to placebo: 9.2% versus 1.8%, respectively. In both analyses, OC000459 was associated with significant improvement on the Standardized Asthma quality-of-life questionnaire: mean difference from placebo was 0.29 in the full study population and 0.37 in the per-protocol population. Nighttime symptom scores were improved as well.

Geometric mean sputum eosinophil count decreased from 2.1% to 0.7% in the OC000459 group, although this was not significant compared to placebo. Adverse events were similar between treatments, although the OC000459 group had a lower rate of respiratory infections.

The CRTH2 antagonist OC000459 leads to improvements in lung function and clinical outcomes in steroid-free patients with moderate persistent asthma. The study supports the hypothesis that CRTH2 receptors are involved in asthmatic symptoms, airflow limitation, and airway inflammation. Further clinical evaluation of OC000459 for asthma treatment is warranted.

COMMENT: *Following a decade of biotech industry targets that, applied to asthma, were mostly "flame-outs," there are now new approaches to therapeutic targeting in asthma. Included in these is the importance of PGD_2-dependent activation of Th2 cells, eosinophils, and basophils. CRTH2 is the receptor that mediates this activation, and this study explored the effect of a twice-daily oral CRTH2 antagonist on asthma. The positive effects on symptoms, lung function, and sputum eosinophils suggest that this therapy has promise. It remains to be seen whether the CRTH2 antagonist confers an advantage over traditional therapeutics such as inhaled corticosteroids, long-acting beta agonists, and leukotriene modifiers.*
S.A.T.

Barnes N, Pavord I, Chuchalin A, et al: A randomized, double-blind, placebo-controlled study of the CRTH2 antagonist OC000459 in moderate persistent asthma.
Clin Exp Allergy. 2011;41:1356-2222. ♦♦

Bariatric Surgery Leads to Improved Asthma Outcomes

THERE are still many questions about the relationship between obesity and asthma. Obese asthma patients may not respond as well to standard asthma treatment. This study evaluated the outcomes of bariatric surgery in a group of obese patients with asthma.

The prospective study included 23 asthma patients undergoing bariatric surgery for severe obesity--mean body mass index 51. The researchers performed a cross-sectional comparison with 21 nonasthmatic patients undergoing bariatric surgery. They also analyzed 12-month postoperative outcomes in the asthma patients.

Most of the patients were women; mean age at bariatric surgery was 43 years. At baseline, the asthma patients had lower FEV_1, lower forced vital capacity, and lower numbers of lymphocytes in bronchoalveolar lavage fluid.

At 12 months' follow-up, the asthma patients' mean body mass index had decreased to 37.5. Clinical asthma measures improved after bariatric surgery: mean asthma control score decreased from 1.55 to 0.74, while asthma quality of life score improved from 4.87 to 5.87. Methacholine PC_{20} improved from 3.9 to 7.28; the change in airway responsiveness was greater for patients with normal baseline IgE levels. Bariatric surgery was also followed by an increased proportion of lymphocytes in bronchoalveolar lavage fluid and increased production of cytokines by CD4+ T cells.

For obese patients with asthma, bariatric surgery is followed by improved asthma outcomes. Changes include improvement in airway hyperresponsiveness, but only in patients with initially normal serum IgE levels. Based on the dichotomous effects on airway physiology and T cell function, obesity-related asthma may be a distinct phenotype requiring a different approach to treatment.

COMMENT: *The interrelationship of asthma and obesity is noteworthy. This study reports the effects of bariatric surgery on asthma, compared to a nonasthmatic control group having the same surgery. Asthmatic patients experienced improvements in asthma symptom scores and quality of life scores; interestingly, their methacholine responsiveness improved by almost twofold. Improvements were greater in patients with normal IgE levels compared to those with elevated levels, indicating yet another phenotypic distinction in asthma.*
R.J.M

Dixon AE, Pratley RE, Forgione PM, et al: Effects of obesity and bariatric surgery on airway hyperresponsiveness, asthma control, and inflammation.
J Allergy Clin Immunol. 2011;128:508-515. ♦♦

Single-Dose Omalizumab Brings Lasting Improvement in Refractory CIU

SOME patients with chronic idiopathic urticaria do not have a good response to initial treatment with nonsedating H_1-antihistamines. Studies have suggested that anti-IgE therapy might be beneficial in CIU. This phase 2 trial evaluated the effects of omalizumab in patients with CIU refractory to H_1-antihistamines.

The placebo-controlled dose-ranging study included 90 U.S. and German patients with continued CIU symptoms--urticaria activity scores over 7 days (UAS7) of 12 or higher--despite treatment with H_1-antihistamines. Patients were randomly assigned to receive placebo or a single subcutaneous dose of omalizumab: 75, 300, or 600 mg. Efficacy outcomes were assessed through 4 weeks after treatment, and safety was monitored for another 12 weeks.

The two higher doses of omalizumab yielded significant improvement in CIU symptoms. Mean reduction in UAS7 was -19.9 in the 300 mg dose group and -14.6 in the 600 mg group, compared to -6.9 in the placebo group. Weekly hive and itch scores also improved. For all outcomes, improvements were noted after 1 to 2 weeks. Adverse events were similar for the omalizumab and placebo groups.

In patients with CIU that does not respond to H_1-antihistamines, omalizumab yields symptomatic improvement. A single 300 or 600 mg dose produces significant and lasting reductions in CIU symptoms, compared to placebo. Further studies, including longer treatment durations, are needed.

COMMENT: *Omalizumab, the anti-IgE monoclonal antibody, has proven efficacy against asthma. Other uses are being studied. In this report, patients with CIU for more than 3 months were given a single dose of omalizumab and scored for the following 4 weeks. Omalizumab doses of 300 and 600 mg improved CIU symptom scores for at least 4 weeks. The study was too short to say how long the control would be maintained, or if later doses would prolong the benefit. It is tempting to speculate that omalizumab's effect on CIU might be due to some molecular effect other than lowering IgE levels.*
R.J.M.

Saini S, Rosen KE, Hsieh H-J, et al: A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H_1-antihistamine-refractory chronic idiopathic urticaria.
J Allergy Clin Immunol. 2011;128:567-573. ♦♦

Lebrikizumab Shows Benefits in Asthma Patients with IL-13 Profile

IN patients with asthma, variations in expression of interleukin-13 (IL-13) may contribute to clinical variability in response to treatment with inhaled glucocorticoids. This raises the possibility that patients showing a pretreatment profile consistent with IL-13 activity might benefit from treatment with the anti-IL-13 monoclonal antibody lebrikizumab.

This hypothesis was tested in a randomized trial including 219 adults with asthma who had a poor clinical response to inhaled glucocorticoid therapy. Mean baseline FEV_1 was 65% of predicted, despite a mean inhaled glucocorticoid dose of 580 µg/d. Eighty percent of patients were taking a long-acting beta-agonist.

One group of patients received lebrikizumab, 250 mg sc once monthly for 6 months, while the other group received placebo. Outcomes of interest were change in prebronchodilator FEV_1 through week 12 and asthma exacerbations through week 24. Subgroup analyses included serum levels of periostin-- a matricellular protein induced by IL-13 that may play a role in airway remodeling. Fifty-two percent of patients had a high periostin level before treatment.

At 12 weeks, the mean increase in FEV_1 was greater in the lebrikizumab group: 9.8% versus 5.3%. The difference was even greater among patients with a high baseline periostin level: 14.0% versus 5.8%, respectively. In contrast, for patients with low periostin at baseline, the increase was 5.1% with lebrikizumab versus 3.5% with placebo. There was a nonsignificant trend toward a lower exacerbation rate in the lebrikizumab group, with no change in asthma symptoms.

Patients in the lebrikizumab group had a higher rate of musculoskeletal side effects: 13.2% versus 5.4% in the placebo group. Lebrikizumab was also associated with a greater decline in exhaled nitric oxide, especially in the high-periostin subgroup.

Anti-IL-13 therapy with lebrikizumab may improve lung function for adult asthma patients who do not respond to inhaled glucocorticoids. This treatment appears most beneficial in patients with high pretreatment periostin levels, consistent with IL-13 activity. Larger studies are needed to confirm the findings.

COMMENT: *It's often stated that asthma is a heterogeneous disease. In molecular terms, one of the differentiating features of uncontrolled asthma is the level of periostin, which is secreted by bronchial epithelial cells into the underlying matrix and which probably contributes to airway remodeling. Periostin is induced by, and is a surrogate marker for, IL-13. This paper reports on the effects of the IL-13 inhibitor lebrikizumab in uncontrolled moderate-to-severe asthma. There were two interesting points. First, patients with high periostin levels responded better than the low periostin group, foretelling a time when therapy might be preselected based on phenotype. Second, positive effects were seen on FEV_1 but not on asthma symptom score, rescue medication use, or nocturnal awakening. This raises questions about the usefulness of subjective symptom scores for following asthma.*
R.J.M.

Corren J, Lemanske RF, Hanania NA, et al: Lebrikizumab treatment in adults with asthma.
N Engl J Med. 2011;365:1088-1098. ♦♦

Early-life Rhinovirus Illness Linked to Decreased Lung Function

VIRAL respiratory infections during early life, including respiratory syncytial virus (RSV) and rhinovirus (RV), contribute to the development of childhood asthma. However, there are few data on how specific viral infections affect later lung function. This study evaluated the effects of specific viral causes of early-life wheezing illness on pulmonary function later in childhood.

A cohort of 238 children at high risk of asthma and allergic disease were followed up from birth to age 8. When early-life wheezing illnesses occurred, diagnostic studies were performed to identify the causative viruses. The children underwent annual lung function studies using spirometry or impulse oscillometry.

On mixed-effect linear regression analysis, early-life wheezing illness caused by RV was associated with significant reductions in spirometric values, including FEV_1, $FEV_{0.5}$, and FEF_{25-75}. Early-life RV illness was also associated with more negative reactance at 5 Hz on impulse oscillometry. In contrast, RSV and other viral causes of wheezing were unrelated to pulmonary function measures later in childhood. Children with asthma at age 6 to 8 had significantly lower values for FEF_{25-75}.

In children at high risk of asthma, early-life wheezing illness caused by RV appears to have the greatest impact on pulmonary function later in childhood, compared to other respiratory viruses. Further studies into the mechanisms of these associations are needed, and may aid in developing new approaches to intervening in the progression from early childhood wheezing to asthma.

COMMENT: *Viral-induced wheezing illnesses have been shown to predispose the young child to have recurrent wheezing and lower lung function during childhood. Although RSV has previously been recognized as increasing the risk of asthma, these researchers report that it is really early RV illness that was of prognostic significance for lower lung function. This was a carefully designed, prospective study that not only measured viral serology during illnesses, but also measured lung function, either by spirometry or by impulse oscillometry. The data suggest that young children with wheezing during RV infections clearly are predisposed to have asthma.*
S.M.F.

Guilbert TW, Singh AM, Danov Z, et al: Decreased lung function after preschool wheezing rhinovirus illnesses in children at risk to develop asthma.
J Allergy Clin Immunol. 2011;128:532-538. ♦♦

Algorithm Improves Asthma Management during Pregnancy

THE goal of asthma management in pregnant women is to control the mother's disease while minimizing drug exposure to the fetus. Studies of exhaled nitric oxide (eNO) to guide asthma therapy in nonpregnant women have yielded mixed results. This trial compared the use of eNO versus symptoms for guiding asthma management during pregnancy.

The Australian study included 220 pregnant, nonsmoking women with asthma, seen at two antenatal clinics before 22 weeks' gestation. Patients were randomly assigned to undergo monthly treatment adjustments guided by clinical symptoms or eNO. In the intervention group, inhaled corticosteroid (ICS) therapy was adjusted upward if eNO was greater than 29 ppb or downward if eNO was less than 16 ppb. If eNO was not elevated, symptoms were managed with the minimum dose of ICS plus a long-acting β_2-agonist. Exacerbations and other outcomes were assessed in masked fashion.

The total rate of moderate to severe exacerbations was 0.288 in women assigned to eNO-guided therapy versus 0.615 in the symptom-adjusted group. The eNO algorithm was associated with an incidence rate ratio of 0.496, with a number needed to treat of 6. It was also associated with improved quality of life scores and a lower neonatal hospitalization rate: 8% versus 17%.

For pregnant women with asthma, a management algorithm based on eNO measurement appears superior to symptom-based treatment adjustments. The study algorithm reduces the rate of moderate or severe exacerbations during pregnancy by about one-half. Further studies are needed to confirm these results in routine prenatal care and other settings.

COMMENT: *There are few prospective clinical trials dealing with treatment options for asthmatic pregnant women. This study is a welcome addition. The authors present an algorithm using eNO for adjusting ICS doses and Asthma Control Test-7 for adjusting long-acting β-agonist dose. These measures were clinically beneficial in the form of fewer exacerbations, improved quality of life, and fewer infant hospitalizations. This algorithm may be helpful in justifying appropriate use of controller medications to our obstetric colleagues. In addition, we may be able to administer a "Goldilocks" dose to our patients. There may be justification for measurement of eNO after all.*
S.F.W.

Powell H, Murphy VE, Taylor DR, et al: Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial.
Lancet. 2011; 378: 983-990. ♦♦

Administrative Data Can Help Improve Asthma Outcomes

THERE is growing interest in the use of administrative data to improve asthma outcomes in large patient populations. This may be done by reaching out to patients with uncontrolled disease and by identifying providers with inadequate quality of care. This article describes efforts to use administrative, survey, and telephone data to assess asthma severity, impairment, risk, and quality of life among asthma patients in the Kaiser Permanente population. ➤➤

The most commonly used administrative marker of persistent asthma is the Healthcare Effectiveness Data and Information Set (HEDIS) definition, based on number and types of asthma visits and medication dispensing. The Kaiser Permanente experience suggests that the HEDIS criteria provide a good surrogate for persistent asthma based on patient surveys. As such, this criteria set has been used to guide asthma population management and quality of care assessments for two consecutive years.

The population management approach assesses asthma impairment based on numbers of short-acting β-agonist (SABA) canisters dispensed, along with validated mail or phone surveys. Risks related to asthma control have been assessed using pharmacy data on SABA canisters, in addition to oral steroid prescriptions and data on past emergency visits. An asthma medication ratio--calculated by dividing controlled medications by controllers plus SABAs--has proven to be related to improved asthma outcomes, and thus is a useful indicator of the quality of asthma care.

These are examples of the use of administrative data plus patient surveys to assess asthma severity, impairment, risk, and quality of care in large, "real world" patient populations. Some of these approaches may be relevant to smaller populations, such as those in individual or group practices. The article includes specific criteria for identifying uncontrolled, undertreated, or higher-risk asthma.

COMMENT: *It is becoming very common for health care insurers (including federal and state governments) to demand measures of quality of care. Asthma is often one of the first diseases to be included, along with diabetes, hip replacement, and hypertension. In Minnesota, the state-mandated quality of care measurement for asthma is action plans for all asthmatics. This has many shortcomings, not the least of which is that it only measures a process, not outcomes. Action plans are unnecessary for patients with intermittent asthma, and their use hasn't been proven to improve outcomes. This paper reviews Kaiser Permanente's use of indicators that correlate better with outcomes. The so-called medication ratio measure may be worth considering. These are some of the things doctors have to know these days. Compensation and credentialing may depend on which measures are chosen. Be alert: Big Brother is most certainly watching.*
R.J.M.
Schatz M, Zeiger RS: Improving asthma outcomes in large populations.
J Allergy Clin Immunol. 2011;128:273-277. ♦♦

Specific and Functional IgE Found in Intrinsic Asthma

INTRINSIC ASTHMA was originally described as asthma not triggered by environmental exposures--ie, asthma without allergy. Like atopic asthma, intrinsic asthma is associated with a Th2 bias and mucosal IgE production. However, the specificity and functionality of IgE in intrinsic asthma remain unknown. Local IgE responses to dust mite were evaluated in patients with intrinsic asthma.

The study included 29 patients with intrinsic asthma, who had negative results on skin prick testing to dust mite and other common allergens; along with 24 allergic asthma patients and 25 controls. Sputum samples were obtained for enzyme-linked immunosorbent assay measurement of specific IgE antibodies to *Dermatophagoides pteronyssinus* (Der p) and to the recombinant major allergens rDer p1 and rDer p2. Allergen-specific whole-lung challenges were performed in a subgroup of participants in each group. Basophil activation testing was performed to examine IgE functionality to trigger effector cells, based on surface expression of CD203c.

Patients with intrinsic asthma had increased total IgE and Der p-specific IgE in sputum, compared to nonatopic controls. However, the intrinsic asthma group had no immediate asthmatic response to Der p exposure, which produced immediate bronchoconstriction in all allergic asthma patients. In vitro studies showed that sputum Der p-specific IgE from patients with intrinsic asthma recognized the major Der p1 and Der p2 allergens. These specific IgE antibodies also triggered activation of blood basophils from atopic donors.

The study confirms production of IgE in intrinsic asthma, including IgE that specifically recognizes Der p antigens. However, even though this IgE is specific to major allergens and shows functionality to activate effector cells, it does not lead to clinical responses to Der p exposure. The results suggest that patients with intrinsic asthma lack a "second signal" promoting IgE-mediated asthmatic responses via FcεRI.

COMMENT: *This is another very important study linking local IgE production to persistent asthma. Local IgE production is particularly important in understanding the endotype expression of what has been previously thought to be intrinsic asthma. Follow-up research may provide groundbreaking information.*
B.E.C.
Mouthuy J, Detry B, Sohy C, et al: Presence in sputum of functional dust mite-specific IgE antibodies in intrinsic asthma.
Am J Respir Crit Care Med. 2011;184:206-214. ♦♦

Low Vitamin D Linked to EIB in Kids with Asthma

LOW serum vitamin D levels have been associated with reduced lung function in adults, and with asthma onset and severity in children. This study looked at the association between vitamin D and severity of exercise-induced bronchoconstriction (EIB) in a sample of asthmatic children.

Forty-five Italian children with intermittent asthma underwent measurement of 25-hydroxyvitamin D. Vitamin D status was then evaluated for associations with the pulmonary function response to a standardized exercise challenge. ➤➤

Vitamin D level was in the "desirable" range of at least 30 to 40 ng/mL in only 11.1% of the asthmatic children and 11.9% of healthy controls. Rates of vitamin D deficiency--less than 20 mg/dL--were 51.1% and 42.4%, respectively. The rate of positive responses to exercise challenge (ΔFEV_1 10% or greater) was 46.7%

Serum 25-hydroxyvitamin D level was positively correlated with both the forced vital capacity and FEV_1 responses to exercise challenge. Mean 25-hydroxyvitamin D level was 16.2 ng/mL for children with a positive response to exercise challenge compared to 23.4 ng/mL for those with a negative response. None of the small group of children with sufficient vitamin D status had EIB.

The study shows a high rate of lower than desirable vitamin D levels among asthmatic and nonasthmatic children, even in a Mediterranean country. Children with asthma and low vitamin D levels have decreased lung function and increased reactivity to exercise. Interventional trials examining the effects of vitamin D supplementation on relevant outcomes in asthma patients with low vitamin D status are urgently needed.

COMMENT: *There has been an explosion of evidence regarding the association of vitamin D and poor asthma control and increased asthma symptoms. This is yet another study that shows the pervasive effect of low vitamin D levels (89% of the cohort) and increasing symptoms of EIB. I have surely changed my practice patterns to measure 25-OH vitamin D in the majority of patients with asthma that is difficult to control.*
B.E.C.

Chinellato I, Piazza M, Sandri M, et al: Serum vitamin D levels and exercise-induced bronchoconstriction in children with asthma.
Eur Respir J. 2011;37:1366-1370. ♦♦

CLINICAL TIDBITS

Do Patients with CUA Need Extensive Lab Tests?

PATIENTS with urticaria or angioedema lasting 6 weeks or longer are considered to have chronic urticaria/angioedema (CUA). There is ongoing debate over the recommended laboratory evaluation for this group of patients.

The researchers analyzed the results of laboratory testing in a random sample of 356 patients with CUA seen at their allergy clinic from 2001 to 2009. Most of the patients were female and white, mean age 48 years. Most had urticaria, alone or with angioedema. Of the total 1,872 laboratory tests ordered, 17% were abnormal. This included a 34% of complete blood counts and 9.4% of complete metabolic panels.

Thirty patients had abnormal laboratory results prompting further tests. The additional tests led to a change in management for just 1 patient (who had a history of hypothyroidism).

In CUA patients referred to an allergy clinic, abnormal laboratory test results are relatively common, but rarely lead to changes in clinical management. The authors suggest antihistamine dose adjustment before ordering extensive laboratory tests for patients with CUA.

COMMENT: *In patients with CUA, the etiology is seldom identified. This study of the tests that are "routinely" ordered in patients with CUA shows low numbers of abnormal tests found among the cohort. When abnormal findings led to a more extensive workup, only one patient benefited from a change in management. This study supports our current practice of performing a focused laboratory evaluation. The authors suggest limiting laboratory tests and considering an increase in the dose of a second-generation antihistamine (up before four times conventional dosing).*
V.H.-T.

Tarbox JA, Gutta RC, Radojicic C, Lang DM: Utility of routine laboratory testing in management of chronic urticaria/angioedema.
Ann Allergy Asthma Immunol. 2011;107:239-243. ♦♦

When Using an EpiPen, Do You Need to Count to 10?

TO ensure adequate delivery of epinephrine during an anaphylactic attack, patients are instructed to hold the EpiPen in place "while slowly counting to 10." This study looked at how duration of injection affected the amount of epinephrine absorbed into muscle tissue.

The experimental study used marbleized beef to simulate human muscle tissue. Samples were injected with EpiPens for durations of 1 to 10 seconds. The total amount of epinephrine released was assessed by weighing the specimens with a highly precise scale.

At all injection times--including 1 second--at least 95.9% of the epinephrine was absorbed into the beef. There was no duration at which the percentage of epinephrine absorbed was less than that observed with a 10-second injection time.

When using an EpiPen, longer injection times do not seem to increase the amount of epinephrine injected or absorbed into muscle. Even if the needle is removed after 1 second, the patient may still receive most of the epinephrine dose.

COMMENT: *This study questions a practice that we have long followed in the treatment of anaphylaxis. The authors looked at the time epinephrine needs to reach muscle. This study, while performed on dead animal tissue, reminds us about the need for epinephrine to be delivered under pressure. There was no linear relationship between the time spent holding the epinephrine in place and amount of epinephrine actually injected. The authors challenge us to consider that holding the device for 1 second may be as effective as holding it for 10 seconds. This is particularly important, since many studies have reported that both patients and physicians incorrectly used the epinephrine autoinjector. We may consider reassurance for patients who are concerned that they "didn't remember" to count to 10 during* ➤➤

an allergic emergency.
V.H.-T.
Baker TW, Webber CM, Stolfi A, Gonzalez-Reyes E: The TEN study: time epinephrine needs to reach muscle.
Ann Allergy Asthma Immunol. 2011;107:235-238. ♦♦

In Utero Tobacco Smoke Exposure Increases Persistent Asthma Risk

PAST studies of how exposure to tobacco smoke during gestation affects childhood respiratory health have yielded inconsistent results. Few studies have evaluated possible differences by racial/ethnic group.

The parents of 295 Mexican, Puerto Rican, and black children with asthma, aged 8 to 16 years, were asked about tobacco use by the mother while she was pregnant with the child. In utero tobacco exposure was evaluated for association with persistent asthma and other clinical outcomes.

Children with persistent asthma were more likely than those with intermittent asthma to have a history of in utero exposure to tobacco smoke: odds ratio (OR) 3.57. There was no association with current exposure, and no modifying effect of exposure to the parents' smoking during the first 2 years of life. In utero exposure was also associated with increased rates of nocturnal symptoms, OR 2.77; daily symptoms, OR 2.73; and emergency department visits, OR 3.85.

In this sample of black and Latino children, in utero exposure to tobacco smoke is linked to an increased risk of persistent asthma. Encouraging pregnant women to quit smoking may help to reduce the incidence of persistent asthma among children in these minority groups.

COMMENT: *While no one would argue that in utero tobacco smoke exposure has deleterious effects, the unfortunate reality is that some children are still subjected to this exposure. Are population differences likely to influence asthma outcomes among children of mothers who smoked during their pregnancies? With genetic variance and asthma predisposition in certain groups, differences are possible. While this may be true, in this assessment, all mothers who smoked during pregnancy increased the odds of their children having persistent asthma!*
K.R.M.
Akuete K, Oh SS, Thyne S, et al: Ethnic variability in persistent asthma after in utero tobacco exposure.
Pediatrics. 2011;128:e623-e630. ♦♦

Transient Tachypnea of Newborn Responds to β -Agonist

INFANTS with transient tachypnea of the newborn (TTN) are at risk of respiratory distress related to persistent fetal lung fluid. This randomized trial evaluated the safety and efficacy of treatment with inhaled salbutamol for infants with TTN.

Fifty-four infants with TTN, gestational age 34 to 39 weeks, were assigned to blinded therapy with nebulized salbutamol (32 infants) or normal saline (22 infants). The first dose of salbutamol was followed by significant improvements in median TTN clinical score: from 8 to 2.5, compared to 7 at both times in the placebo group. Salbutamol also led to improvements in respiratory rate, fraction of inspired oxygen, and level of respiratory support.

Posttreament pH, partial pressure of arterial oxygen, and partial pressure of arterial carbon dioxide were all better in infants assigned to salbutamol. They left the hospital a median of 2 days sooner than infants in the placebo group.

The results support the use of inhaled β_2 = agonist therapy for infants with TTN. Salbutamol leads to improved clinical outcomes and laboratory values, with no adverse events.

COMMENT: *Transient tachypnea of the newborn has been associated with future asthma risk in children, in studies over the past decade. Response of TTN to β-agonist therapy suggests greater support for this association.*
K.R.M.
Armangil D, Yurdakök M, Korkmaz A, et al: Inhaled beta-2 agonist salbutamol for the treatment of transient tachypnea of the newborn.
J Pediatrics. 2011;159:398-403. ♦♦

Capsaicin Nasal Spray Relieves Nonallergic Rhinitis Symptoms

SINUS Buster is a proprietary homeopathic product containing Capsaicin annum and Eucalyptol, marketed for the treatment of "sinus symptoms." The efficacy of this capsaicin-containing nasal spray was evaluated in patients with nonallergic rhinitis (NAR).

The randomized trial included 42 adult patients with rhinitis and a "significant component" of NAR. One group used the Sinus Buster nasal spray twice daily for 2 weeks; the other group received placebo.

Sinus Buster was associated with significant improvement in nasal symptom, including total and individual symptom scores. Average time to first relief was 52.6 seconds, with significant improvement in congestion, sinus pain and pressure, and headache. The effects on nasal congestion and sinus pain were still present at 60 minutes. There were no apparent adverse effects and no rebound congestion or olfactory problems.

This placebo-controlled trial supports the efficacy of a capsaicin-containing nasal spray for patients with congestion and other symptoms of NAR. Used daily for 2 weeks, this product provides safe, sustained symptom relief.

COMMENT: *This provocative study is the first controlled trial demonstrating that intranasal capsaicin, used continuously over 2 weeks, ameliorates rhinitis symptoms in individuals with significant NAR syndromes. Treatment works rapidly and without* ➤➤

adverse events. The findings are significant as there is an urgent need for more focused and effective therapy for this common and often frustrating syndrome.
C.C.R.
Bernstein JA, Davis BP, Picard JK, et al: A randomized, double-blind, parallel trial comparing capsaicin nasal spray with placebo to subjects with significant component of nonallergic rhinitis.
Ann Allergy Asthma Immunol. 2011;107:171-178. ♦♦

Good Correlation between IMMULITE and ImmunoCAP for Food Allergens

THE ImmunoCAP system provides quantitative measures of specific IgE antibody levels for diagnosis of food allergy. This study compared ImmunoCAP measurements of food-specific IgE levels with levels measured using the IMMULITE autoanalyzer.

Both the ImmunoCAP and IMMULITE systems were used to measure IgE antibody levels in serum samples from 328 children with food allergies. All had known IgE positivity (greater than 0.1 kU/L) for egg white, 120 patients; cow's milk, 135 patients; and/or peanut, 304 patients.

For all three allergens, the ImmunoCAP and IMMULITE measurements were highly correlated, with r^2 values of 0.95 for egg white, 0.93 for cow's milk, and 0.95 for peanut. Ratios of IMMULITE to ImmunoCAP values were 4.85, 2.33, and 1.86, respectively. The two sets of specific IgE levels for milk and peanut were not significantly different for children who had either a positive or negative food challenge. (The sample size was too small to perform a similar analysis for egg white.)

The ImmunoCAP and IMMULITE measurements of specific IgE levels to egg white, milk, and peanut are highly correlated with each other. The differences between the two systems are limited, although the IMMULITE values average two to five times higher.

COMMENT: *This provocative study highlights the finding that specific IgE levels to egg white, milk and peanut determined by the IMMULITE and ImmunoCAP systems are highly correlated. Differences between the two systems are minimal, although the IMMULITE values are a mean of 2- to 5-fold higher. The findings are instructive for the practicing allergist: we need to be aware of the differences in results between the two systems in interpretation of food protein allergen sensitivities.*
C.C.R.
Hamilton RG, Mudd K, White ME, Wood RA: Extension of food allergen specific IgE ranges from the ImmunoCAP to the IMMULITE systems.
Ann Allergy Asthma Immunol. 2011;107:139-144. ♦♦

Add-on Tiotropium for Severe Persistent Asthma

SOME patients with severe asthma have persistent symptoms and airway obstruction despite maximal treatment with an inhaled corticosteroid (ICS) plus long-acting β_2-agonist (LABA). The long-acting anticholinergic agent tiotropium was evaluated for use as a bronchodilator in this clinical situation.

The trial included 107 patients with uncontrolled severe asthma despite high-dose ICS/LABA therapy. In randomized, crossover fashion, patients received add-on therapy with tiotropium, 5 or 10 µg/d, or placebo. Each treatment lasted 8 weeks.

Compared to placebo, peak FEV_1 was 139 mL higher with the 5 µg/d dose of tiotropium and 170 mL higher with the 10 µg/d dose. Trough FEV_1 values at the end of the treatment period were also higher with tiotropium versus placebo: 86 and 113 mL, respectively. Tiotropium was also associated with higher daily home peak expiratory flow, but no improvement in asthma symptoms.

The differences between tiotropium doses were not significant. Adverse events were similar, except for a higher rate of dry mouth with tiotropium 10 µg/d.

For patients with severe persistent asthma, adding once-daily tiotropium to maximal ICS/LABA therapy leads to significant improvements in lung function. The results add to previous studies suggesting benefits of tiotropium in asthma patients.

COMMENT: *Options for add-on treatment are limited for patients with severe persistent asthma that is not controlled with ICS and LABAs. This proof-of-concept study showed significant benefit when tiotropium, a long-acting inhaled anticholinergic agent, was added to the regular maintenance regimen. Interestingly, although there was some improvement in peak expiratory flow with the higher dose of tiotropium, there were three times more complaints of dry mouth and essentially no additional improvement in FEV_1. It won't be surprising to see maintenance asthma controllers with ICS, LABA, and tiotropium soon.*
S.M.F.
Kerstjens HAB, Disse B, Schröder-Babo W, et al: Tiotropium improves lung function in patients with severe uncontrolled asthma: a randomized controlled trial.
J Allergy Clin Immunol. 2011;128:308-314. ♦♦

Oral Steroid Shows Benefits in Chronic Rhinosinusitis

ANTIBIOTICS are not completely effective in patients with chronic rhinosinusitis (CRS). Corticosteroids might have benefits in controlling the inflammatory response. This randomized trial evaluated the use of oral methyprednisolone in children with CRS. ➤➤

The study included 48 children, aged 6 to 17 years, with clinically and radiologically confirmed CRS. In addition to oral amoxicillin/clavulanate, patients were assigned to receive oral methylprednisolone or placebo for 30 days. Methylprednisolone was given for 15 days, with a tapering dose thereafter.

Both treatments led to reduced symptom and sinus CT scores. However, methylprednisolone was associated with greater improvement in CT scores, total rhinosinusitis symptoms, and individual symptoms of nasal obstruction, postnasal discharge, and cough. Rates of abnormal CT scans at the end of the study were 14% with methylprednisolone versus 48% with placebo. The methylprednisolone group also had a nonsignificantly lower rate of clinical relapse: 25% versus 43%.

Adding oral methylprednisolone to antibiotics has clinical benefits for children with CRS. Symptoms and CT scores are both significantly reduced for children receiving the systemic corticosteroid, compared to placebo.

COMMENT: *This was a relatively small study, but it showed that using systemic corticosteroids as an adjunct to antibiotic treatment for children with CRS was significantly more effective in reducing symptoms including nasal congestion, postnasal drainage and cough, and it also improved CT imaging scores. Although the 15-day course of corticosteroids is somewhat longer than what we usually use, the response to treatment with systemic corticosteroids added to the antibiotic was impressive.*
S.M.F.

Ozturk F, Bakirtas A, Ileri F, Turktas I: Efficacy and tolerability of systemic methylprednisolone in children and adolescents with chronic rhinosinusitis: a double-blind, placebo-controlled randomized trial.
J Allergy Clin Immunol. 2011;128:348-352. ♦♦

Air Cleaners Help Asthmatic Kids Living with Smokers

DESPITE advice to eliminate smoking, some children with asthma are still exposed to secondhand smoke at home. This randomized trial evaluated two interventions for inner-city children with asthma living with a smoker.

The study included 126 inner-city children with asthma who lived in a home with a smoker. Children were assigned to receive air cleaners with high-efficiency particulate air (HEPA) filters; air cleaners plus visits with a health coach; or, as a control, a waiting period followed by an air cleaner.

Both air cleaner groups showed significant reductions in indoor particulate matter (PM) concentrations: mean $PM_{2.5}$ concentration decreased by -19.9 $\mu g/m^3$ with air cleaner only and -16.1 $\mu g/m^3$ with air cleaner plus health coach. For $PM_{2.5-10}$, the values were -8.7 and =10.6 $\mu g/m^3$, respectively. The air cleaners did not reduce air nicotine and urine cotinine levels, however. Both intervention groups also had increased symptom-free days.

For inner-city asthmatic children living with smokers, air cleaners with HEPA filters can reduce indoor PM levels and increase symptom-free days. However, even with the addition of a health coach, air cleaners do not prevent secondhand smoke exposure.

COMMENT: *This interesting study found that using HEPA filter air cleaners in homes of inner-city asthmatic children exposed to second-hand smoke resulted in a 14% to 18% improvement in asthma symptom-free days. There was no additional benefit with nurse-counselor home visits. There was documented improvement in PM levels in homes with air cleaners, but no significant change in nicotine levels. This could be explained by the fact that the HEPA filters, which are good for filtering PM, are not particularly good for filtering out nicotine, even with charcoal filters. Interestingly, the authors point out that the improvement in symptom-free days compares to the 20% improvement seen in studies of added leukotriene receptor antagonists in similar populations, although the cost of the air cleaners is less. Something to ponder....*
S.M.F.

Butz AM, Matsui EC, Breysse P, et al: A randomized trial of air cleaners and a health coach to improve indoor air quality for inner-city children with asthma and secondhand smoke exposure.
Arch Pediatr Adolesc Med. 2011;165:741-748. ♦♦

Early FSC Has Benefits after Asthma Exacerbation

FOR patients with acute asthma exacerbations, prompt treatment with inhaled anti-inflammatory agents might have clinical benefits. This retrospective study evaluated the outcomes of early treatment with fluticasone propionate/salmeterol in a single inhaler (FSC) after asthma exacerbations.

Insurance claims data were used to identify 14,861 patients receiving FSC after an initial asthma exacerbation. Treatment with FSC was classified as early in 10,793 patients and late in 4,068. Outcomes were compared for propensity-matched cases and controls: 3,555 in both groups. Mean follow-up was about 2 years.

Early FSC treatment was associated with a longer time to first asthma-related exacerbation: hazard ratio 0.82. Short-acting β-agonist prescriptions were 3.3 with early FSC versus 3.6 with late FSC. Early FSC was associated with higher outpatient pharmacy costs but lower emergency department costs.

Early treatment with FSC after asthma exacerbation may lower the risk of future exacerbations. Total asthma related costs are similar with early vs late FSC treatment.

COMMENTS: *In this novel study, earlier use of FSC following asthma exacerbation was related to reduced risk of future asthma exacerbation and decreased utilization of rescue medications. Such results have been demonstrated for other combination therapy--ie, formoterol and budesonide--which have been the state of the art in GINA guidelines for the past 10 years.* ➤➤

Could combination therapy with FSC provide maintenance as well as rescue? Further studies are needed to test this postulate.
C.C.R.
Hagiwara M, Delea TE, Stanford RH: Retrospective comparison of early versus late treatment with fluticasone propionate/salmeterol after an asthma exacerbation.
J Asthma. 2011;48:721-728. ♦♦

Can MMP Measurement Determine Aspirin Sensitivity?

MATRIX metalloproteins (MMPs) have been shown to contribute to progressive tissue changes in asthma. They may also play a pathogenetic role in chronic rhinosinusitis (CRS) and nasal polyposis (NP). Expression of MMP-9 and its inhibitor, tissue inhibitor of metalloproteinase-1 (TIMP-1), was studied in NP patients with and without aspirin sensitivity.

The study used nasal polyp tissue from 6 aspirin-sensitive and 6 aspirin-tolerant patients undergoing sinus surgery for CRS with NP. Tissues from patients with CRS without NP were studied for comparison. Expression of MMP-9 and TIMP-1 was measured by immunofluorescence technique.

Aspirin-sensitive CRS/NP patients had reduced expression of TIMP-1, compared to aspirin-tolerant CRS/NP patients and controls with CRS without NP. Patients with aspirin-sensitive CRS/NP also had an increased MMP-9/TIMP-1 ratio. However, there were no significant differences in MMP-9 expression.

In patients with aspirin sensitivity, lower expression of TIMP-1 may promote the effects of MMP-9 expression, thus favoring tissue remodeling and inflammation. Further studies of the role of MMP-9 and TIMP-1 in nasal polyp formation and management of CRS/NP are needed.

COMMENT: *Research has investigated the role of MMPs in asthma and, more recently, CRS. This study compared the levels of these enzymes in patients with NP and CRS. Since patients with aspirin sensitivity may be more difficult to treat and have more severe asthma, identification of these patients would be helpful. Patients with aspirin sensitivity had decreased TIMP-1, compared to patients with NP who were aspirin tolerant and controls. The results are a reminder of the importance of these enzymes in patients with NP. A future treatment for these patients may lie in preventing the remodeling of tissue by targeting MMPs.*
V.H.-T.
Mudd, PA, Katial RK, Alam R, Hohensee S, et al: Variations in expression of matrix metalloproteinase-9 and tissue inhibitor of metalloproteinase-1 in nasal mucosa of aspirin-sensitive versus aspirin-tolerant patients with nasal polyposis.
Ann Allergy Asthma Immunol. 2011;107:353-359. ♦♦

Urinary 3-Bromotyrosine: Candidate Asthma Biomarker?

EXHALED nitric oxide has important limitations as an asthma risk marker. Urinary 3-bromotyrosine (By-Tyr) is a relatively specific marker of eosinophil-catalyzed protein oxidation. This study evaluated urinary By-Tyr as a measure of asthma control and asthma risk in children.

The prospective study included 57 consecutive children with asthma, followed up over 6 weeks. Urinary By-Tyr levels were significantly correlated with Asthma Control Questionnaire scores both at baseline and follow-up. Children with high urinary By-Tyr at baseline were 18 times more likely to have inadequate asthma control and 4 times more likely to have an asthma exacerbation during follow-up. Exhaled NO was not a good indicator of asthma control or exacerbation risk.

This short-term follow-up study suggests that urinary By-Tyr is a promising marker of asthma control and exacerbation risk in children. Further studies are needed to explore this possibility, as well as the contribution of eosinophil-driven oxidative pathways to asthma symptoms and exacerbations.

COMMENT: *Exhaled nitric oxide levels are variably correlated with asthma flares in children, limiting their use as a predictive tool. An easily measured biomarker that correlates with disease progression or could predict control would be ideal. One drawback to this study is the 6-week study period; whether 3-bromotyrosine would continue to be as predictive over a longer timeframe is not certain. Also, levels of By-Tyr were not assessed in a normal, control population (or in those with less severe asthma), matched for demographic characteristics.*
K.R.M.
Wedes SH, Wu W, Comhair SAA, et al: Urinary bromotyrosine measures asthma control and predicts asthma exacerbations in children.
J Pediatrics. 2011;159:248-255. ♦♦

REVIEWS OF NOTE

COMMENT: *This entertaining Point/Counterpoint summarizes the utility of measuring sputum eosinophils in severe asthma. It is a detailed procedure requiring a trained technician but can help with classifying these severe cases. Dr. Peters' personal observation of the frequency of sputum eosinophilia in subjects compliant with inhaled corticosteroids (14%) should help investigators assess a screen fail rate in clinical trials of newer antieosinophilic compounds.*
S.F.W.
Hargreave FE, Nair P: Point: Is measuring sputum eosinophils useful in the management of severe asthma? Yes.
Chest, 2011;139;1270-1272.
Peters S: Counterpoint: Is measuring sputum eosinophils useful in the management of severe asthma? No, not for the vast majority of patients. ➤➤

Chest. 2011;139;1273-1275.
Hargreave FE, Nair P: Rebuttal.
Chest. 2011;139;1275-1277.
Peters S: Rebuttal.
Chest. 2011;139;1277. ♦♦

COMMENT: *Establishing the dose response for allergen immunotherapy was a major achievement of our specialty, and much of the credit is due to brilliant clinical studies carried out at Johns Hopkins in the 1960s. And though the dose response required for efficacy with both subcutaneous and sublingual immunotherapy has been clearly established, adequate standardization of the allergens we use is far from complete. Immunotherapy continues to be knowingly administered in homeopathic doses in many practices, especially among those who are not board-certified allergy/immunology specialists. This study reminds us that despite the established scientific dogma, much work remains to be done as we strive for optimal immunotherapy treatment for our patients.*
S.A.T.
Calderón MA, Larenas D, Kleine-Tebbe J, et al: European Academy of Allergy and Clinical Immunology task force report on 'dose-response relationship in allergen-specific immunotherapy.'
Allergy. 2011; 66:1345-1359. ♦♦

COMMENT: *The American Thoracic Society has issued a very important statement regarding the clinical applications of exhaled nitric oxide measurement, as well as a comprehensive review of work-related asthma exacerbations.*
B.E.C.
Dweik RA, Boggs PB, Erzurum SC, et al: An official ATS clinical practice guideline:
interpretation of exhaled nitric oxide levels (FE_{NO}) for clinical applications.
Am J Respir Crit Care Med. 2011;184:602-615.
Henneberger PK, Redlich CA, Callahan DB: An official American Thoracic Society statement: work-exacerbated asthma.
Am J Respir Crit Care Med. 2011;184:368-378. ♦♦

COMMENT: *This article is divided into two parts. A summary of the benefits and shortcomings of respiratory delivered medication (eg, MDI, MDI plus spacer, DPI, nebulized) is presented. The remainder of the article outlines proper CPT coding of aerosolized medication. There is virtual panoply of examples, which should benefit a practice's billing department and "minimize lost revenue from underbilling as well as wasted administrative effort handling denied claims," according to the authors.*
S.F.W.
Sims MW: Aerosol therapy for obstructive lung diseases: device selection and practice management issues.
Chest. 2011;140;781-788. ♦♦

COMMENT: *This review adds to our knowledge of the interaction between airway and bone marrow with respect to allergens, which has been known for years. Recently, viral infections of the respiratory tract have been demonstrated to involve similar pathways. Signals triggered as a result of viral infection in airway tissue result in upregulation of the high affinity IgE receptor (FcεRI) on local dendritic cells, which turn over rapidly during infection, and also in their bone marrow precursors. In atopic subjects with a ready supply of aeroallergen-specific IgE and concomitant exposure to specific allergens, this sets the scene for a potentially self-sustaining inflammatory cascade.*
S.F.W.
Holt PG, Sly PD: Interaction between adaptive and innate immune pathways in the pathogenesis of atopic asthma: operation of a lung/bone marrow axis.
Chest. 2011;139:1165-1171. ♦♦

COMMENT: *This retrospective cross-sectional chart study reviews typical neurologic features found in ataxia-telangiectasia--including those found at presentation, and at various ages as the disease progresses. In addition to neurologic symptoms, the finding of small head circumference is a consistent phenomenon in these patients.*
K.R.M.
Nissenkorn A, Levi YB, Vilnozi D, et al: Neurologic presentation in children with ataxia-telangiectasia: is small head circumference a hallmark of the disease?
J Pediatr. 2011; 159:466-471. ♦♦