AllergyWatch®

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

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Does SLIT Prevent Asthma?

SUBLINGUAL immunotherapy (SLIT) has emerged as an effective alternative to subcutaneous immunotherapy for the treatment of allergic rhinitis and asthma. Some studies have reported additional benefits of SLIT, including reductions in new-onset asthma and new allergic sensitizations. These preventive effects were evaluated in a randomized trial of SLIT in children.

The Italian study included 216 children, mean age 10 years, with allergic rhinitis; 131 also had intermittent asthma. In open-label fashion, 144 children were assigned to receive 3 years of SLIT plus drug therapy; the remaining 72 children received drug therapy only. In the SLIT group, all patients received SLIT for a single allergen--most commonly mite, followed by grasses. Clinical scores were assessed each year during allergen season; pulmonary function, methacholine challenge, and skin prick tests were performed at the beginning and end of the study. The study evaluated SLIT's effects in preventing the onset of persistent asthma, preventing new sensitizations, and reducing bronchial hyperreactivity.

The dropout rate was 9.7% in children assigned to SLIT and 8.3% in the control group. The rate of new sensitizations was 3.1% with SLIT, compared to 34.8% with drug therapy only--odds ratio (OR) 16.85 in the control group. At 3 years, mild persistent asthma had developed in 1.5% of children in the SLIT group, compared with 28.8% of those receiving drug therapy only: odds ratio 0.04 with SLIT.

The SLIT group had lower rates of new sensitizations, OR 0.06, and positive methacholine challenge tests, OR 0.24. Children assigned to SLIT also had lower clinical scores, beginning at the 1-year assessment and continuing through years 2 and 3. Adherence rates were high; there was only one case of systemic itching in a child receiving SLIT.

Three years of SLIT dramatically reduces new cases of mild persistent asthma among children with allergic rhinitis. The results also show a lower rate of new➤➤

CONTENTS

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The following journals have been selected as the primary focus of review in the preparation of materials within "AllergyWatch®".

- Annals of Allergy, Asthma and Immunology
- Journal of Allergy and Clinical Immunology
- American Journal of Respiratory and Critical Care Medicine
- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
- Journal of Pediatrics
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- European Respiratory Journal
- Pediatric Allergy and Immunology

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sensitizations and decreased bronchial hyperreactivity in children assigned to SLIT. These preventive effects are in addition to the symptom reduction achieved with SLIT.

COMMENT: *The literature on SLIT continues to grow, although the discrepancies between the European and North American experience are perplexing. This study can be criticized as an open trial, but the study design is otherwise reasonable and the results are impressive. The decrease in intermittent asthma in both groups is surprising for a study of 10-year-olds with allergy. Also, the low occurrence of a family history of allergy in this allergic population seems odd. Monotherapy was used with the allergen determined by nasal challenge in polysensitized individuals--not typical allergen selection in the United States. Stay tuned, more news will be forthcoming.*
D. K. L.
Marogna M, Tomassetti D, Bernasconi A et al: Preventive effects of sublingual immunotherapy in childhood: an open randomized controlled study.
Ann Allergy Asthma Immunol. 2008;101:206-211. ♦♦

Breast-Feeding Doesn't Affect Allergy Outcomes at Age 7 or 8

THE protective effects of breast-feeding against the development of asthma and allergic disease are still being debated. Although early wheezing is reduced in breast-fed infants, some recent reports suggest that breast-feeding may actually increase the risks of asthma, wheezing, and atopy at older ages. These issues were addressed using longitudinal data from a British birth cohort.

The analysis included data on from the Avon Longitudinal Study of Parents and Children, including follow-up through age 8. Logistic regression was performed to evaluate the relationship between breast-feeding and a wide range of asthma and allergy outcomes. The analysis included data on 7,245 children tested for atopy at age 7--of these, 6,551 underwent pulmonary function testing at age 8 and 3,920 underwent methacholine challenge testing at age 8.

About one-fourth of the children were breast-fed for at least 6 months. Through age 3, breast-fed children were at lower risk of wheezing--odds ratio (OR) 0.80 for those breast-fed for 6 months or longer, compared to no breast-feeding. There was no significant effect on outcomes at age 7 to 8, including wheezing, atopy, or bronchial hyperresponsiveness. A similar pattern emerged on Bayesian analysis to account for possibility that infants who wheezed were breast-fed longer.

The longitudinal data support the protective effect of breast-feeding on wheezing during the first 3 years of life. However, breast-fed children show no reduction in allergic disease or atopy at older ages. There is also no evidence that breast-feeding increases the risk of asthma or atopy at later ages, even in children of asthmatic mothers.

COMMENT: *There is a growing body of literature on primary prevention of allergy by dietary manipulations, and the net results are confusing. This large longitudinal study with lots of controls for potential confounders found that breast-feeding was protective for wheezing in the first 3 years of life, but not wheezing, atopy, or bronchial hyperresponsiveness at 7 to 8 years of age. An accompanying editorial* (**J Allergy Clin Immunol**. 2008;122:29-33) *puts the existing published data into some perspective, and cautions against simple conclusions about infant feeding. This issue is messier than a 2-year-old's dinner tray!*
R. J. M.
Elliott L, Henderson J, Northstone K, et al: Prospective study of breast-feeding in relation to wheeze, atopy, and bronchial hyperresponsiveness in the Avon Longitudinal Study of Parents and Children (ALSPAC).
J Allergy Clin Immunol. 2008;122:49-54. ♦♦

Ex-Preterm Infants Have Normal Lung Function as Young Adults

LONG-TERM follow-up studies of preterm infants have reported neurodevelopmental sequelae persisting into young adulthood. However, there are few data on respiratory morbidity in this group of patients. A group of preterm infants were followed up to age 21 to assess respiratory symptoms and lung function in young adulthood.

The study included 60 subjects who were preterm infants at birth in 1979-80. Median gestational age at birth was 31.5 weeks and median birthweight 1,440 g; none of the infants received surfactant therapy. At a median age of 21.7 years, the subjects underwent evaluation including assessment of respiratory symptoms, pulmonary function testing, and methacholine challenge testing. Fifty healthy controls were studied for comparison.

When evaluated in mid-childhood, the ex-preterm infants had increased rates of respiratory symptoms, airway obstruction, and airway hyperresponsiveness. In young adulthood, they continued to have more respiratory symptoms than controls--odds ratio (OR) 4.2. However, spirometry results were similar between groups; mean z scores for FEV_1, forced mid-expiratory flow, and forced vital capacity were not significantly different for the ex-preterm infants versus controls. Rates of increased airway hyperresponsiveness were 23% and 19%, respectively.

These findings in preterm infants born before the surfactant era show continued excess respiratory symptoms at age 21. However, the ex-preterm infants have no evidence of persistent airway obstruction or airway hyperresponsiveness in young adulthood. These patients, particularly those who smoke, need continued follow-up into late adulthood.

COMMENT: *This is an extremely reassuring article with the largest follow-up of ex-preterm infants: 60 subjects for almost 22 years. Although respiratory symptoms were still present, impaired lung function and airway hyperresponsiveness were not significant concerns. We should look for even better outcomes going forward, as this study was initiated before the routine use of surfactant in neonatal ICUs.*
B. E. C.
Narang I, Rosenthal M, Cremonesini D, et al: Longitudinal evaluation of airway function 21 years after preterm birth.
Am J Respir Crit Care Med. 2008;178:74-80. ♦♦

Asthma Linked to Rhinovirus in Lower Airway

INFECTION with human rhinovirus (HRV), the cause of the common cold, may be an important asthma risk factor and a trigger for asthmatic attacks. This study examined the possible association between asthma severity and chronic lower airway infection with HRV.

Two techniques were used to test for HRV in bronchial mucosal biopsy specimens from patients with stable asthma and nonasthmatic controls. Indirect in situ reverse transcription-polymerase chain reaction (RT-PCR) was performed in 30 asthma patients and 23 controls and immunohistochemistry in 14 patients and 6 controls. The findings were compared with the clinical features of asthma.

Immunohistochemistry was positive for HRV in 64.3% of bronchial biopsy specimens from asthma patients versus 33.3% of nonasthmatic controls. The more sensitive RT-PCR technique showed HRV in the lower airways of 73% of asthma patients versus 22% of controls. Among the asthma patients, positive tests for HRV were associated with decreased FEV_1 and other pulmonary function measures. Patients with HRV in the lower airways also had higher numbers of blood eosinophils and leukocytes and greater eosinophilic infiltration of the bronchial mucosa.

Patients with asthma are more likely to have HRV in the lower airway, a finding associated with clinical features of increased asthma severity. The results suggest that chronic HRV infection may be related to the presence and severity of asthma. Longitudinal studies are needed to confirm this association.

COMMENT: *This study continues to expand our knowledge regarding the persistence of lower airway infections--first with chlamydia, then mycoplasma, now rhinovirus. The role of persistent viral infections in the inceptions and persistence of asthma is an extremely important pathophysiologic mechanism for recurrent disease. We hope that intervention strategies can be developed to identify and address this significant immunopathologic process.*
B. E. C.
Wośś M, Sanak M, Soja J, et al: The presence of rhinovirus in lower airways of patients with bronchial asthma.
Am J Respir Crit Care Med. 2008;177:1082-1089. ♦♦

Impaired Phagocytosis and Apoptosis in Poorly Controlled Asthma

IN asthmatic children, respiratory infections may be an important risk factor for poor disease control, although the mechanisms of this association are unclear. Studies in adult asthma patients have suggested increased activation of the alveolar macrophages (AMs)--the primary airway cells involved in innate immune defenses--and decreased phagocytosis of apoptotic cells. This study evaluated AM phagocytosis in children with poorly controlled asthma.

The study included 28 children with poorly controlled asthma--12 moderate and 16 severe--and 10 nonasthmatic children with chronic cough who received inhaled corticosteroids. Unstimulated and lipopolysaccharide-stimulated phagocytosis were compared between the two groups of children and with a group of 10 healthy adults. An immunostaining assay was performed to assess apoptosis. ➤➤

Unstimulated phagocytosis was significantly reduced among children with poorly controlled asthma. The phagocytic index was 4,361 relative fluorescence units (RFU) in children with moderate asthma and 3,153 RFU in those with severe asthma, compared to 9,042 RFU in the children with chronic cough and 9,330 RFU in the healthy adults. Assessment of stimulated phagocytosis yielded similar results. The children with severe asthma had increased AM apoptosis, a finding that was correlated with the phagocytic index. The impairment in phagocytic function could not be explained by corticosteroid treatment or other potential confounders.

Children with poorly controlled asthma have impaired phagocytic function, with increased apoptosis and decreased phagocytosis of bacteria. Added to other recent reports, the findings support the hypothesis that bacterial infection may contribute to asthma morbidity. Future research should look at how impaired AM phagocytosis is related to bacterial phagocytosis and viral clearance in poorly controlled asthma.

COMMENT: *Children with poorly controlled asthma tend to have a difficult time with recurrent respiratory infections. Analyzing bronchoalveolar lavage fluid (BAL) from children with poorly controlled asthma and comparing this to BAL from normal adults and children with cough or other reasons for bronchoscopy, these researchers found that AMs collected from BAL in the asthmatic children had reduced phagocytosis and increased apoptosis. Impaired function of the AM may contribute to the severity of respiratory infections in these children.*
S. M. F.

Fitzpatrick AM, Holguin F, Teague WG, Brown LAS: Alveolar macrophage phagocytosis is impaired in children with poorly controlled asthma.
J Allergy Clin Immunol. 2008;121:1372-1378. ♦♦

Good Asthma Control with Adjustable-Dose Budesonide/Formoterol pMDI

COMPARED to the fixed-dose budesonide/formoterol dry powder inhaler (DPI), the adjustable-dose DPI offers equivalent or better asthma control with lower use of inhaled corticosteroid and reduced costs. This study compared the adjustable- and fixed-dose budesonide/formoterol pressurized metered-dose inhalers (pMDI) with the fixed-dose fluticasone propionate/salmeterol DPI in patients with moderate to severe asthma.

The open-label, phase 3 trial included 1,225 adolescent to adult patients with moderate to severe asthma, drawn from 145 U.S. centers. During a 10- to 14-day run-in period, the patients remained on their current medication. They were then randomly assigned in a 2:1 ratio to treatment with the fixed-dose budesonide/formoterol pMDI, 160/4.5 µg x 2 inhalations twice daily; or the fixed-dose fluticasone propionate/salmeterol DPI, 250/50 µg x 1 inhalation twice daily.

After 1 month of treatment, patients assigned to the fixed-dose fluticasone propionate/salmeterol DPI remained on that treatment. Those who had been using the fixed-dose budesonide/formoterol pMDI were assigned in a 1:1 ratio to continue the same treatment or to start treatment with the adjustable-dose budesonide/formoterol pMDI. In the latter group, the dose was adjustable from 2 inhalations (320/9 µg) twice daily to two inhalations (320/9 µg) once daily or 4 inhalations (640/18 µg) once daily. Treatment continued for 6 months.

The asthma exacerbation rate was not significantly different between the three groups, ranging from 0.196 to 0.240 exacerbations per patient-treatment year. Other efficacy outcomes were also similar, including asthma symptoms and lung function measures. The daily number of drug inhalations was lower with the adjustable-dose versus the fixed-dose budesonide/formoterol pMDI: mean 3 versus 4 inhalations per day. Seventy-seven percent of patients assigned to the adjustable-dose group were able to step down from 2 inhalations twice daily to 2 inhalations once daily. All treatments were well tolerated.

For patients with moderate to severe asthma, the adjustable-dose budesonide/formoterol pMDI provides disease control similar to that of the fixed-dose budesonide/formoterol pMDI or the fixed-dose fluticasone propionate/salmeterol DPI. The adjustable-dose inhaler reduces the amount of medication required; the clinical significance of this effect is unknown.

COMMENT: *In this large, well-designed, prospective, open-label study, 1,225 patients with persistent asthma adjusted their combination inhaler medication following a rigid protocol over a 7-month period. Even those following the adjustable-dose regimen had similar outcomes to those on the fixed-dose study arms. This is reassuring to practitioners, since we all know that most patients aren't as compliant as we would like.*
S. M. F.

Busse WW, Shah SR, Somerville L, et al: Comparison of adjustable- and fixed-dose budesonide/formoterol pressurized metered-dose inhaler and fixed-dose fluticasone propionate/salmeterol dry powder inhaler in asthma patients.
J Allergy Clin Immunol. 2008;121:1407-1414. ♦♦

SLIT for Bee Allergy?

SPECIFIC immunotherapy with hymenoptera venom offers near-complete protection against allergic reactions to bee stings. The effectiveness of sublingual immunotherapy (SLIT) for respiratory allergies is now well established. This randomized trial evaluated the effectiveness of SLIT for patients with hymenoptera allergy.

The double-blind trial included 30 patients with hymenoptera allergy: 18 men and 12 women, mean age 44.5 years. All had a history of large local reactions to honeybee stings and were monosensitized to honeybee. Responses to a sting challenge were assessed at➤➤

baseline; patients were then randomly assigned to 6 months of SLIT or placebo. The SLIT regimen began with a 6-week buildup period, followed by a maintenance dose of 525 µg of venom per month. The sting challenge was repeated at the end of treatment.

Twenty-six patients completed the study, with one dropout in the SLIT group and three in the placebo group. In response to sting challenge, peak maximal diameter of the skin reaction decreased from a median of 20.5 to 8.5 cm with SLIT, compared with no significant change in the placebo group (23.0 to 20.5 cm). Fifty-seven percent of patients had at least a 50% reduction in the size of the skin reaction. The SLIT group also had a significant increase in total specific IgG levels. There were no adverse events related to SLIT.

Initial evaluation supports the effectiveness of SLIT for patients with large local reactions to honeybee stings. Active SLIT reduces the size of the skin reactions, compared to placebo, with good safety outcomes. Further evaluations of SLIT for hymenoptera allergy are warranted, including dose-ranging studies and trials in patients with systemic reactions.

COMMENT: *In this proof-of-concept study, impressive immunologic changes in specific IgE and IgG and reductions in size of local reactions were seen after 6 months of SLIT. These patients only had large local reactions to bee stings, so whether SLIT will work in insect sting anaphylaxis remains to be seen. We hope future studies will show SLIT is also effective in patients with stinging insect anaphylaxis.*
S. M. F.

Severino MG, Cortellini G, Bonadonna P, et al: Sublingual immunotherapy (SLIT) for large local reactions caused by honeybee sting: a double-blind, placebo-controlled trial.
J Allergy Clin Immunol. 2008;122:44-48. ♦♦

Five-Year Experience with Pediatric Anaphylaxis

ALTHOUGH anaphylaxis is much more common in children, few reports have focused on pediatric anaphylaxis. Most cases of anaphylaxis in children are caused by foods and are seen in the emergency department (ED). The authors review a 5-year experience with pediatric anaphylaxis at an Australian children's hospital ED.

From 1998 to 2003, the ED treated 123 episodes of anaphylaxis in 117 children. The median age was 2.4 years; one child died after reacting to peanut. Forty-eight percent of reactions occurred at home. Eighty-five percent of episodes were triggered by foods: 18% by peanut, 13% by cashew nut, and 11% by cow's milk. For all identifiable triggers, the median time from exposure to anaphylaxis was 10 minutes. Time to the start of ED treatment was 40 minutes after onset. A previous episode of anaphylaxis was documented for 17% of patients.

Ninety-seven percent of children had respiratory features, most commonly wheezing, shortness of breath, cough and stridor. Skin features were also present in 97%, with most children having urticaria and angioedema. Eighty-five percent of children received some form of epinephrine. In 52% of cases, epinephrine was given subcutaneously.

The results provide insights into the clinical characteristics of children seen in the ED for anaphylactic reactions. Most are reacting to foods, especially peanuts and tree nuts, and are experiencing their first episode of anaphylaxis. The findings raise concerns about the timing and appropriate use of epinephrine for pediatric anaphylaxis.

COMMENT: *This study focused on the clinical presentation and causes of pediatric anaphylaxis presenting to the ED. Not surprisingly, the most common culprits were peanuts and tree nuts. Of particular concern is the fact that epinephrine administration was frequently delayed, and in the ED it was more likely to be administered subcutaneously than intramuscularly.*
S. A. T.

de Silva IL, Mehr SS, Tey D, Tang MLK: Paediatric anaphylaxis: a 5 year retrospective review.
Allergy. 2008:63:1071-1076. ♦♦

Why Can't AD Skin Kill Bacteria?

ATOPIC dermatitis (AD) is characterized by colonization and infection of the skin with *Staphylococcus aureus*. These patients also have overexpression of Th2 cytokines, hindering the skin's antimicrobial responses. The authors recently demonstrated that human β-defensin-3 (HBD-3) plays a key role in rapid killing of *S. aureus* in the skin. They evaluated the effectiveness in *S. aureus* killing in the skin of patients with AD, including the role of HBD-3.

Skin biopsies were obtained from 10 patients with AD and 10 healthy controls. Synthesis and mobilization of HBD-3 onto surface-associated *S. aureus* were compared between AD and normal skin. Further studies were performed to examine how Th2 cytokines influenced the synthesis and mobilization of HBD-3 by cultured keratinocytes and their effectiveness in killing *S. aureus*.

Keratinocytes from AD patients killed *S. aureus* less effectively than cells from healthy subjects. Although there was no difference in constitutive expression of HBD-3 by epidermal keratinocytes from AD patients versus controls, the AD cells showed defective mobilization of HBD-3. The Th2 cytokines interleukin (IL)-4 and IL-13 inhibited the mobilization and *S. aureus*-killing effects of HBD-3. Antibodies against IL-4, IL-10, and IL-13 enhanced mobilization of HBD-3 onto the surface of *S. aureus* in AD skin samples.

Colonization and infection with *S. aureus* in the skin of AD patients appears to be related to increased levels of Th2 cytokines, which inhibit mobilization of HBD-3 from epidermal keratinocytes. Treatments to inhibit Th2 cytokines might help in achieving bactericidal concentrations of HBD-3. If effective, this approach could be a useful alternative to antibiotic therapy in patients with AD. ➤➤

COMMENT: *One of the deficiencies in the skin of people with AD is the inability to effectively kill* S. aureus. *It has been shown that HBD-3, constitutively expressed in normal keratinocytes, is a vitally important molecular killer of* S. aureus. *This study shows that increased levels of the pro-allergic Th2 cytokines IL-4, IL-10, and IL-13 inhibit the mobilization of bactericidal HBD-3 from the keratinocytes onto* S. aureus *cells, suggesting how allergy and infection combine in AD. Piece by piece, the mysteries of AD are being demystified.*
R. J. M.

Kisich KO, Carspecken CW, Fiéve S, et al: Defective killing of Staphylococcus aureus *in atopic dermatitis is associated with reduced mobilization of human β-defensin-3.*
J Allergy Clin Immunol. 2008;122:62-68. ♦♦

Acid-Suppressing Drugs May Affect Food Allergies

FOOD allergens have been classified as complete (class 1) allergens, which cross-link IgE and are the primary source of sensitization; and incomplete (class 2) allergens--sometimes called nonsensitizing elicitors--which elicit symptoms only after sensitization with cross-reactive allergens. Digestion assays developed to predict the allergenic potential of food proteins use simulated gastric fluid to imitate the effects of proteolysis in the stomach. However, changes in gastric digestion capacity can occur at different stages of life, both physiologically and as a result of disease.

Various classes of acid-suppressing medications--including H2-receptor blockers and proton-pump inhibitors--are widely used and are generally considered safe for long-term treatment. Through varying mechanisms, these drugs work by raising the pH in the stomach. This alteration in gastric digestive function could have implications for food allergies, allowing digestion-labile food allergens to remain stable during gastric transit. Studies in mice and humans have suggested an increased risk of new sensitization to foods during treatment with acid-suppressing drugs. The change in gastric digestion capacity might also affect allergic responses in previously sensitized patients, with severe reactions occurring at much lower intakes of food proteins.

Based on these data, the authors suggest that the current classification of class 1 and class 2 food allergens should be modified to incorporate the concept of allergen persistence. Test protocols accounting for impaired digestive capacity may have important implications for patient safety, including the risk of new sensitizations and lowered thresholds for allergic reactions to foods. These risks should be borne in mind in prescribing acid-suppressing medications, including measures to reduce exposure and allergist follow-up for patients on long-term acid-reducing therapy.

COMMENT: *Food allergies arise from sensitization of the immune system by intact or largely-intact food proteins. Digestion of such proteins normally begins in the stomach and is known to be partly dependent on an acid pH. What, then, might be the role of acid inhibitor medications like proton-pump inhibitors, H2 blockers, and sucralfate in the genesis of food allergies? This review urges caution in prescribing such medications without limits or in inappropriate circumstances. Should pediatricians really be prescribing these medications for infants who are merely "spitters"? Should adults with gastroesophageal reflux disease be given them for years on end? Remember the law of unintended consequences.*
R. J. M.

Untersmayr E, Jensen-Jarolim E: The role of protein digestibility and antacids on food allergy outcomes.
J Allergy Clin Immunol. 2008;121:1301-1308. ♦♦

FOCUS ON PREVENTION OF ALLERGIC DISEASE

Genetics and Cytokine Responses Affect Asthma Risk in Children Exposed to Tobacco Smoke

STUDIES in adults have suggested that smoking may influence not only the expression of β2-adrenergic receptor genes (*ADRB2*), but also the associations between *ADRB2* variants and asthma. It is unknown whether exposure to tobacco smoke in utero or to secondhand smoke during childhood has similar effects in children. The effects of these two types of tobacco smoke exposure on genetic associations with wheezing were examined using data from a population-based study of children.

The analysis included data on 3,128 children from the Children's Health Study. All had available data on asthma outcomes, exposure to maternal smoking in utero and to secondhand smoke at home, and genotyping data on two well-characterized *ADRB2* single nucleotide polymorphisms: *Arg16Gly* and *Glu27Gln*.

Both types of exposure to tobacco smoke were significantly associated with childhood wheezing. Among *Arg16* homozygotes, in utero exposure to tobacco smoke was associated with a threefold increase in lifetime wheezing risk, compared to nonexposed children with at least one *Gly16* allele. Similarly, in children homozygous for *Arg16*, risk of lifetime, current, and nocturnal wheezing increased along with the number of smokers at home. Comparable associations emerged on comparison of children recruited in different years and on diplotype-based analyses. Analysis of *Glu27Gln* genotype showed no such associations.

The effects of the *Arg16Gly* variant on childhood wheezing risk is modified by exposure to tobacco smoke, in utero or during childhood. Smoke-related increases in wheezing risk are greater for children who are *Arg16* homozygotes and for those with two copies of the *Arg16-Gln27* diplotype. Studies of the association between *ADRB2* and asthma must consider the effects of exposure to smoking.

ALTHOUGH the adverse health effects of exposure to environmental tobacco smoke in children are well-documented, the mechanisms of these effects are unclear. Data from the Tucson Children's Respiratory ➤➤

Study were used to assess the effects of parental smoking on children's immune responses, and whether such effects are independent of in utero exposure to maternal smoking.

The analysis included prospective data on 512 children and their parents. Detailed information on parental smoking was collected from the prenatal period until the children were 11 years old. At that time, peripheral blood mononuclear cells were collected from the children for measurement of interferon-γ and interleukin-4 (IL-4) in response to mitogen stimulation.

After adjustment for covariates, children whose parents smoked were more likely to be in the lower two quartiles of IFN-γ production: adjusted odds ratio 1.61. Decreased IFN-γ production was associated with active wheezing, although not with positive skin-prick test results. Interferon-γ production showed an inverse dose-response relationship with maternal smoking, paternal smoking, and parental pack-years of smoking. The associations with paternal smoking and parental pack-years remained significant even for children not exposed in utero. Parental smoking was unrelated to IL-4 production.

Parents' smoking affects immune system function in school-age children. Children's production of interferon-γ decreases as exposure to parents' tobacco smoke increases, independent of in utero exposure.

COMMENT: *A complex interaction among environmental and genetic risks is thought to mediate development of asthma. In the first of these studies, a possible link between tobacco smoke exposure and genetics of* ADRB2 *receptors is found. This could explain why chronic tobacco smoke exposure leads to a higher risk of asthma/wheeze some children, while others seem to be less affected in this noxious environment. Children homozygous for the* Arg16 *variant were deemed at highest risk. The second study uses the cohort from the Tucson Children's Respiratory Study to assess levels of interferon-γ and IL-4 in children exposed to environmental tobacco smoke. The higher the exposure levels, the lower the interferon-γ levels and more likely the child had recent wheezing. Both studies add to our armamentarium as we continue to advise parents not to smoke around their children.*
K. R. M.

Wang C, Salam MT, Islam T, et al: Effects of in utero and childhood tobacco smoke exposure and β2-adrenergic receptor genotype on childhood asthma and wheezing.
Pediatrics. 2008;122:e107-e114.

Tebow G, Sherrill DL, Lohman IC, et al: Effects of parental smoking on interferon γ production in children.
Pediatrics. 2008;121:e1563-e1569. ♦♦

Nuts during Pregnancy May Increase Childhood Asthma Risk

THE maternal diet during pregnancy might influence fetal airway development and Th2-cell responses, thus affecting the risk of childhood asthma or allergic disease. The relationship between maternal diet and childhood asthma risk was assessed in a birth cohort study with follow-up to age 8.

In the Prevention and Incidence of Asthma and Mite Allergy study, 4,126 pregnant women--1,327 atopic and 2,819 nonatopic--provided information on consumption of specific types of allergenic foods during the previous month. The children's prevalence of asthma symptoms was longitudinally assessed from age 1 to 8 years. Follow-up information was available for 2,832 children.

The children's longitudinal outcomes were unrelated to maternal consumption of vegetables, fish, egg, milk, or nuts during pregnancy. However, children whose mothers reported daily consumption of nut products (eg, peanut butter) were at increased risk of childhood wheezing: odds ratio (OR) 1.42, compared to those whose mothers rarely ate nuts. Daily consumption of nut products was also linked to increased rates of childhood dyspnea, OR 1.58; steroid use, OR 1.62; and asthma symptoms, OR 1.47. Daily fruit consumption had a small, borderline-significant protective effect against wheezing.

High consumption of nuts and nut products during pregnancy may be associated with an increase in childhood asthma symptoms. Additional research is needed to make evidence-based dietary recommendations for expectant mothers.

COMMENT: *This study does not support recent recommendations by the American Academy of Pediatrics* (**Pediatrics**. 2008;121:183-191) *and a recent article* (**J Allergy Clin Immunol**. 2008;122:29-33) *suggesting that there is no compelling evidence for maternal dietary avoidance. We must continue to view this form of primary prevention as work in progress and to be carefully mindful of weighing new data as they are presented.*
B. E. C.

Willers SM, Wijga AH, Brunekreef B, et al: Maternal food consumption during pregnancy and the longitudinal development of childhood asthma.
Am J Respir Crit Care Med. 2008;178:124-131. ♦♦

Dietary Recommendations in Atopic Infants: Are We Making Things Worse?

IT is still unclear how age at the introduction of solid foods affects children's risk of atopy. Associations between the introduction of cow's milk and other food products on the risk of atopic symptoms by age 2 were evaluated.

The analysis included 2,258 infants from the Dutch KOALA Birth Cohort Study. The introduction of cow's milk products and other food products was evaluated as a predictor of atopic manifestations during the first 2 years of life, including eczema, atopic dermatitis, recurrent wheezing, and sensitization to foods and other allergens.

Later introduction of cow's milk products was associated with an increased risk of eczema. The adjusted odds ratio for eczema at age 2 was 1.55 for infants aged 7 to 9 months at introduction of cow's milk products, compared to those aged 0 to 3 months. For infants ➤➤

older than 9 months, the odds ratio was 2.29. Risk of any sensitization at age 2 was increased for infants with delayed introduction of other food products: adjusted odds ratios were 3.69 for introduction at 4 to 6 months and 4.31 for older than 7 months, compared to 3 months. The results were similar on exclusion of infants with early symptoms of eczema and recurrent wheezing, to account for possible reverse causation.

Delaying introduction of cow's milk and other food products may not reduce the risk of allergic disease in early childhood, and may increase some risks. Although the protective effects of breast-feeding are unquestioned, the data do not show any additional benefit of delaying introduction of cow's milk products or other foods.

COMMENT: *Evidence-based medicine continues to upend or at least challenge "conventional wisdom" in the arena of dietary prevention in food allergy. The findings of this study are fascinating, if proven to be true, as we have collectively been recommending delay in introduction of cows' milk and other foods in "at-risk" infants for years. The authors made every attempt to address reverse causation in this large birth cohort study, but one cannot be absolutely certain unless the study is randomized and prospective.*
K. R. M.

Snijders BEP, Thijs C, van Ree R, van den Brandt PA: Age at first introduction of cow milk products and other food products in relation to infant atopic manifestations in the first 2 years of life: the KOALA Birth Cohort Study.
Pediatrics. 2008;122:e115-e122. ♦♦

Hydrolyzed Formulas Reduce Long-Term Allergy Risk

HYDROLYZED infant formulas were developed to reduce the allergenicity of cow's milk-based formulas, with the aim of preventing the development of allergic diseases in high-risk infants. Long-term follow-up data were analyzed to assess the preventive effects of three different hydrolyzed formula products.

The German Infant Nutritional Intervention study included 2,252 infants with a family history of atopy and insufficient breast-feeding. Infants were randomized to receive partially hydrolyzed whey formula, extensively hydrolyzed whey formula, extensively hydrolyzed casein formula, or conventional cow's milk formula. The infants received their assigned formula for the first 4 months of life. Rates of physician-diagnosed allergic diseases were compared at age 6 months.

On intention-to-treat analysis, the risk of physician-diagnosed allergic manifestations was lower for children assigned to the hydrolyzed formulas, compared to cow's milk formula. Relative risks were 0.82 for partially hydrolyzed whey formula, 0.90 for extensively hydrolyzed whey formula, and 0.80 for extensively hydrolyzed casein formula. The hydrolyzed formulas were also associated with lower rates of atopic eczema: relative risks 0.79, 0.92, and 0.71, respectively.

All of these preventive benefits were stronger on per-protocol analysis. None of the other specific allergic manifestations was significantly different between groups.

Among high-risk infants, 4 months of feeding with hydrolyzed formulas is associated with a lower risk of allergic manifestations and atopic eczema up to age 6. When breast-feeding is insufficient for any reason, hydrolyzed formulas may be the best option for prevention of childhood allergic disease.

COMMENT: *The relationship between infants' diet and atopy is intriguing but difficult to define. In this study, infants were fed hydrolyzed formulas for just 4 months in infancy, and then followed for 6 years. The control group received unhydrolyzed cow's milk formula. There was a persistent protective effect of hydrolyzed casein and whey formulas on the development of eczema and other manifestations of allergy, even at 6 years of age. Other studies have downplayed the protective effect of breast-feeding. We still don't know what to recommend to our patients.*
R. J. M.

Von Berg A, Filipiak-Pittroff B, Krämer U, et al: Preventive effect of hydrolyzed infant formulas persists until age 6 years: long-term results from the German Infant Nutritional Intervention Study (GINI).
J Allergy Clin Immunol. 2008;121:1442-1447. ♦♦

A Fishy Subject - Revisited

THE prevalence of childhood asthma is lower in Mediterranean countries. One possible explanation is the so-called Mediterranean diet, characterized by a high ratio of monounsaturated to saturated fats; high intake of fruits, vegetables, legumes, and grains; and moderate intake of milk and dairy products. Associations between the Mediterranean diet and the risk of wheezing in preschool children were assessed.

The analysis included data on 1,784 Spanish preschoolers, 20% of whom had parent-reported wheezing in the previous year. Data on food consumption were used to assign a Mediterranean diet score for each child.

The Mediterranean diet was significantly associated with current wheezing, though not with obesity, in this sample of preschoolers. Many other factors were associated with wheezing as well, including obstetric factors, exposures during pregnancy and early childhood, other allergic symptoms, maternal characteristics, physician activity, and having a cat at home. On multivariate analysis, independent risk factors for current wheezing were eczema, adjusted odds ratio (aOR) 2.35; rhinoconjunctivitis, aOR 2.78; paternal asthma, aOR 3.89; and acetaminophen use, aOR 2.38. The Mediterranean diet was an independent protective factor: aOR 0.54 for children in the highest quartile of Mediterranean diet score. Older age was also a protective factor, aOR 0.67 per year.

Preschool-aged children who eat a Mediterranean diet have lower rates of current wheezing. This dietary protective effect is independent of obesity and physical activity level. Further study is needed to determine the preventive benefits of specific foods.

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COMMENT: *Yet another study in the genre of dietary-modification-as-therapy suggests that a Mediterranean diet may reduce risk of wheeze in preschool children. Unfortunately, this was an entirely retrospective analysis, relying on parental recall for all food intake and symptom data (some of which occurred years earlier), with no review of medical records. Other recent, and more rigorous, prospective studies have not suggested an influence of omega-3 dietary supplementation on either asthma or atopy.*
K. R. M.
Castro-Rodriguez JA, Garcia-Marcos L, Rojas JDA, et al: Mediterranean diet as a protective factor for wheezing in preschool children.
J Pediatr. 2008;152:823-828. ♦♦

Breast-Feeding Doesn't Affect Allergy Risk in Young Adulthood

SOME studies suggest that breast-feeding lowers the risk of allergic diseases, while others report an increased risk. This report assesses the protective effects of breast-feeding against allergic diseases into young adulthood.

The cross-sectional survey study included 9,615 Japanese university students. When asked about their history of allergic diseases, 47.2% reported allergic rhinitis, 17.4% reported atopic dermatitis, and 9.3% reported asthma. Students reporting any one of these three conditions were more likely to have the other two.

Factors associated with an increased prevalence of allergic rhinitis on logistic regression analysis were male sex, odds ratio (OR) 1.5; and maternal or paternal history of allergic rhinitis, OR 2.2 and 1.6, respectively. Respondents who had a family member with atopic dermatitis were at higher risk: ORs were 2.7 for maternal history, 3.8 for paternal history, and 1.9 for sibling history. Family history also increased the risk of asthma, with ORs of 4.9, 4.0, and 3.3, respectively. History of breast-feeding was not related to any of the three diagnoses.

Subject-reported history of breast-feeding versus formula-feeding during infancy is unrelated to the prevalence of allergic diseases in young adulthood. The results underscore the importance of family history of allergy.

COMMENT: *This study is subject to the limitations of data based on questionnaires and influenced by recall bias. However, it adds to growing evidence that breast-feeding, although desirable for multiple reasons, does little to reduce the likelihood of developing allergic sensitivity or symptoms.*
D. K. L.
Karino S, Okuda T, Uehara U, Toyo-oka T: Breastfeeding and prevalence of allergic diseases in Japanese university students.
Ann Allergy Asthma Immunol. 2008;101;:153-159. ♦♦

Turkish Study Finds Very Low Rates of Food Reactions

NO previous studies have comprehensively evaluated the prevalence of food allergy and nonallergic food hypersensitivity (FA/NAFH) in Turkey and surrounding countries. In Turkey, the Mediterranean diet is common, as is the "Eastern food culture diet," which includes red meat and various spices. The prevalence of adverse reactions to foods was evaluated in a Turkish population-based study.

The study included a random sample of 11,816 adults in Istanbul, including respondents from both the European and Asian sides of the city. In response to a questionnaire, 9.5% of subjects had suspected FA/NAFH. They were invited for a clinical evaluation including double-blind placebo-controlled food challenges.

The findings suggested a very low point prevalence of FA/NAFH, including "possible" cases--as low as 0.3%. On food challenges, the rates of both diagnoses were 0.1%. The main risk factor for FA/NAFH was family history of atopy: adjusted odds ratio 4.3. The most common related allergic disease was itching dermatitis or urticaria, adjusted odds ratio 3.9.

Turkey appears to have a very low population prevalence of FA/NAFH, compared with Western and Northern Europe. The explanation for this finding is unknown; genetic, cultural, or dietary factors may be involved.

COMMENT: *We know the prevalence of food allergy has been increasing rapidly in the United States and Western Europe. This Turkish study suggests that the prevalence of food allergy in Turkey is much lower. These data will no doubt serve as a starting point for subsequent studies to help us understand what factors are responsible for this difference.*
S. A. T.
Gelincik A, Büyüköztürk S, Gül H, et al: Confirmed prevalence of food allergy and non-allergic food hypersensitivity in a Mediterranean population.
Clin Exp Allergy. 2008;38:1333-1341. ♦♦

Can We Predict Response to LTRAs?

IN children and adults, leukotriene receptor antagonists (LTRAs) are an effective treatment for asthma. The factors affecting susceptibility to the therapeutic effects of LTRAs are unknown. This placebo-controlled study sought to identify predictors of susceptibility to LTRAs in children with asthma.

Twenty-seven school-age children with asthma were randomly assigned to receive montelukast or placebo in addition to their current controller medications. At baseline and throughout the 5-month treatment period, the children underwent measurement of urinary leukotriene E_4 (LTE_4) and cotinine. Fractional exhaled nitric oxide (FENO) and albuterol use were monitored as well.

Before randomization, LTE_4 was significantly and positively correlated with albuterol use 2 days ➤➤

later. Albuterol use per interquartile increase in LTE_4 decreased by 12% in children starting treatment with montelukast, compared to a 2% increase in those assigned to placebo. The reductions in LTE_4-related albuterol use were greater in girls than boys and greater in children who had higher cotinine levels, reflecting higher exposure to cigarette smoke. Higher levels of LTE_4 in terms of FENO were associated with significant reductions in LTE_4-related albuterol use.

In children with asthma, increases in urinary LTE_4 predict increased use of albuterol a few days later. These LTE_4-related increases in albuterol use and the degree of responsiveness to montelukast are greater in children with higher exposure to tobacco smoke, and may be greater in girls. The ratio of LTE_4 to FENO might be a useful predictor of individual responses to montelukast.

COMMENT: *We all see asthmatic patients who have a dramatic response to LTRA, while in others the effect of LTRA is disappointing. This randomized, placebo-controlled prospective study used urinary LTE_4 levels, FENO, and frequency of albuterol use to monitor clinical response in asthmatic children receiving inhaled corticosteroids. The biologic phenotype related to LTRA responsiveness tended to involve female sex, higher baseline LTE_4 levels, exposure to secondhand tobacco smoke, and higher LTE_4/FENO ratios.*
S. M. F.
Rabinovitch N, Strand M, Stuhlman K, Gelfand EW: Exposure to tobacco smoke increases leukotriene E_4-related albuterol usage and response to montelukast.
J Allergy Clin Immunol. 2008;121:1365-1371. ♦♦

Can We Use Specific IgE to Diagnose Peanut and Tree Nut Allergy?

INFORMATION on diagnostic specific IgE levels for food allergies might provide a valuable alternative to double-blind, placebo-controlled food challenge. The investigators evaluated the diagnostic utility of specific IgE levels for identifying patients with symptomatic allergies to peanut, tree nuts, and seeds, as well as assessing the relationships among these allergens.

The study included 324 patients--61% male, median age 6 years--referred for evaluation of suspected peanut or tree nut allergies. Diagnostic evaluation included the medical history and, when appropriate, skin prick test results and specific IgE levels. Serum samples from each patient were tested for specific IgE antibodies to peanut, tree nuts, and seeds using the ImmunoCAP assay.

In addition to food allergies, 57% of the patients had atopic dermatitis and 58% had asthma. Seventy-two percent had a convincing history of peanut allergy. Of this group, 86% had positive ImmunoCAP results (over 0.35 kUA/L) to tree nuts. Thirty-four percent were clinically reactive to one or more tree nuts. Logistic regression analysis was performed to estimate the relationship between diagnosis of allergy and allergen-specific IgE levels.

Based on this analysis, the investigators proposed diagnostic decision points associated with 90% to 95% predicted probability of clinical reactivity to peanut and walnut. Probability curves for peanut, sesame seeds, and various tree nuts were constructed as well. The analysis showed strong correlations between cashew and pistachio and between pecan and walnut.

The study suggests useful specific IgE cutoff points as an aid to the clinical evaluation of allergy to peanut, tree nuts, and seeds. It also provides data on which tree nut allergies are more and less likely in patients allergic to peanut.

COMMENT: *One almost needs to be a statistician to correctly apply quantitative data to patient decisions. Thus in regard to food allergies and quantitative specific IgE assays, one must know for each individual food the positive and negative predictive values of the assay. And not all assays are comparable with each other. In reference to allergies to peanuts and tree nuts, this study proposes "decision points" for the ImmunoCAP assay. Unfortunately, while those points have favorable positive predictive ability, we must recognize that they lack good negative predictive ability. This means that many people with true clinical reactivity will be missed and may be inappropriately reassured of their safety. Bearing those points in mind, this paper includes a very useful table of correlations among peanut and individual tree nuts and sesame seeds. For example, peanut-specific IgE levels have a correlation of 46% with hazelnut levels, but only 4% with walnut, and so on. You will find a surfeit of such kernels in this paper. Bon appétit!*
R. J. M.
Maloney JM, Rudengren M, Ahlstedt S, et al: The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy.
J Allergy Clin Immunol. 2008;122:145-151. ♦♦

CLINICAL TIDBITS

CRS Occurs with Allergic and Nonallergic Rhinitis

THERE are conflicting data regarding the association between allergy and CRS. This study compared the rate of CRS between patients with persistent nonallergic versus allergic rhinitis.

The study included 115 patients with persistent rhinitis symptoms: 78 females and 37 females, mean age 32 years. Individual and global CRS symptoms were assessed and rated, along with the impact on quality of life. In addition to skin prick tests for common allergens, patients underwent rhinoscopy and paranasal sinus CT to confirm the diagnosis of CRS.

Allergic rhinitis was diagnosed in 68.7% of patients, asthma in 22.6%, and CRS in 45.2%. The characteristics of CRS were not significantly different between patients with and without allergies. However, some symptoms were more severe in nonallergic patients; CT staging scores were higher as well. The only significant difference on rhinoscopy was the presence of nasal purulence in patients with allergic rhinitis. ➤➤

Among patients with persistent rhinitis, CRS may occur in those with and without allergies. The results question whether atopy plays any role in the pathogenesis of CRS, and suggest that allergy-specific treatments will not be effective for most patients.

COMMENT: *Nonallergic rhinitis is defined by the absence of sensitivity to known allergens. This diagnosis by default is a major challenge in formulating a treatment regimen or in associating nonallergic rhinitis with other conditions, such as rhinosinusitis. How different is the pathophysiology of allergic rhinitis from nonallergic rhinitis? Could local IgE production explain rhinitis without positive skin tests? Could allergic rhinitis and nonallergic rhinitis be similar conditions on different ends of the spectrum? Could allergic patch tests identify sensitivity in some subjects with nonallergic rhinitis? These are questions to ponder.*
D. K. L.

Gelincik A, Büyüköztürk S, Aslan, I et al: Allergic vs nonallergic rhinitis: which is more predisposing to chronic rhinosinusitis?
Ann Allergy Asthma Immunol. 2008:101:18-22. ♦♦

Is There a Better Cat Allergen?

CAT dander extract, comprising several different allergens, is widely used for the diagnosis of cat allergy. The authors previously reported the development of a recombinant major cat allergen, rFel d 1, with the same properties as natural cat allergen. Here they report on the presence of IgE and IgG4 antibodies to rFel d 1 in two populations of patients with cat allergy.

The study included a Swedish population of 27 children and 31 adults with cat allergy and an Australian population of 41 adults and 41 children. All patients had rhinoconjunctivitis and/or asthma. The IgE responses to rFel d 1 and CDE were strongly correlated with each other, although levels of IgE to rFel d 1 averaged 30% higher. IgE antibodies to rFel d 1 were present in 98% of the cat-allergic patients, compared to none of a control group. For children with the highest levels of IgE to rFel d 1, the odds ratio for asthma was 3.23. Median IgE levels were 19.4 kU/L for children with asthma versus 6.6 kU/L for those with rhinoconjunctivitis and 3.0 kU/L for adults with asthma. Asthmatic children also had higher IgG4 levels than asthmatic adults.

For the diagnosis of cat allergy, the recombinant allergen evaluated in this study appears at least as sensitive as CDE. Children with high levels of IgE to rFel d 1 may be at particularly high risk of asthma.

COMMENT: *These authors found that ImmunoCAP testing with recombinant Fel d 1, but not with conventional CDE, was predictive of asthma in cat-allergic children. They argue that using rFel d 1 as an in vitro test reagent may be superior to using the conventional extract. These results are provocative, but further studies are necessary to fully validate this reagent.*
S. A. T.

Grönlund H, Adédoyin J, Reininger R, et al: Higher immunoglobulin E antibody levels to recombinant Fel d 1 in cat-allergic children with asthma compared with rhinoconjunctivitis.
Clin Exp Allergy. 2008;38:1275-1281. ♦♦

Intermittent Tacrolimus Controls Chronic Eczema in Adults

RECENT reports suggest that a proactive approach to treatment of atopic dermatitis (AD)--consisting of intermittent use of topical anti-inflammatory drugs given at low doses--can control acute AD while preventing exacerbations. This study evaluated a proactive approach to AD treatment using topical tacrolimus every 2 weeks.

For up to 6 weeks, 257 adult patients with AD used 0.1% tacrolimus ointment twice daily in open-label fashion. After reaching an investigator global assessment score of 2 or less, patients were randomized to continued twice-weekly treatment with tacrolimus or inactive vehicle for 12 months. If exacerbations occurred, twice-daily tacrolimus treatment was resumed.

Two hundred twenty-four patients were randomized. Patients assigned to proactive tacrolimus had a median of 2 fewer disease exacerbations requiring treatment intervention. Fifty-seven percent of patients in the proactive treatment group had no exacerbations requiring treatment, compared to 30% in the reactive group. The proactive approach was also associated with fewer days of exacerbation treatment, 12.4 versus 31.5 days; and a longer time to first exacerbation, 142 versus 15 days. Adverse events were similar between groups.

The findings support a proactive approach to topical tacrolimus treatment in adult patients with AD. For most patients, twice-weekly tacrolimus effectively reduces and/or delays AD exacerbations.

COMMENT: *Clinicians' hands are often tied when recommending treatment for atopic dermatitis. Barriers to long-term disease control include concerns about topical steroid side effects, the FDA warning regarding calcineurin inhibitor safety, and the lack of FDA approval for long-term use of either of these classes of medication. There is considerable evidence that a proactive treatment approach can control the disease while also minimizing cumulative exposure to medications. This study demonstrated sustained control of atopic dermatitis in adults using tacrolimus administered just twice a week.*
S. A. T.

Wollenberg A, Reitamo S, Girolomoni G, Lahfa M, et al: Proactive treatment of atopic dermatitis in adults with 0.1% tacrolimus ointment.
Allergy. 2008;63:742-750. ♦♦

REVIEWS OF NOTE

COMMENT: *Chronic obstructive pulmonary disease is often underrecognized and can appear as severe persistent as well as mild asymptomatic airway obstruction. This is a summary with algorithms. Interestingly, as opposed to asthma, inhaled corticosteroids should not be prescribed alone in patients with COPD, but rather in combination with a long-acting beta-agonist.*
S. M. F.
Celli BR: Update on the management of COPD.
Chest. 2008;133:1451-1462. ♦♦

COMMENT: *This consensus document was jointly developed by the European Academy of Allergology and Clinical Immunology and the American Academy of Allergy, Asthma and Immunology. It is an excellent practical summary of how to recognize and treat athletes who experience exercise-induced symptoms from rhinitis, asthma, hives, and/or anaphylaxis.*
S. A. T.
Schwartz LB, Delgado L, Craig T, et al: Exercise-induced hypersensitivity syndromes in recreational and competitive athletes: a PRACTALL consensus report (what the general practitioner should know about sports and allergy).
Allergy. 2008;63:953-961. ♦♦

COMMENT: *Controversy still exists concerning an increased risk for serious asthma-related adverse events in patients receiving long-acting beta-agonists. These authors examined in a meta-analysis whether the incidences of severe asthma related events differ in persons receiving salmeterol plus inhaled corticosteroids compared with inhaled corticosteroids alone in randomized, controlled trials. They conclude that salmeterol combined with inhaled corticosteroids decreases the risk for severe exacerbations, doesn't alter the risk for asthma-related hospitalizations, and may not alter the risk for asthma-related deaths or intubations compared with inhaled corticosteroids alone.*
M. F.
Bateman E, Nelson H, Bousquet J, et al: Meta-analysis: effects of adding salmeterol to inhaled corticosteroids on serious asthma-related events.
Ann Intern Med. 2008;149:33-42. ♦♦

COMMENT: *Common variable immunodeficiency (CVID) is a primary immunodeficiency most commonly encountered in clinical practice. Appropriate diagnosis and management will have a significant effect on morbidity and mortality as well as financial aspects of health care. As discussed in this seminar, primary immunodeficiencies comprise many diseases caused by genetic defects primarily affecting the immune system. About 150 such diseases have been identified, with more than 120 associated genetic defects. Although primary immunodeficiencies are quite rare in incidence, the prevalence can range from 1 in 500 to 1 in 500,000 in the general population, depending on the diagnostic skills and medical resources available in different countries. Advances in diagnostic laboratory methods, including B-cell subset analysis and genetic testing, coupled with new insights into the molecular basis of immune dysfunction in some patients with CVID, have enabled advances in the clinical classification of this heterogeneous disease.*
M. F.
Park MA, Li JT, Hagan JB, et al: Common variable immunodeficiency: a new look at an old disease.
Lancet. 2008:372:489-502. ♦♦

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