AllergyWatch®

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

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Reduce Your Asthma Risk . . . Eat Fish!

SOME evidence suggests that a diet high in fish or cod oil might reduce the risk of asthma and atopic diseases. Studies of this issue have yielded conflicting results, and have not addressed the long-term protective effects of fish consumption in childhood. Data from a large, population-based study were used to assess the association between fish and cod oil intake and adult asthma.

In the Respiratory Health in Northern Europe (RHINE) study, 16,187 subjects in five northern European countries responded to a mail questionnaire. The survey included data on fish intake in childhood and fish and cod oil intake in adulthood, as well as on asthma and asthma symptoms. Multiple logistic regression analysis was performed to evaluate associations between fish and cod oil consumption and asthma outcomes, with adjustment for age, sex, body mass index, adult hayfever, type of dwelling, smoking, and study center. In a subsample of 2,459 subjects participating in the European Community Respiratory Health Survey, data were also available on family history of hayfever and asthma and on parental smoking during pregnancy.

Fish consumption was much higher for subjects in Iceland and Norway than in Sweden, Estonia, and Denmark. Adults who at fish less than once weekly had increased asthma symptoms. However, there was no apparent protective effect at higher levels of fish consumption. Subjects reporting no fish intake in childhood were at increased risk of asthma and had earlier asthma onset. Otherwise, there was no dose-response association between childhood fish intake and adult asthma. There was a U-shaped association between adult cod oil consumption and asthma, with subjects who took cod oil never and daily having the highest asthma rates.

For adults, eating fish at least once weekly is associated with a lower rate of asthma symptoms. Children who never eat fish may be at increased risk of adult ➤➤

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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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asthma. Prospective studies with more complete dietary data are needed to evaluate this possible threshold effect of fish consumption.

COMMENT: *These findings from the RHINE study reveal a striking inverse relationship between asthma and eating fish, particularly in patients who had never eaten fish during childhood. These results are strengthened by the large study size and adjustment for confounding variables. However, a prospective study is needed to confirm these observations.*
S. A. T.

Laerum BN, Wentzel-Larsen T, Gulsvik A, et al: Relationship of fish and cod oil intake with adult asthma.
Clin Exp Allergy. 2007;37:1616-1623. ♦♦

High Rate of Oat Allergy in Children with Atopic Dermatitis

SOME of the emollients and moisturizers used as adjuvant treatments for atopic dermatitis (AD) have ingredients with possible anti-inflammatory properties, such as oat proteins. There have been several reports of patients with contact allergy to oat proteins in moisturizers. The prevalence and clinical significance of sensitization to oat were assessed in a large group of children with AD.

The prospective study included 302 children with AD who were referred for allergy testing over a 3.5-year period. In addition to the European standard series, the children underwent patch testing and skin prick testing for sensitization to oat proteins at concentrations of 1%, 3%, and 5%. Thirty-two patients with evidence of oat sensitization underwent oral food challenge and 25 underwent repeated open application test.

Patch testing was positive for oat sensitization in 14.6% of children, while 19.2% had positive skin prick tests. For children aged 2 years or younger, the rate of positive patch test results was 45.5%. Among children with oat sensitization, oral food challenge was positive in 15.6% and the repeated open application test in 28.0%. Patch testing was positive for oat sensitization in 32% of children who used skin products containing oat, compared with none of those who did not use oat products.

The study documents a high prevalence of oat sensitization among children with AD referred for allergy testing. This may reflect repeated use of oat-containing products in predisposed children with impairment of the epidermal barrier. Sensitization rates are particularly high for children aged 2 and under; the authors recommend avoiding the use of topical products containing oat protein in infants with AD

COMMENT: *Oatmeal baths and oat creams have a reputation for soothing angry skin, and there are even limited data supporting the use of oat cream as a steroid-sparing agent in AD. However, this French study found an alarming rate of sensitization to oat protein among children who used oat cream emollients, including some with positive oral challenges to oat. Caution is therefore warranted when using these creams regularly.*
S. A. T.

Boussault P. Léauté-Labrèze C, Saubusse E, et al: Oat sensitization in children with atopic dermatitis: prevalence, risks and associated factors.
Allergy. 2007;62:1251-1256. ♦♦

Beta-2 Receptor Polymorphisms Affect Salbutamol Response in COPD

REVERSIBILITY of airflow obstruction in response to bronchodilators is a key clinical concern in patients with chronic obstructive pulmonary disease (COPD). Two common polymorphism of the β_2-adrenergic ➤➤

receptor gene (*ADRB2*)--Arg16Gly and Glin27Glu--have been shown to affect responses to β_2-agonists in asthma patients. The effects of these polymorphisms on short-term bronchodilator responses were studied in patients with COPD.

The study included 246 Japanese patients with COPD who were enrolled in a longitudinal cohort study. All underwent genotyping of *ADRB2* at codons 16 and 27. Short-term bronchodilator responses to salbutamol were compared for patients in different genotype groups.

The prevalence of the Arg16Gly and Glu27Gln polymorphisms was similar to the expected number. Patients with the Arg16 allele had a reduced bronchodilator response to salbutamol. Mean differences between postbronchodilator and prebronchodilator FEV_1 were 2.19 in Gly16 homozygotes vs 2.09 in Arg16Gly16 heterozygotes and 2.01 in Arg16 homozygotes. The Arg16Gly polymorphism was associated with reduced bronchodilator responsiveness independent of severity of airflow limitation, age, and smoking. Responses to salbutamol were also reduced among subjects with the most common Arg16-Gln27 haplotype.

Common *ADRB2* polymorphisms affect short-term bronchodilator responses to salbutamol in patients with COPD. These genetic factors may be an important source of variability in responsiveness to β_2-adrenergic agonists in patients with chronic obstructive airway diseases.

COMMENTS: *It is not surprising that Arg/Arg polymorphism of the β_2 receptor in lungs of patients with COPD would demonstrate a diminished response similar to that in asthmatics. However, this is the first study investigating β_2 receptor polymorphisms in COPD. Although the effect is small, the therapeutic implications are important. Aside from therapeutic decisions in COPD, the diminished response to short-acting beta-agonists augments our knowledge about polymorphisms in asthma.*
S. F. W.

Hizawa N, Makita H, Nasuhara Y, et al: β_2-Adrenergic receptor genetic polymorphisms and short-term bronchodilator responses in patients with COPD.
Chest. 2007;132:1485-1492. ♦♦

Interleukin-4Ra Inhibitor Reduces Late-Phase Asthmatic Responses

ALLERGIC asthma has been linked to upregulation of T-helper 2 (Th2) cytokines such as interleukin (IL)-4 and IL-13, which may participate in the physiologic response to allergen challenge. Pitrakinra is a newly developed recombinant human IL-4 variant that inhibits binding to IL-4Rα receptor complexes, thus interfering with the activities of both IL-4 and IL-13. The effects of pitrakinra on late-phase responses to allergen challenge were studied in patients with atopic asthma.

The authors present data from two randomized, double-blind phase 2a clinical trials of pitrakinra in patients with atopic asthma. The first study included 24 patients, who received once-daily subcutaneous treatment with pitrakinra, 25 mg, or placebo. In the second study, 32 patients received twice-daily treatment with nebulized pitrakinra, 60 mg, or placebo. Responses to inhaled allergen challenge were assessed before and after 4 weeks of treatment. In the first study, the main outcome of interest was maximum percentage decrease in FEV_1 over 4 to 10 hours after allergen challenge. In the second study, the average percentage decrease in FEV_1 was the primary endpoint.

In the first study, the maximum percentage decrease in FEV_1 was 17.1% for patients receiving pitrakinra, compared with 23.1% in the placebo group. In the second study, the average percentage decrease in FEV_1 was 4.4% with pitrakinra, compared to 15.9% with placebo. This endpoint was 3.7 times lower with pitrakinra than with placebo.

Subcutaneous pitrakinra was associated with significant reductions in asthma-related adverse events and events requiring β-agonist medications. The number of asthma-related adverse events was too low for analysis in the study of nebulized pitrakinra.

Treatment with the IL-4Rα inhibitor pitrakinra is associated with significant reductions in late-phase responses to allergen challenge in patients with atopic asthma. More study is needed to determine whether the effects of pitrakinra result from inhibition of IL-13 alone or of both IL-13 and IL-4.

COMMENT: *This small study involving pitrakinra, an inhibitor of IL4Rα, is an exciting demonstration of physiologic features of asthma attributable to airway remodeling and exacerbations. Suppression of allergen-induced late-phase measures of airway obstruction and exhaled nitric oxide was especially shown after inhalation of pitrakinra. However, subcutaneous administration also demonstrated effects. The implication for disease modification by suppressing IL-4/13 activation of IL4Rα is tantalizing. Larger studies with added clinical endpoints will help clarify this.*
S. F. W.

Wenzel S, Wilbraham D, Fuller R, et al: Effect of an interleukin-4 variant on late phase asthmatic response to allergen challenge in asthmatic patients: results of two phase 2a studies.
Lancet. 2007;370:1422-1431. ♦♦

Wheezy Preschoolers Have Pathologic Features of Asthma

EOSINOPHILIC airway inflammation, a key pathologic feature of asthma, has been reported in children as young as 3 years old. It is unclear when the finding of epithelial reticular basement membrane (RBM) thickening develops--neither eosinophilic inflammation nor airway wall remodeling has been found in wheezy infants. These asthma characteristics were evaluated in preschoolers with severe, recurrent wheezing.

The study included endobronchial biopsy specimens from infants and children, 3 months to 5 years old, ➤➤

who were undergoing clinically indicated bronchoscopy. There were 16 children with wheezing confirmed by video questionnaire (median age 29 months) and 14 with parent-reported wheezing. Another 10 nonasthmatic children with stridor served as controls. Biopsy specimens were examined to compare eosinophilic inflammation (volume fraction of immunologically distinct inflammatory cells) and RBM thickness between groups.

Median RBM thickness was 4.6 µm in children with confirmed wheezing, compared to 3.5 µm in those with reported wheezing and 3.8 µm in controls. Median values for eosinophil density were 1.07% in confirmed wheezers, 0.72% in reported wheezers, and 0.0% in controls. Both values were higher in the confirmed wheezers than in the nonasthmatic controls. Percentages of other inflammatory cells were similar between groups.

Among children with confirmed severe, recurrent wheezing, pathologic evidence of asthma can be found as early as 1 to 3 years of age. This is consistent with the timing of initial lung function abnormalities among preschool-aged children with wheezing. Treatment during this critical period may have the potential to affect the natural history of childhood asthma.

COMMENT: *In this study the pathologic features of allergic asthma are seen in preschool children between 1 and 3 years of age. The findings fit with the previously reported data that early sensitization and high-level exposure predict persistent asthma (see Illi et al, Lancet. 2006;368:763-770). This presupposes that the immunopathologic changes of allergic asthma begin very early, which suggests the need for aggressive early intervention to modulate the allergic diathesis.*
B. E. C.
Saglani S, Payne DN, Zhu J, et al: Early detection of airway wall remodeling and eosinophilic inflammation in preschool wheezers.
Am J Respir Crit Care Med. 2007;176:858-864. ♦♦

Home Cleaning Sprays Linked to Adult Asthma

PREVIOUS studies have shown that cleaning workers, especially those involved in domestic cleaning, are at increased risk of asthma. The use of specific cleaning products, such as bleach and sprays, may contribute to this risk. This study evaluated possible respiratory effects of using common household cleaning products.

The analysis, part of the follow-up of the European Community Respiratory Health Survey, included 3,503 adult subjects who reported doing the cleaning and washing in their homes and were free of asthma at baseline. More than two-thirds were women; mean age was 43 years. In follow-up interviews, subjects were asked about their use of 15 specific cleaning products. Associations between cleaning product use and asthma--defined in terms of physician diagnosis, asthma symptoms, or use of asthma medications--were assessed.

Forty-two percent of respondents used household cleaning sprays at least once weekly. Subjects in this group had increased rates of asthma symptoms or medication use, relative risk (RR) 1.49, and wheezing, RR 1.39. Using home-cleaning sprays at least 4 days weekly was associated with more than double the incidence of physician-diagnosed asthma: RR 2.11. The relationship between cleaning products and asthma was consistent across subgroups and was unmodified by atopy. Risk increased not only with frequency of use, but also with the number of different sprays used. Much of the increase was related to glass cleaners, furniture sprays, and air fresheners.

Adults who are frequent users of household cleaning sprays may be at increased risk of asthma. Confirmatory studies are needed, including efforts to identify the causative chemicals and other factors affecting exposure.

COMMENT: *This study again supports the very clear association with indoor and environmental irritants as a precursor for asthma and as a risk factor for persistence of symptoms. This ties in quite nicely to published data from the California Air Resources Board regarding the increased incidence of childhood asthma in populations in areas of high outdoor pollution.*
B. E. C.
Zock J-P, Plana E, Jarvis D, et al: The use of household cleaning sprays and adult asthma: an international longitudinal study.
Am J Respir Crit Care Med. 2007;176:735-741. ♦♦

Allergic Rhinitis Increases Risk of New BHR

CROSS-sectional studies have shown that allergic rhinitis is strongly linked to bronchial hyperresponsiveness (BHR), even in people without asthma. This suggests that upper and lower airway dysfunction often occur together and may share many of the same risk factors. Follow-up studies of subjects with allergic rhinitis, including measures of bronchial responsiveness, are needed to understand these associations. A large group of subjects with and without allergic rhinitis were monitored for the development of BHR over long-term follow-up.

The analysis included follow-up data on 3,719 subjects from the European Community Respiratory Health Survey who were free of BHR at baseline. The study definition of allergic rhinitis was a history of nasal allergy with positive specific IgE to common allergens.

At 9 year's follow-up, BHR developed in 9.7% of subjects with allergic rhinitis, 7.0% of those with atopy but not allergic rhinitis, and 5.5% of those with neither condition. Compared to the latter group, odds ratios for BHR were 2.44 for subjects with allergic rhinitis and 1.35 for those with atopy alone, after adjustment for sex, smoking, body mass index, and FEV_1. Among subjects with allergic rhinitis, the risk of BHR was particularly high for those with monosensitization to cat, OR 7.90; or dust mites, OR 2.84.

In a group of 372 subjects with BHR at baseline, 35.3% of those with allergic rhinitis had no further BHR during follow-up, compared to 51.8% of those with-➤➤

out allergic rhinitis--OR 0.51. Patients with rhinitis who were treated with nasal steroids were more likely to have their BHR go into "remission," OR 0.33.

This long-term follow-up study shows that subjects with allergic rhinitis are more likely to develop new-onset BHR, even compared to atopic subjects without allergic rhinitis. Treatment for allergic rhinitis improves the chances that BHR will resolve. The results further strengthen the association between allergic rhinitis and lower airway inflammation.

COMMENT: *This large study allows us to better understand and reinforce the one-airway hypothesis, with rhinitis preceding BHR. This tendency is greater with environmental allergies, which supports data from recent studies in children (see Illi et al, Lancet 2006;308:763-770). Intervention with nasal steroids also allowed for a significant reduction in BHR.*
B. E. C.

Shaaban R, Zureik M, Soussan D, et al: Allergic rhinitis and onset of bronchial hyperresponsiveness: a population-based study.
Am J Respir Crit Care Med. 2007;176:659-666. ♦♦

More Frequent Exacerbations Lead to Faster Remodeling

WORSENING airway inflammation associated with asthma exacerbations is thought to lead to increased airway structural changes, or remodeling. However, it remains unclear whether asthma patients with more frequent exacerbations have faster declines in lung function. Patients with moderate to severe asthma were followed up to assess the relationship between exacerbations and the rate of decline in lung function.

The study included a historical cohort of nonsmoking patients who had moderate to severe asthma before starting treatment with inhaled corticosteroids. Over a median follow-up of 11 years, 60.2% of subjects had one or more severe exacerbations (requiring hospitalization or causing a significant and reversible reduction in FEV_1). Lung function outcomes were compared for patients above and below the median exacerbation rate of 0.10 per year.

Patients who took oral corticosteroids and those with more severe obstruction at baseline had higher exacerbation rates. Patients with more frequent exacerbations had a faster rate of decline in FEV_1--median difference 16.9 mL/y--compared to those with less frequent exacerbations. The difference was independent of risk factors for severe exacerbations. One severe exacerbation per year was associated with an additional 30.2 mL annual decrease in FEV_1.

For patients with moderate to severe asthma, an increased exacerbation rate is associated with a faster rate of decline in pulmonary function at long-term follow-up. Thus exacerbations correspond to periods of accelerated airway remodeling. Prevention of exacerbations is an important outcome in clinical trials of asthma treatment.

COMMENT: *This excellent review and accompanying editorial by Malcom Sears (Eur Respir J. 2007;30:411-413) reinforce the data that severe asthma exacerbations are a significant risk factor for increased loss of lung function over time. The findings support the hypothesis that recurrent bouts of severe airway inflammation are a predictor of decreased lung function.*
B. E. C.

Bai TR, Vonk JM, Postma DS, Boezen HM: Severe exacerbations predict excess lung function decline in asthma.
Eur Respir J. 2007;30:452-456. ♦♦

Can Early Dietary Intervention Alter the Course of Eczema?

THE mechanism by which breast-feeding protects against allergy is unclear; avoidance of cow's milk and other potential allergens may play a role. This study evaluated maternal history of allergy as a potential modifier of breast-feeding's protective effect against early allergic disease.

The analysis included data on 2,705 Dutch infants from the KOALA Birth Cohort Study. Mothers provided information on atopic disease manifestations in questionnaires completed at 34 weeks' gestation and from 3 to 24 months after birth. Blood samples were collected for measurement of total and specific IgE. The relationship between breast feeding and allergic disease during the first 2 years of life was compared for three groups defined by maternal allergy/asthma status: no maternal history, maternal allergy but not asthma, and maternal asthma.

For infants whose mothers had no allergy or asthma, longer durations of breast-feeding were associated with a reduced risk of eczema. There was also a significant trend for infants of mothers with allergy but not asthma. However, duration of breast-feeding did not affect eczema risk for infants of mothers with asthma. Across maternal allergy/asthma groups, infants who were breast-fed longer were at lower risk of recurrent wheezing.

The reduction in eczema risk associated with prolonged breast-feeding is affected by maternal history of allergy and asthma. The protective effect is weaker for infants of mothers with a history of allergy but not asthma, and disappears for infants of asthmatic mothers. Prolonged breast-feeding protects against recurrent wheezing regardless of maternal allergy/asthma status, possibly by reducing the rate of respiratory infections.

Snijders BEP, Thijs C, Dagnelie PC, et al: Breast-feeding duration and infant atopic manifestations, by maternal allergic status, in the first 2 years of life (KOALA Study).
J Pediatr. 2007;151:347-351. ♦♦

TO reduce the risk of allergic disease, infant feeding guidelines call for exclusive breast-feeding➤➤

through the first 6 months of life, before the introduction of solid foods. However, there is no firm scientific evidence that delaying solid foods prevents atopic disease. This cohort study analyzed the relationship between age at introduction of solid foods and the development of eczema.

The German Infant Nutritional Intervention Program included a birth cohort of 5,991 infants recruited from 1995 to 1998. Families with a history of allergy were asked to participate in an intervention study, in which mothers were encouraged to breast-feed for at least 6 months. The mothers were also advised not to introduce solid foods until after 4 months of age, and then only gradually, avoiding potentially allergenic foods for the first year. Families with no history of allergy, and those who declined to participate in the intervention trial, served as a nonintervention subgroup. The main outcomes of interest were physician-diagnosed eczema and eczema symptoms.

Follow-up data were available on 4,753 infants. In addition to family history of allergy, the intervention and nonintervention groups differed in terms of feeding practices. Infants in the nonintervention group were less likely to be breast-fed, more likely to be started on solid foods within the first 4 months, and more likely to receive potentially allergenic foods within the first year.

Rates of physician-diagnosed eczema at 2 years were 12.9% in the intervention group and 9.5% in the nonintervention group. Neither group showed any relationship between eczema and the timing or diversity of solid foods. For infants in the intervention group, delaying potentially allergenic foods until after 6 months did not reduce the risk of eczema. Avoidance of soybeans and nuts was associated with a reduced risk of eczema in the nonintervention group. However, the rate of eczema was increased for nonintervention infants who did not receive egg for the first year.

Delaying introduction of solid foods until after the first 4 months of life does not reduce the risk of eczema in infants and young children. There is also no protective effect of avoiding potentially allergenic foods beyond the first 6 months. The results question the current recommendations to delay introduction of solid foods for the prevention of allergy.

Filipak B, Zutavern A, Koletzko S, et al: Solid food introduction in relation to eczema: results from a four-year prospective birth cohort study.
J Pediatr. 2007;151:352-358. ♦♦

MORE than 80% of infants with moderate to severe atopic eczema reportedly have IgE food sensitization to cow's milk, egg, and/or peanut. However, these findings may be biased by the fact that the infants were referred for evaluation at an allergy department. Rates of IgE food sensitization were assessed in a consecutive group of infants with moderate atopic eczema referred to a dermatology clinic.

The prospective study included 51 consecutive infants referred to a university-affiliated dermatology department for evaluation of moderate atopic eczema. The infants were 39 boys and 12 girls, median age 34 weeks. Evaluation of food allergies included skin prick testing in 51 infants and CAP-FEIA measurement of specific IgE antibodies in 41. The diagnosis of IgE food sensitization was made when the results of either test were greater than the 95% predictive cutoff point for positive results on food challenge.

Skin prick tests led to the diagnosis of IgE food sensitization in 86% of infants. Seventy-three percent of the infants were sensitized to egg, 51% to peanut, and 16% to cow's milk. Based on CAP-FEIA, IgE food sensitization was present in 83% of infants: 80% to egg and 23% to cow's milk. Ninety percent of infants were diagnosed as having IgE sensitization to at least one food, based on the results of either test.

Like those referred for allergy evaluation, infants with moderate atopic eczema seen in a dermatology department have very high rates of IgE food sensitization. The authors recommend routine screening for food sensitization and allergies in 6- to 12-month-old infants with moderate atopic eczema. Further study is needed to demonstrate the clinical benefits of dietary modifications for infants with eczema.

COMMENT: *Despite lack of definitive evidence, various recommendations have been made over the years regarding the feeding of infants--most notably by the World Health Organization and the American Academy of Pediatrics--in an attempt to reduce or delay the onset of atopic disease. These three consecutive articles from the* Journal of Pediatrics *further explore the relationship between early dietary practice and eczema.*

Taken together, these studies suggest that dietary modifications as currently recommended do not prevent the natural progression of early atopic dermatitis. The guilt felt by some parents, that they "caused" their childís dermatitis by lack of adherence to a specific preventive diet, should be assuaged. More rigorous dietary restriction either in utero or while breast-feeding might (or might not) achieve the desired result, but such restriction would need to be balanced against excessive limitation of the maternal diet. Certainly, more research in this area is warranted before specific recommendations can be made.
K. R. M.
Hill DJ, Heine RG, Hosking CS, et al: IgE food sensitization in infants with eczema attending a dermatology department.
J Pediatr. 2007;151:359-363. ♦♦

The Obesity Epidemic Again Impacts Childhood Asthma

THERE is a complex pattern of interrelationships among asthma and overweight/obesity. Previous data from the Childhood Asthma Management Program (CAMP) have linked increased weight to decreased pulmonary function among children with mild to moderate asthma. This study analyzed the relationship between body weight and psychologic functioning in asthmatic children from the CAMP.

The analysis included 1,005 children, aged 5 to 12 years, with mild to moderate asthma. Patients were assessed regularly over 4.5 years' follow-up. Psychologic assessments included measures of cog-➤➤

nitive functioning and emotions and behavior (the Child Behavior Checklist). Relationships among body mass index (BMI), psychologic characteristics, and demographic factors were evaluated.

Baseline rates of overweight, defined as BMI at or above the 95th percentile for age, were not significantly different for children with mild to moderate asthma compared to the general population: 14.1% vs 14.5%. However, asthmatic children had higher rates of "overweight risk," defined as BMI between the 85th and 95th percentile: 17.1% vs 14.1%, respectively. There was no increase in either category during follow-up. Black and Hispanic children with asthma had higher rates of overweight and overweight risk, although no more so than children of the same racial groups in the general population.

Asthmatic children who were overweight at baseline had lower IQ scores, higher scores for social withdrawal, and increased levels of internalized psychologic distress. There was also a trend toward an increased frequency of depression. As they got older, overweight children with asthma had increased rates of behavior problem and decreased levels of physical activity.

Children with mild-to-moderate asthma have increased rates of "overweight risk" than children in the general population. Asthmatic children who are overweight appear to have increased psychologic problems, including psychologic distress. Additional mental health problems may develop in adolescence. The authors note that their results may underestimate the true psychologic comorbidity associated with asthma and overweight, as the study excluded children with severe asthma and those living in poverty.

Bender BG, Fuhlbrigge A, Walders N, Zhang L: Overweight, race, and psychologic distress in children in the Childhood Asthma Management Program. **Pediatrics**. 2007;120:805-813. ♦♦

AMONG children hospitalized for asthma, those who are overweight have increased lengths of stay. However, the effects of overweight on the risk of hospital admission for asthma are unclear. This study compared hospitalization rates for overweight vs non-overweight children seen in the emergency department (ED) for asthma.

The retrospective analysis included all children over age 2 who were seen for asthma exacerbations at a children's hospital ED during 2005. Patients with other chronic medical conditions in addition to asthma were excluded. Rates of hospital admission were compared for children who were overweight (over 95% weight-for-age percentile) vs non-overweight children.

During the study year, 813 children made a total of 884 ED visits for asthma. The hospital admission rate was 27%, with an ICU admission rate of 4%. Hospitalization risk was higher for children with a higher clinical asthma score, but was unaffected by patient age, sex, or poverty.

In 23% of visits, the child was overweight. Overweight children were older than non-overweight children, 8.5 vs 7.3 years; and were more likely to live in an impoverished area, 37% vs 28%. On adjusted analysis, overweight children were more likely to be hospitalized than non-overweight children: odds ratio (OR) 1.76. This was despite the lack of difference in clinical asthma score or therapeutic interventions in the ED. Non-white children were less likely to be hospitalized: OR 0.62 for black and 0.52 for Hispanic children.

Among children seen in the ED for asthma exacerbations, those who are overweight are more likely to be admitted to the hospital. The reasons for this association are unclear, but it highlights another key area in which being overweight adversely affects the health of American children.

COMMENT: *Childhood obesity is in itself a tragedy; this problem further compounds the difficulty of treating asthma in the United States. In the CAMP study, being borderline overweight was identified as a risk factor in mild to moderate asthma. However, the study excluded patients with severe disease, likely underestimating the overall risk. Additional psychologic effects on those participants were noted, not surprisingly. A separate study finds that childhood overweight worsens asthma exacerbations, actually increasing the odds of asthma hospitalization and ICU admission. Our daily efforts are focused on preventing poor asthma outcomes, but we are losing ground. Tackling obesity requires serious patient and family motivation.*
K. R. M.
Carroll CL, Stoltz P, Raykov N, et al: Childhood overweight increases hospital admission rates for asthma. **Pediatrics**. 2007;120:734-740. ♦♦

ANCA Levels May Not Reflect Disease Activity in Wegener Granulomatosis

IN patients with Wegener granulomatosis, monitoring of disease activity and prediction of relapses are key aspects of clinical management. Measurement of antineutrophil cytoplasmic antibodies (ANCA) is an established diagnostic technique, but there is ongoing debate over the use of ANCA levels as a guide to treatment. This study compared two ANCA components, pro-proteinase 3 (PR3)-ANCA and mature-PR3-ANCA, for associations with disease activity and relapse in Wegener granulomatosis.

The prospective study included 156 patients from eight U.S. centers participating in a clinical trial of etanercept. All patients were enrolled during active disease episodes. Disease activity was measured using the Birmingham Vasculitis Activity Score for Wegener granluomatosis, with specified definitions of remission and relapse. Capture enzyme-linked immunosorbent assay was used to measure PR3-ANCA levels. Levels of PR3-ANCA and mature-PR3-ANCA were compared as indicators of disease activity and predictors of remission or relapse.

Overall, there was only a weak correlation between ANCA levels and disease activity. On an individual➤➤

basis, variations in ANCA levels over time were more strongly related to disease activity, but still explained less than 10% of the variation. Decreased levels of pro-PR3-ANCA or mature-PR3-ANCA did not predict a shorter time to remission, and increases in the same levels did not predict relapse. Forty percent of patients experienced a relapse within 1 year after a rise in mature-PR3-ANCA and 43% after a rise in pro-PR3-ANCA.

In patients with Wegener granulomatosis, PR3-ANCA levels do not reflect clinical disease activity. In addition, changes in pro-PR3-ANCA or mature-PR-ANCA cannot predict disease remission or relapse. Thus ANCA levels should not be used to guide immunosuppressive treatment--the authors call for better predictors of relapse and safer alternatives to treatment for this disease.

COMMENT: *This interesting study evaluated whether pro-PR3 ANCA is a better measure of disease activity in Wegener granulomatosis--characterized by necrotizing granulomatous inflammation and vasculitis, most commonly affecting the respiratory tract and kidneys--than mature-PR3-ANCA. The authors also sought to determine whether either measure is associated with remission time or relapse rate. They found that pro-PR3-ANCA is no better than mature-PR3-ANCA, and that decreases in PR3-ANCA are not associated with shorter time to remission or relapse rate.*
M. F.

Finkielman JD, Merkel PA, Schroeder D, et al: Antiproteinase 3 antineutrophil cytoplasmic antibodies and disease activity in Wegener granulomatosis.
Ann Intern Med. 2007;147:611-619. ♦♦

Is Omalizumab Cost-Effective?

OMALIZUMAB, which has been approved for the treatment of moderate to severe asthma, is the most expensive asthma medication. The wholesale cost of the drug is nearly $1,300 per patient-month, in addition to clinic visits and other additional costs. The authors performed a formal cost-effectiveness analysis of omalizumab for moderate to severe asthma.

The Asthma Policy Model was used to simulate the use of omalizumab in adult patients with severe, uncontrolled asthma. The model incorporated published clinical and economic data to project the 10-year outcomes including quality-adjusted life-years (QALYs), costs, and cost-effectiveness--of adding omalizumab to inhaled corticosteroid treatment. Cost-effectiveness was assessed under differing clinical and economic circumstances.

At baseline rates of acute asthma events, omalizumab provided an additional 1.7 quality-adjusted life-months at an incremental cost of $131,000 over 10 years. Thus omalizumab treatment had a cost-effectiveness ratio of $821,000 per QALY gained. On sensitivity analysis, omalizumab would achieve a cost-effectiveness ratio of $100,000 per QALY--similar to that of other widely accepted therapies--at a monthly drug cost of less than $200. Omalizumab would also be cost-effective at an acute event rate five times higher than baseline.

For most patients with moderate to severe asthma, omalizumab is not a cost-effective therapy. The current price of the drug is not justified by the clinical benefit and resource savings achieved. Omalizumab's cost-effectiveness ratio is highly sensitive to price.

COMMENT: *As physicians, it is our responsibility to deliver cost-effective care to our patients. In an affluent society, cost is sometimes de-emphasized in comparison to effectiveness. But with omalizumab, at a cost of about $1,300 per patient per month just for the agent, cost cannot be overlooked. This analysis concludes that unless the cost of omalizumab drops to less than $200 per month, it cannot be considered cost-effective.*
R. J. M.

Wu AC, Paltiel AD, Kuntz KM, et al: Cost-effectiveness of omalizumab in adults with severe asthma: results from the Asthma Policy Model.
J Allergy Clin Immunol. 2007;120:1146-1152. ♦♦

Airway Colonization in Infancy Linked to Early Childhood Asthma

STUDIES of bronchoalveolar lavage fluid from young children with severe recurrent wheezing suggest that bacterial colonization may contribute to the initiating events of early asthma. The association between hypopharyngeal colonization with specific bacteria and the development of early childhood asthma was evaluated.

The longitudinal study included children of asthmatic mothers, identified from a Danish birth cohort study. At age 1 month, aspirates from the airways of 321 asymptomatic infants were cultured for *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus*. The children were prospectively followed up for the occurrence of wheezing through the first 5 years of life. Other assessments included measurement of blood eosinophil count and total and specific IgE at age 4 and pulmonary function testing and diagnostic assessment for asthma at age 5.

Cultures at age 1 month showed colonization with *S. pneumoniae*, *M. catarrhalis*, and/or *H. influenzae* in 21% of infants. Colonization with these organisms was associated with an increased risk of persistent wheezing, hazard ratio (HR) 2.40. Wheezing was unrelated to the presence of *S. aureus*.

Early colonization with *S. pneumoniae*, *M. catarrhalis*, and/or *H. influenzae* was also significantly associated with acute severe exacerbations of wheezing, HR 2.99; and hospitalization for wheezing, HR 3.85. The same bacteria were associated with increased blood eosinophil counts and total IgE at age 4, although not with specific IgE. Thirty-three percent of infants colonized with one or more of the three bacteria had asthma at age 5, compared to 10% of non-colonized infants. Rates of reversibility of airway resistance after β_2-➤➤

agonist administration were 23% and 18%, respectively.

Hypopharyngeal colonization with *S. pneumoniae*, *M. catarrhalis*, and/or *H. influenzae* during infancy is associated with increased rates of recurrent wheezing and asthma by preschool age. The results are consistent with reports of neutrophilic inflammation in young children with severe recurrent wheezing. This finding may lead to new directions in research toward the prevention of early childhood asthma and allergy.

COMMENT: *This is a longitudinal study of a cohort of children from 1 month to 5 years of age. Colonization of the neonates' hypopharynx with three bacterial pathogens* (S. pneumoniae, M. catarrhalis, *and* H. influenzae), *alone or in combination, was associated with a 2-to-4-fold greater chance of significant wheezing illness/asthma by the age of 5 years, and with elevated levels of total IgE and blood eosinophils. It is not known how this association might work, but it should give allergy fellows a target for more research.*
R. J. M.

Bisgaard H, Hermansen MN, Buchvald F, et al: Childhood asthma after bacterial colonization of the airway in neonates.
N Engl J Med. 2007;357:1487-1495. ♦♦

Cytokine Production in Infancy Predicts Childhood Wheezing Risk

PREVIOUS studies have linked decreased cytokine production during infancy to an increased risk of allergic sensitization and wheezing in early life. Interferon-γ (IFN-γ) responses might be one mechanism by which exposures such as day care or pets influence the risk of asthma and allergies, although the effects on development of asthma later in life remain unclear. The relationship between cytokine production in infancy and the development of wheezing during childhood was evaluated.

The study included 118 healthy infants, mean age 9.4 months. Production of IFN-γ and interleukin-2 (IL-2) were measured in mitogen-stimulated mononuclear cells. At intervals from 2 to 13 years, the children were followed by questionnaire for the occurrence of wheezing. Associations between cytokine production in infancy and wheezing from early childhood to adolescence were assessed.

Infants with low production of IFN-γ at 9 months were about twice as likely to develop wheezing between age 2 and 13 years: relative risk 2.29. There was also a borderline-significant increase in wheezing among children with borderline IFN-γ production in infancy. Production of IL-2 at 9 months was unrelated to wheezing outcomes. Interferon-γ production in infancy was related to toddler wheezing, occurring only before age 6 years; and to chronic wheezing, occurring before and after age 6. However, IFN-γ was not related to school-age wheezing, occurring only after age 6.

Cytokine production during infancy is inversely associated with the development of certain wheezing phenotypes later in childhood. The results raise the possibility that treatments to increase IFN-γ production during infancy might reduce these risks, or that measuring cytokine production might identify a group of infants at increased risk of childhood wheezing.

COMMENT: *Evaluating data from the Tucson Children's Respiratory Study, these researchers found an inverse correlation between in vitro leukocyte IFN-γ production and risk for wheezing in childhood. Interestingly IL-2 production was not related to childhood wheezing. This suggests that even characteristics of the immune system, specifically low IFN-γ in very early life can predict the likelihood of developing wheezing.*
S. M. F.

Stern DA, Guerra S, Halonen M, et al: Low IFN-γ production in the first year of life as a predictor of wheeze during childhood.
J Allergy Clin Immunol. 2007;120:835-841. ♦♦

Atopy Explains Most Cases of Asthma

ALTHOUGH atopy is a known risk factor for asthma, it remains unclear what proportion of asthma cases are attributable to atopy. This question was addressed using data from the Third National Health and Nutrition Examination Survey (NHANES III).

The analysis included data on 10,508 NHANES III subjects who underwent skin testing with a panel of 10 allergens. Subjects with one or more positive results on allergen-specific tests were considered to have atopy. The association between atopy and physician-diagnosed asthma was assessed.

Based on this representative sample, it was estimated that 56.3% of cases of asthma in the United States are attributable to atopy. The adjusted odds ratio for the association between atopy and asthma was 3.5. The percentage of cases related to atopy was higher for men vs women, for subjects in the highest category of education vs lower categories, and for subjects living in highly populated vs less-populated areas.

In unadjusted analyses, all positive allergen-specific tests were associated with asthma. However, after adjustment for all tests, three allergens were independently associated with an increased risk of asthma: cat, *Alternaria*, and white oak. There was also an inverse association with perennial rye. Positive tests for cat allergen accounted for 29.3% of cases of asthma.

These nationally representative data suggest that more than half of cases of asthma in the United States are attributable to atopy. However, only certain allergens appear independently related to asthma. Immunotherapy or other interventions to interfere with the pathway between atopy and asthma have great potential to reduce the number of asthma cases.

COMMENT: *The NHANES III survey collects data from over 30,000 patients. Allergy skin tests were completed in over 10,000 patients. Because of the large sample, the finding that 56% of asthma cases were* ➤➤

attributable to allergy is compelling. The authors suggest that measures which block the asthma-allergy pathway, such as immunotherapy, could reduce the overall impact of asthma.
S. M. F.
Arbes SJ, Gergen PJ, Vaughn B: Asthma cases attributable to atopy: results from the Third National Health and Nutrition Examination Survey.
J Allergy Clin Immunol. 2007;120:1139-1145. ♦♦

How Many EpiPens for Patients at Risk of Food Anaphylaxis?

ANAPHYLACTIC reactions to food are commonly seen in U.S. emergency departments (EDs). Self-injectable epinephrine is recommended for all patients at risk of such reactions. Recent studies, based on limited data, have suggested that these patients should have two doses of self-injectable epinephrine available at all times. This study evaluated the need for multiple doses of epinephrine in patients with food-induced anaphylaxis.

The retrospective study included 34 patients seen at a single ED for acute allergic reactions to foods over a 13-month period. The timing of symptom onset was assessed, along with the number of epinephrine doses given before and after the patient arrived in the ED.

Of 19 patients with anaphylaxis, 12 received at least one dose of epinephrine. Of these, three received two doses. Although the numbers were too small for statistical analysis, multiple doses of epinephrine appeared more likely for patients with anaphylactic reactions to peanut or tree nut, and for those with hypotension. Time since ingestion did not appear to affect the likelihood of requiring more than one dose of epinephrine.

Sixteen percent of patients seen in the ED for food-induced anaphylaxis require multiple doses of epinephrine, this small study suggests. The results strengthen the recommendation that patients at risk of such reactions carry two doses of self-injectable epinephrine.

COMMENT: *This paper adds additional support for the idea of having two doses of epinephrine available for treatment of anaphylaxis to foods--particularly for patients with peanut, tree nut, and shellfish sensitivity. The data show that 16% of ED-treated subjects needed two doses of epinephrine. This is similar to the findings of a previous survey showing that 25% of patients with food-induced anaphylaxis need two doses. A limitation of this paper is only ED patients are included, implying that the need for a second dose is likely lower than 16% if we assume subjects treated without coming to the ED are more likely to use one dose. We need two to be prepared.*
D. K. L.
Oren E, Banerji A, Clark S, Camargo CA Jr: Food-induced anaphylaxis and repeated epinephrine treatments.
Ann Allergy Asthma Immunol. 2007;99:429-432. ♦♦

Allergies May Play a Causal Role in Chronic Middle Ear Disease

NASAL allergies may contribute to the development of chronic secretory otitis media (SOM), or otitis media with effusion. Nasal allergy was evaluated as a potential cause of chronic SOM in adults, including the use of nasal provocation testing combined with tympanometry.

The study included 69 patients, aged 16 to 26, referred to an allergy department for evaluation of long-standing bilateral chronic SOM. All patients had suspected nasal allergy, with obstruction and other recurrent symptoms of rhinitis. The patients underwent nasal provocation tests, including a total of 173 nasal challenges with various inhalant allergens performed by rhinometry. These tests were combined with pure-tone air conduction tympanometry to assess middle ear responses in relation to nasal responses. Forty-two patients with allergic rhinitis but no history of middle ear disease underwent similar tests for comparison.

Seventy-eight percent of the SOM patients had varying types of positive nasal responses. Of the total 129 nasal responses, 117 were associated with changes in middle ear pressure. In control subjects with allergic rhinitis only, there were no significant tympanometric changes accompanying nasal responses.

Allergy leading to eustachian tube dysfunction may contribute to chronic SOM in some adult patients. Allergen nasal provocation tests combined with tympanometry are a useful diagnostic tool, with potential implications for treatment.

COMMENT: *The association between allergic rhinitis and middle ear disease is a clinical observation that is not well explained. The fact that many patients with allergic rhinitis do not develop otitis media with effusion argues that a predisposing factor, possibly anatomic, is necessary for the development of ear disease. The new study confirms this point. Some might argue that the dose of allergen used for the nasal challenge exceeds natural exposure and yields results that do not reflect real world. The challenge remains as to how to treat these subjects, since most evidence indicates that effective nasal therapy does not improve the ear disease.*
D. K. L.
Pelikan Z: The role of nasal allergy in chronic secretory otitis media.
Ann Allergy Asthma Immunol. 2007;99:401-407. ♦♦

CLINICAL TIDBITS

Experience Shows Value of Human C1-INH Concentrate for HAE

HEREDITARY angioedema (HAE) is caused by inherited deficiency of C1-inhibitor (C1-INH). Human C1-INH (hC1-INH) concentrate is of proven effectiveness for the treatment of acute attacks and ➤➤

short-term prevention, and may also be useful for long-term prevention. A 10-year experience with hC1-INH concentrate at a Hungarian HAE center is reported.

Since 1996, the authors have used hC1-INH concentrate to treat a total of 468 acute edematous attacks in patients with HAE. At a dose of 500 U, hC1-INH concentrate provided prompt relief of severe abdominal and subcutaneous and laryngeal edema. In no case did the attacks progress after treatment or recur within 72 hours. Patients continued to respond to the same dose of hC1-INH concentrate after repeated treatments. The experience included effective treatment of 94 attacks in children and 6 in pregnant women. There were no adverse reactions or viral infections, and no evidence of antibodies to the purified protein.

The experience supports the safety and effectiveness of hC1-INH concentrate for treatment of HAE attacks and short-term prophylaxis. This treatment should be available to all patients with HAE.

COMMENT: *This report documents the unique Hungarian experience of 10 years' use of purified, lyophilized human plasma-derived C1-INH, which appears to be very effective and safe for patients with acute attacks of HAE. It was most effective when administered early in the onset of an attack. The hC1-INH concentrate was even helpful for short-term prophylaxis in patients requiring general anesthesia and safe in pregnant patients. Hereditary angioedema is a life-threatening condition; patients will be thankful when this safe and effective therapeutic option is available here in the United States.*

S. M. F.

Farkas H, Jakab L, Temesszentandrási G, et al: Hereditary angioedema (HAE): a decade of human C1-inhibitor concentrate therapy.

J Allergy Clin Immunol. 2007;120:941-947. ♦♦

Montelukast Reduces Local Reactions to Immunotherapy

LOCAL reactions (LRs) to allergen immunotherapy are a frequent problem that can limit patient adherence. Antihistamine pretreatment can reduce LRs, but does not usually prevent them. Montelukast was evaluated as an alternative approach to managing LRs associated with immunotherapy.

Fifteen patients undergoing rush immunotherapy for severe reactions to hymenoptera venom were randomly assigned to premedication with placebo, montelukast 10 mg, or desloratadine 10 mg. Montelukast delayed the appearance of LRs larger than 3 cm, compared with placebo. There was no difference in LRs after pretreatment with desloratadine versus placebo. No significant difference could be shown between montelukast and desloratadine. There was no difference in itching between the three groups.

Montelukast appears to reduce LRs in patients undergoing allergen immunotherapy. This small pilot study finds no significant difference between desloratadine and placebo in reducing LRs.

COMMENT: *Local reactions are common with specific immunotherapy, and premedication with antihistamines has been shown to beneficially influence LRs. This interesting study evaluated montelukast versus desloratadine in patients with severe anaphylactic reactions to Hymenoptera in a rush protocol. Compared to placebo, LRs were significantly delayed by montelukast, but not desloradatine. However, because of the small sample size, the authors could not conclude that montelukast prevented systemic reactions.*

M. F.

Wöhrl S, Gamper S, Hemmer W, et al: Premedication with montelukast reduces local reactions of allergen immunotherapy.

Int Arch Allergy Immunol 2007;144:137ñ142. ♦♦

Do Food Additives Affect Behavior?

CONCERNS have been raised over possible behavioral effects of artificial color and additives (AFCA) in children. In randomized, double-blind fashion, 153 preschool and school-aged children were given drinks containing sodium benzoate plus one of two mixes of AFCA, or a placebo drink. Parent and teacher ratings were used to calculate a global hyperactivity score. The older children underwent a computerized attention test as well.

One of the two AFCA mixes had a significant adverse effect on hyperactivity score in preschoolers, compared with the placebo drink: effect size 0.20. The other drink had no such effect. The association was unchanged on analysis of children who consumed more than 85% of the drink and had no missing data.

The latter analysis showed a significant effect of both AFCA drinks on hyperactivity scores in older children: effect sizes were 0.12 and 0.17, respectively. The results lend credence to concerns about the behavioral effects of AFCA in children.

COMMENT: *Behavioral reactions to AFCA remain a controversial subject. It has been suggested that these additives affect behavior in children. This randomized, double-blind, placebo-controlled trial evaluated the behavioral effects of AFCA in 3-year-old and 8- to 9-year-old children, based on ratings by teachers and parents. Of interest, artificial color or sodium benzoate preservative or both resulted in increased hyperactivity in the general population, not just in children with attention deficit-hyperactivity disorder. Some limitations are the lack of control when challenges were ingested related to timing of hyperactive measures and the need for extensive resources to obtain multisource measures of hyperactivity.*

M. F.

McCann D, Barrett A, Cooper A, et al: Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded, placebo-controlled trial.

Lancet. 2007;370:1560-1567. ♦♦

REVIEWS OF NOTE

COMMENT: *You may think you know what bronchopulmonary dysplasia (BPD) is, but you are probably deluding yourself. It is* quite *different from asthma in almost every respect, and asthma medications frequently are useless. Did you know that there is an "old form" and a "new form" of BPD? There really are more questions than answers about BPD, and this review covers them nicely.*
R. J. M.
Baraldi E, Filippone M: Chronic lung disease after premature birth.
New Engl J Med. 2007;357:1946-1955. ♦♦

COMMENT: *Patients of all ages with gastrointestinal complaints commonly present to allergists, looking for a food allergy. Celiac disease occurs in 1% of the population, and has diverse symptoms going well beyond diarrhea. In fact, did you know that constipation can be the presenting complaint? This article reviews the spectrum of celiac disease and its complications, diagnostic tests, and treatments.*
R. J. M.
Green PHR, Cellier C: Celiac disease.
N Engl J Med. 2007;357:1731-1743. ♦♦

COMMENT: *It is well-proven that leukotrienes are mediators in the pathogenesis of asthma. You may not be aware that they play roles in cancer, cardiovascular disease, and infection. Leukotrienes and cytokines talk to, and regulate, each other. These facts and more are found in this excellent review.*
R. J. M.
Peters-Golden M, Henderson WR Jr: Leukotrienes.
N Engl J Med. 2007;357:1841-1854. ♦♦

COMMENT: *In children, a number of conditions mimic asthma and should be considered in the differential diagnosis, either at the time of initial evaluation or during re-evaluation of poorly responsive asthma. This is a thorough review of such asthma "masqueraders."*
K. R. M.
Weinberger M, Abu-Hasan M: Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma.
Pediatrics. 2007;120:855. ♦♦

COMMENT: *This second article in the immunodeficiency series provides practical recommendations for the interpretation of pneumococcal antibody responses in the evaluation of functional immunodeficiency. The information is influenced by the opinions of the authors, but they have extensive experience. The biggest challenges are a lack of standardized testing among different laboratories and a definition of normal values and normal responses among different age groups, since age influences the response to most pneumococcal polysaccharides. Despite the shortcomings in our current knowledge, this assay is a useful arrow in our hunt for immunodeficiency.*
D. K. L.
Paris K, Sorensen RU: Assessment and clinical interpretation of polysaccharide and antibody responses.
Ann Allergy Asthma Immunol. 2007;99:462-464. ♦♦

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