ALLERGYWATCH®

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

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Diphenhydramine Impairs Driving Ability Worse Than Alcohol

A driving simulator was used to compare the effects of the first- and second-generation antihistamines and alcohol on various driving performance measures. The subjects were 40 volunteers with seasonal allergic rhinitis to ragweed. In crossover fashion, the patients performed a 1-hour driving task in the Iowa Driving Simulator after taking diphenhydramine 50 mg, fexofenadine 60 mg, alcohol sufficient to produce a blood alcohol concentration of 0.1%, or placebo. The task simulated good driving conditions on a two-lane highway with a blacktop surface. The main outcome was coherence, which reflects the driver's ability to match the speed of a vehicle ahead of them. Lane keeping, response to an unexpected blocking vehicle, and other driving performance measures were assessed, along with self-reported drowsiness.

Coherence was significantly lower when the subjects took diphenhydramine compared with fexofenadine, alcohol, or placebo. Alcohol did not affect coherence, but it did significantly reduce performance on secondary tasks, including lane keeping (as did diphenhydramine) and response to a blocking vehicle. Overall driving performance was worst with diphenhydramine. The subjects' self-perceived drowsiness did not correlate well with their driving performance.

The results suggest that first-generation antihistamines may affect driving performance at least as badly as alcohol. This can be ascribed to the drowsiness produced by diphenhydramine, although subjective drowsiness does not predict driving performance. Second-generation antihistamines do not cause drowsiness and do not affect driving performance.

COMMENT: *This article underscores the importance of nonsedating drugs in the treatment of allergic rhinitis. Benadryl continues to be the largest-selling over-the-counter treatment for allergic rhinitis, yet is use is associated with greater impairment than the use of alcohol. Importantly, self-reported drowsiness was shown not to be an adequate predictor of performance.* ➤➤

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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
- Thorax
- Archives of Pediatric and Adolescent Medicine
- New England Journal of Medicine
- JAMA
- Lancet
- British Medical Journal
- American Journal of Medicine
- Mayo Clinic Proceedings

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Patients, physicians, and health plans need to be educated regarding these important findings.
A. M.
Weiler JM, Bloomfield JR, Woodworth GG, et al: Effects of fexofenadine, diphenhydramine, and alcohol on driving performance: a randomized, placebo-controlled trial in the Iowa Driving Simulator.
Ann Intern Med 132:354-363, 2000. ♦♦

AlaSTAT Finds 5% to 8% Population Prevalence of IgE to Latex

A highly sensitive enzyme-linked immunosorbent assay was used to examine the prevalence of IgE to natural rubber latex (NRL) in a large group of unselected blood donors. Three independent U.S. laboratories used the AlaSTAT microtiter plate test for antilatex IgE in a large population sample. The subjects were 1,997 consecutive blood donors: 56% men and 44% women. Ninety percent of the donors were classified as white, and only 10% black or "other." The prevalence of IgE to NRL was assessed, along with the performance characteristics of the AlaSTAT test at the different laboratories.

At the generally accepted cutoff point of 0.35 kU/L, the prevalence of IgE to NRL at the different laboratories ranged from 5.4% to 7.6%. For specific samples, the rate of agreement between sites was greater than 90%. Reproducibility was greatest for samples at or above the class II cutoff point of 0.7 kU/L. The three laboratories had similar percentages of positive values.

The prevalence of IgE to NRL is similar across laboratories using the AlaSTAT microtiter plate test. The large study supports previous studies reporting the prevalence of latex-specific IgE in blood donors. The results suggest that values not reaching the class II cutoff point should be considered equivocal.

COMMENT: *Diagnosis of latex allergy is a growing clinical problem in patient management and occupational assessment. This paper provides data on the prevalence of IgE to natural rubber latex in the largest blood-donor population reported to date: 1,997 subjects. Food and Drug Administration-approved technology was used in three laboratories. The prevalence of IgE to natural latex is 5.4% to 7.6%. If a more specific cutoff value is used to identify specific IgE, the prevalence of antibody is 3.9% to 4.8%. These data are necessary to interpret prevalence studies of latex allergy in at-risk populations. Minority populations were underrepresented in the study. The natural history of asymptomatic individuals with elevated NRL IgE remains to be determined.*
D. K. L.
Saxon A, Ownby D, Huard T, et al: Prevalence of IgE to natural rubber latex in unselected blood donors and performance characteristics of AlaSTAT testing.
Ann Allergy Asthma Immunol 84:199-206, 2000. ♦♦

Normal Peak Flow Does Not Exclude Airway Obstruction in Children

HOME peak expiratory flow (PEF) monitoring is an important part of modern care for moderate to severe asthma. However, there is concern that asthmatic children with air trapping—associated with an increased residual volume to total lung capacity (RV/TLC) ratio—may generate an initial burst sufficient to produce a normal PEF reading. This could lead to dangerous underestimation of the degree of airway obstruction. This study assessed the relationship between air trapping on the negative predictive value of PEF in terms of FEV_1 and forced expiratory flow at 25% to 75% of vital capacity ($FEF_{25-75\%}$). ➤➤

The study included 244 children and adolescents with asthma of varying severity: FEV_1 ranged from 28% to 134% of predicted. Analysis of 367 sets of pulmonary function tests found that 30% of patients with normal PEF measurements had abnormalities of FEV_1 or $FEF_{25-75\%}$. The ability of a normal PEF value to predict normal FEV_1 and $FEF_{25-75\%}$ decreased as air trapping increased: from 83% to 53% at the lowest to the highest RV/TLC ratio.

The results suggest that asthmatic children with higher degrees of air trapping are more likely to have false-negative results on PEF testing. Air trapping is well correlated with disease severity, so a normal PEF value in a patient with moderate to severe asthma should not be taken at face value. In the current study, 43% of children tested had an FEV_1 of less than 80% predicted, despite being asymptomatic.

COMMENT: *We have long known that peak flow measurements are less sensitive to small- airways obstruction than spirometry, and that variations in effort can introduce inaccuracies. This study shows that the degree of inaccuracy is related to the severity of airways obstruction. In other words, children who have the greatest decrease in FEV_1 and $FEF_{25-75\%}$ are most likely to have falsely normal peak flows. This is because such patients can briefly achieve high flow rates during a forced expiratory maneuver, but then their flows decline rapidly as they exhale. The take-home message is that peak flows alone should not be relied on to detect airways obstruction, either in the office or at home. Symptoms must also be used in action plans. When peak flows are monitored, their trend is a better indicator of asthma control than their actual values.*
J. M. P.
Eid N, Yandell B, Howell L, et al: Can peak expiratory flow predict airflow obstruction in children with asthma? **Pediatrics** 105:354-358, 2000. ♦♦

Compliance with Self-Administered Epinephrine Is Low

FOOD allergy is a common cause of anaphylaxis in children, causing severe and potentially fatal reactions. A self-injectable epinephrine kit is routinely prescribed for these patients. Compliance with and competence to use self-administered epinephrine were studied in 101 families of children with food allergy.

The children's mean age was 6 years. Eighty-six percent of the parents, or adolescent patients, said they carried self-injectable epinephrine with them at all times. However, only 71% of this group had the device with them at the time of the study, and 10% of these had an expired device. Overall, just 55% of families had an unexpired epinephrine kit with them. Just 32% were able to demonstrate correct use of the device. Further study of a group of 29 pediatricians found that only 18% were familiar with and could demonstrate use of any self-injectable epinephrine device.

Many families of children with food allergy do not carry self-injectable epinephrine kits with them, and many of those who do carry the devices do not know how to use them. Most pediatricians are unfamiliar with these devices. The parents of food-allergic children should be shown how to administer epinephrine, encouraged to review the technique periodically, and reminded to check the expiration date.

COMMENT: *Though it is routine to prescribe injectable epinephrine to patients with food allergy who are at risk of anaphylaxis, it has long been suspected that compliance with this recommendation is poor. Yet the degree of noncompliance is always surprising. This study suggests that only 32% of children whose families had been properly instructed about the need to carry an up-to-date Epi-Pen and how to use it actually were prepared to treat anaphylaxis in the event that it occurred. In addition, many pediatricians were not familiar enough with the device even to teach patients about its use. Clearly, additional postgraduate education is needed if deaths due to food-induced anaphylaxis are to be avoided.*
J. M. P.
Sicherer SH, Forman JA, Noone SA: Use assessment of self-administered epinephrine among food-allergic children and pediatricians. **Pediatrics** 105:359-362, 2000. ♦♦

Itraconazole Can Benefit Patients with Allergic Bronchopulmonary Aspergillosis

ALLERGIC bronchopulmonary aspergilliosis (ABPA) is common among patients with corticosteroid-dependent asthma, but often goes unrecognized. Patients with ABPA are generally treated with systemic corticosteroids. However, the long-term benefits of this treatment are unclear. Promising results have been achieved with the oral antifungal agent itraconazole. Fifty-five adult patients with corticosteroid-dependent ABPA were randomized to receive either itraconazole 200 mg twice daily or placebo. Mean age was 48 and 54 years, respectively; there were fewer men in the itraconazole group. In each patient, the diagnosis of ABPA was made according to immunologic and pulmonary function criteria. About half of each group had bronchiectasis. After a 16-week double-blind phase, all patients received itraconazole 200 once daily for 12 weeks.

Forty-six percent of patients in the itraconazole group had a positive response, including a 50% or greater reduction in corticosteroid dose and a 25% or greater reduction in serum IgE. The response rate in the placebo group was 19%. The adverse event rate was 89% and 85%, respectively. Two patients in each group had serious complications, although these were not ascribed to the assigned treatment. Itraconazole was discontinued because of pregnancy in one patient and constipation in another. During the open-label phase, 36% of patients who had not responded previously had a response, and none of the patients who had previously responded had a relapse.

Many patients with corticosteroid-dependent ABPA can benefit from the addition of oral itraconazole therapy, without added toxicity. Itraconazole may act by reducing colonization and proliferation of aspergillus, and may also have an anti-inflammatory effect. ➤➤

The optimal duration of treatment is unknown.

COMMENT: *Allergic bronchopulmonary aspergillosis (ABPA) is an allergic disease promoted by a resident fungus in the airway. The standard treatment to date has been to suppress the allergy with systemic corticosteroids. This study included 55 ABPA patients averaging about 50 years of age, almost half of whom already had associated bronchiectasis. Concurrent treatment with the antimicrobial drug itraconazole for 4 months was of clear benefit to about half of the patients. A longer course of therapy is likely to improve the response rate.*
R. J. M.
Stevens DA, Schwartz HH, Lee JY, et al: A randomized trial of itraconazole in allergic bronchopulmonary aspergillosis. **N Engl J Med** 342:756-762, 2000. ♦♦

Microbial Exposure Affects Risk of Respiratory Allergy

THE controversial "hygiene hypothesis" states that early childhood exposure to infectious agents reduces the risk of later atopic sensitization. Previous studies have suggested that stimulation of gut-associated lymphoid tissue is essential to avoid atopic sensitization to environmental allergens. This study examined the relationship between markers of exposure to orofecal and foodborne infections and respiratory allergies in a group of Italian military cadets. The subjects were assessed for allergic rhinitis or asthma by questionnaire, examination, and skin tests. Serum samples were obtained for measurement of total IgE and IgE antibodies to airborne allergens. Also assessed were antibodies against hepatitis A virus, measles, mumps, rubella, chickenpox, cytomegalovirus, herpes simplex virus type 1, *Toxoplasma gondii*, and *Helicobacter pylori*. Exposure to the various foodborne and orofecal markers was compared for 240 atopic cases and 240 controls without atopy.

The nonatopic controls had higher rates of exposure to orally transmitted microbes than the atopic cases. The difference was significant for *T. gondii*, 26% in controls vs 18% in cases; and hepatitis A virus, 30% vs 16%. The likelihood of atopy decreased as exposure to *H. pylori*, *T. gondii*, and hepatitis A virus increased. Of the overall group of 1,659 cadets, 245 had been exposed to two or more of the three infections. Seven percent of these subjects had allergic rhinitis, and only 0.4% had allergic asthma.

In support of the hygiene hypothesis, heavy exposure to orofecal and foodborne microbes appears to lower the risk of respiratory allergy. Changes in the pattern of commensals and pathogens stimulating the gut-associated lymphoid tissue may have contributed to the increasing rates of allergic rhinitis and asthma in developed countries. The findings raise the possibility of using microbial-based approaches to preventing atopy, without causing infectious disease.

COMMENT: *Many theories have been developed to explain the increased incidence of atopic diseases in developed countries. This epidemiologic study of Italian recruits shows a relationship between exposure to foodborne and orofecal microbes and failure to become atopic. This report gives further credence to the "hygiene hypothesis" of atopy and should stimulate research into dietary manipulation with microbes or their molecules, which could affect the immune system to produce a greater TH1 response.*
M. S. B.
Matricardi PM, Rosmini F, Riondino S, et al: Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study. **BMJ** 320:412-417, 2000. ♦♦

Does Low Airway pH Lead to Asthma Exacerbations?

PREVIOUS studies have shown high airway concentrations of reactive nitrogen and oxygen species in asthma. A low pH in exhaled airway vapor condensate might play a role in the pathophysiology of asthma. Repeated airway pH measurements were made in 22 patients hospitalized for asthma exacerbations and in 19 controls. The mean pH measured in exhaled airway condensate samples was 5.23 in patients with early acute asthma vs 7.8 in those with stable asthma and 7.65 in controls. After more than 48 hours of systemic glucocorticoid therapy, the condensate pH values in acute asthma patients increased significantly. The values normalized over time with anti-inflammatory therapy. However, nebulized albuterol had no effect on condensate pH. Nonasthmatic patients with other forms of airway obstruction had normal condensate pH values.

As in previous studies, the asthma patients had higher levels of endogenous nitrite in condensate than controls. This difference was ascribed to evolution of nitric oxide from endogenous nitrite. In vitro studies showed that 86% of eosinophils necrosed after 48 hours in the pH range associated with acute asthma condensate. There was little evidence of necrosis after incubation at pH 8.0, although 26% of cells showed evidence of apoptosis.

The findings suggest that airway pH may play an important role in acute asthma. Rather than being caused by airflow obstruction per se or asthma medications, the acidification of airway vapor in asthma appears related to some intrinsic abnormality in the regulation of nonvolatile species. Asthma exacerbations may be associated with a sudden reduction in airway pH, leading to eosinophil necrosis with acute release of inflammatory and bronchoconstricting substances. The findings raise the possibility that early treatment to normalize airway pH might interrupt the sequence of events leading to airflow obstruction.

COMMENT: *During acute exacerbations of asthma, patients were found to have low pH in the condensed vapor of expired air. The pH normalized after treatment with corticosteroids but not after treatment with inhaled albuterol. Acidic breath was not found in patients with other forms of obstructive lung disease. These results suggest that monitoring the pH of expired air might be used to guide treatment of asthma and that efforts to correct pH abnormalities might be ther-* ➤➤

apeutically useful. Regulation of airway pH may have a fundamental and previously unsuspected role in the pathophysiology of asthma.
J. R. B.
Hunt JF, Fang K, Malik R, et al: Endogenous airway acidification: implications for asthma pathophysiology.
Am J Respir Crit Care Med 161:694-699, 2000. ♦♦

Combined Salmeterol/Fluticasone Product May Improve Asthma Control

ADDING a long-acting bronchodilator to inhaled corticosteroid therapy can improve pulmonary function and symptom control in patients with asthma. Combining these two medications in a single inhalation device could make asthma treatment simpler and more effective. A new combination product consisting of salmeterol 50 µg and fluticasone propionate 250 µg, given via Diskus device, was evaluated in a randomized trial.

The study included 349 patients requiring regular drug therapy for stable asthma. They were assigned to receive 12 weeks of twice-daily treatment with the salmeterol/fluticasone combination product; either salmeterol or fluticasone alone, at the same doses; or placebo. Main outcome measures were area under the 12-hour serial FEV_1 curve, morning predose FEV_1, and continuation in the study without withdrawal for worsening asthma. Peak expiratory flow, symptom scores, albuterol use, and nighttime wakenings were assessed as well.

The groups had similar demographic and clinical characteristics at baseline. Patients receiving the combination product had a 23% increase from baseline FEV_1, compared with a 4% increase with salmeterol alone, a 13% increase with fluticasone alone, and a 5% decrease with placebo. Salmeterol/fluticasone also yielded a greater sustained mean improvement compared with the other treatments, increasing progressively through the 12-hour dosing interval. The mean area under the 12-hour serial FEV_1 curve also increased to a greater extent. Only 4% of patients in the salmeterol/fluticasone group withdrew because of worsening asthma, compared with 38% with salmeterol only, 22% with fluticasone only, and 62% with placebo. The combination product also brought greater improvements in peak expiratory flow, symptom scores, and albuterol use. All three active treatments were well tolerated.

The combination of salmeterol 50 µg and fluticasone 250 µg, twice daily via Diskus device, offers a safe, simplified approach to asthma treatment. This treatment improves pulmonary function and symptom control. When the combination product is marketed, it will be available in varying strengths of fluticasone, allowing the corticosteroid dose to be titrated to asthma severity.

COMMENT: *A dry powder inhaler combining salmeterol and fluticasone will soon be marketed as Advair. The results of this study indicate the combination will be more effective than either agent used alone for the treatment of patients with moderate persistent asthma. This product is easy to use and a rapid onset, which should improve adherence to treatment. The availability of several strengths of fluticasone in the combination product will allow corticosteroid dosing appropriate for the degree of asthma severity.*
J. R. B.
Shapiro G, Lumry W, Wolfe J, et al: Combined salmeterol 50 µg and fluticasone propionate 250 µg in the Diskus device for the treatment of asthma.
Am J Respir Crit Care Med 161:527-534, 2000. ♦♦

Steroid-Nonresponsive Nasal Polyps Linked to Lung Function Decline

NASAL polyposis (NP) is a common form of chronic rhinosinusitis, often accompanying asthma and/or nonspecific bronchial hyperresponsiveness (BHR). The impact of treatment for NP on asthma outcomes is uncertain, but some studies have suggested that surgery may induce worsening of the asthma. This prospective study evaluated the long-term outcomes of asthma and BHR in 46 patients with NP. All patients were thoroughly evaluated—including nasal symptoms, skin tests, serum total IgE measurement, spirometry, and carbachol challenge—before any treatment for NP. They then received 6 weeks of topical steroid treatment. If there was no clinical response, they proceeded to intranasal ethmoidectomy. The baseline evaluations were repeated after 1 and 4 years.

At baseline, 54% of patients had nonspecific BHR and 35% had a history of asthma. Eighteen patients responded to topical steroids; the remaining 28 were nonresponders and underwent surgery. These 2 groups were similar in all clinical characteristics. At follow-up, the two groups had similar improvements in nasal symptom scores. The pulmonary function results were similar between groups at baseline. However, the steroid nonresponders had significant reductions in FEV_1, FEV_1/forced vital capacity (FVC) ratio, and maximal midexpiratory flow at 1 and 4 years, whereas the responders had no significant change. Neither group had a significant change in BHR during follow-up, or in asthma severity score.

Among patients with NP, those who require surgery after failure of topical steroid therapy have significant declines in pulmonary function during follow-up. In contrast, patients whose NP responds to topical steroids have no change in pulmonary function. The mechanism of airflow obstruction in steroid nonresponders is unknown. These changes are unrelated to the presence of asthma or nonspecific BHR. Because initial lung volumes are similar between groups, the decline in lung function likely results from the nasal surgery, rather than steroid nonresponsiveness.

COMMENT: *A decline in pulmonary function occurred in patients with nasal polyps unresponsive to topical corticosteroids even though they had good relief of nasal symptoms after surgery. These findings might be used to argue against surgical treatment of nasal polyposis as a means of improving associated asthma. However, all patients had improvement in nasal symptoms with either medical or surgical therapy and we do not know what changes* ➤➤

in lung function might have occurred if their polyposis had not been treated.
J. R. B.
Lamblin C, Brichet A, Perez T, et al: Long-term follow-up of pulmonary function in patients with nasal polyposis. **Am J Respir Crit Care Med** 161:406-413, 2000. ♦♦

Magnesium Sulfate Vehicle Improves Response to Nebulized Salbutamol

AMONG other biologic actions, magnesium chloride has a relaxant effect on smooth muscle. However, most previous studies have suggested that adding IV magnesium does not improve the response to treatment for acute asthma. Magnesium sulfate can be safely given via inhalation to patients with stable asthma. This study examined the effects of isotonic magnesium sulfate as a vehicle for nebulized salbutamol given for acute asthma.

The multicenter, randomized trial included 35 patients with acute asthma. All received 2.5 mg of salbutamol via jet nebulizer. The salbutamol was given in isotonic magnesium sulfate in one group and in normal saline in the other. The 2 groups were similar in their baseline characteristics, including peak flow. Patients receiving nebulized magnesium sulfate-salbutamol had nearly double the improvement in peak expiratory flow, compared with the saline-salbutamol group. Twenty minutes after treatment, the percentage increase in peak flow was 57% greater for patients receiving magnesium sulfate. The absolute peak flow values, or the percentage of predicted values, were not significantly different, however. Baseline peak flow was inversely related to percentage increase in peak flow at 20 minutes in the magnesium sulfate group only.

Giving nebulized salbutamol in isotonic magnesium sulfate vehicle significantly improves peak flow in patients with acute asthma, compared with salbutamol in saline. Patients with greater initial obstruction have a greater response to magnesium sulfate plus salbutamol. It remains to be seen whether the improvement in pulmonary function translates into better clinical outcomes.

COMMENT: *This randomized, double-blind controlled study compared treatment in 16 patients with acute asthma with 2.5 mg salbutamol in 3 mL of normal saline solution with 19 patients treated with 2.5 mg salbutamol in 3 mL of isotonic magnesium sulfate via a jet nebulizer. Peak flows were similar in the two groups prior to treatment, but at 20 minutes, the percentage increase in peak flow was 57% greater in the magnesium sulfate group (95% confidence interval: 4% to 100%, P = .04). It is hypothesized that magnesium sulfate may augment the bronchodilator response to salbutamol in acute asthma by increasing the affinity of β-receptors to agonists.*
E. J. B.
Nannini LJ Jr, Pendino JC, Corna RA, et al: Magnesium sulfate as a vehicle for nebulized salbutamol in acute asthma. **Am J Med** 108:193-197, 2000. ♦♦

Early Childhood Eczema Has Good Outcomes, but High Risk of Allergies

ATOPIC dermatitis (AD) in infants and young children is associated with a high risk of respiratory allergy later in life. A group of 94 infants and young children with AD were followed up to 7 years of age to assess the development of clinical allergy, including risk factors for sensitization. The children's mean age was 18 months when first studied. Follow-up evaluations were performed at 42 and 86 months. The family history included atopy in 69% of patients, and AD in 58%. At each assessment, AD was graded for severity, extent of involvement, and treatment. Food allergies were assessed, along with the results of skin prick testing for inhalant allergens.

At baseline, 59 of the children had had food reactions, including 31 who had reacted to milk, egg, fish, or soybean. During follow-up, all but 12 children had reductions in eczema score. However, the percentage with symptoms of bronchial obstruction increased from 26% at baseline to 43% at last follow-up. The percentage with allergic rhinoconjunctivitis increased from 14% to 45%. Fifty-one percent had at least one episode of urticaria. By the end of follow-up, 80 of the 94 children had had symptoms of asthma or allergic rhinoconjunctivitis. Asthma was more likely for children with a family history of eczema, those with a higher eczema score, and those with a food reaction before 36 months of age. Factors associated with sensitization to inhalant allergens included family history of atopy or eczema and onset of eczema before 4 months of age.

The outcome of eczema in young children is usually good. However, these children appear predisposed to atopy, including a high risk of early sensitization to foods and later sensitization to airborne allergens. Family history of eczema is among the risk factors for allergic symptoms or sensitization.

COMMENT: *These investigators studied 94 children with mild to severe atopic dermatitis for up to 7 years. Of the 94 children with eczema, 50% developed allergic rhinitis and 47% developed asthma before age 7. Moreover, 18% became sensitized to inhalant allergens, but did not have respiratory symptoms. Presence of severe eczema at the time of study inclusion was associated with an increased tendency to produce food-specific IgE. During the follow-up, eczema improved in 82 of 94 children.*
E. J. B.
Gustafsson D, Sjöberg O, Foucard T: Development of allergies and asthma in infants and young children with atopic dermatitis—a prospective follow-up to 7 years of age. **Allergy** 55:240-245, 2000. ♦♦

Latex Sensitization Increases Over Time in Children with Spina Bifida

LATEX allergy is a frequent problem, in children with spina bifida, with risk factors including number of previous surgical procedures and the presence of atopy. Previous studies have suggested that the ➤➤

process of sensitization to latex is a dynamic one. This study examined changes in latex sensitization over time—including after latex avoidance measures—in children with spina bifida.

The study included 68 consecutive children with spina bifida. Each was assessed for risk factors for latex sensitization, including number of operations, serum total IgE level, presence of a ventriculoperitoneal shunt, and history of atopy. Skin prick testing with latex and in vitro measurement of latex-specific IgE were performed initially and 2 years later. After the initial test, a latex-free environment was adopted in the hospital, and latex avoidance measures recommended for home use.

At baseline, 26% of the children showed latex sensitization, including 9% with clinical reactions to latex. At 2 years' follow-up, 40% of the children were sensitized to latex, and 17% had symptomatic reactions. Overall, sensitization progressed in 22% of children, despite latex avoidance measures. Four percent of children had a reduction in latex sensitization, from indeterminate to nonsensitized or from sensitized to indeterminate.

This study documents progression of latex sensitization among children with spina bifida, despite latex avoidance measures in the hospital and at home. Latex-specific IgE levels increase progressively from nonsensitized, to indeterminate, to asymptomatic-sensitized, to symptomatic-sensitized children. The findings stress the importance of latex avoidance measures for children with spina bifida, and of periodic assessment for latex sensitization.

COMMENT: *This Spanish study of spina bifida patients provides important information on the natural history of latex allergy in this high-risk patient group. Even with adoption of a latex-free hospital environment, the incidence of positive latex-specific IgE increased from 26% to 40%. In addition, the number of clinically sensitized children almost doubled. These findings emphasize the need for continued vigilance in prescribing avoidance measures and providing ongoing evaluations for children in this high-risk group.*
A. M.

Mazón A, Nieto A, Linana JJ, et al: Latex sensitization in children with spina bifida: follow-up comparative study after two years.
Ann Allergy Asthma Immunol 84:207-201, 2000. ♦♦

Are Some Reactions to Varicella Vaccine Caused by Gelatin?

IT has been suggested that anaphylactic reactions to measles-mumps-rubella (MMR) vaccines are caused by the egg proteins contained in those vaccines. However, previous studies have found specific IgE to gelatin in children with immediate-type reactions to MMR vaccine. Responses to gelatin may also account for non-immediate-type reactions to these vaccines. This study sought evidence of antibodies to gelatin in children with non-immediate-type reactions to varicella vaccine.

Anti-gelatin IgE and IgG were measured in 21 children with non-immediate-type reactions to varicella vaccines. Thirty-three children with immediate-type reactions to varicella vaccine who had anti-gelatin IgE were studied for comparison. Ten percent of the children with non-immediate-type reactions had anti-gelatin IgE, while 29% had anti-gelatin IgG. All of the children with immediate-type reactions had anti-gelatin IgG in addition to anti-gelatin IgE.

Some children with non-immediate-type reactions to varicella vaccine have IgE and IgG antibodies to gelatin. Thus at least some of these reactions may result from immune reactions to gelatin. Many children with such reactions have anti-gelatin IgG without anti-gelatin IgE. The IgG antibodies may have arisen because of dietary factors or previous administration of gelatin-containing vaccines.

COMMENT: *Specific immune responses to gelatin appear to be common in children. In this report, the authors—who have previously detailed possible gelatin reactions in children receiving MMR vaccine—detail their experience with varicella reactions. Since gelatin-specific IgG would be expected in a significant number of normal children, the clinical relevance of these findings remains to be determined. Gelatin-containing vaccines must be administered with caution to children who have experienced immediate reactions to ingested gelatin.*
A. M.

Sakaguchi M, Miyazawa H, Inouye S: Sensitization to gelatin in children with systemic non-immediate-type reactions to varicella vaccines.
Ann Allergy Asthma Immunol 84:341-344, 2000. ♦♦

Low-Dose Budesonide Controls Asthma During Stable Periods

INHALED corticosteroids such as budesonide are effective and well-tolerated medications for asthma control. Recent findings suggest the importance of using the lowest effective daily dose of inhaled corticosteroids to minimize side effects. This study examined the ability of low-dose inhaled budesonide to control symptoms and pulmonary function in patients with moderate, stable asthma. The effects of a short-term increase in budesonide dose for asthma exacerbations were assessed as well.

The randomized trial included 213 patients with moderate asthma in stable condition. For the first month of the study, all patients received high-dose budesonide, 800 μg bid. They were then randomized to receive budesonide at a standard dose of 400 μg bid or a low dose of 100 μg bid. One of the low-dose groups received budesonide 200 μg bid in case of exacerbation. The high-dose group and the other low-dose group received placebo for exacerbations.

All symptoms were well-controlled by high-dose budesonide. Thereafter, symptoms remained controlled by either the standard dose or the low dose of budesonide. Most patients in all groups remained free of exacerbations. The rate of exacerbations was lower among patients receiving the standard dose than those receiving the low dose. Among the low-dose ➤➤

groups, those receiving additional budesonide had fewer exacerbations.

In patients whose asthma is brought under control by high-dose budesonide, disease control can be maintained at a reduced dose—as low as 100 μg bid. Low-dose budesonide controls both asthma symptoms and pulmonary function. In patients receiving low-dose budesonide, exacerbations can be effectively treated using a short-term increase in budesonide dose. Using this approach, the level of disease control is no different from that achieved with the reference dose of budesonide only.

COMMENT: *Using the minimum effective dose of any medication is prudent, though a general dose-response for inhaled steroids clearly exists. Compared with high-dose budesonide, the subjects in this study did just as well using low-dose budesonide as a baseline dose, increasing to high-dose therapy when their asthma flared. While this result implies the potential for reduced side effects and cost, additional studies are necessary before this claim can be made.*
S. A. T.
Foresi A, Morelli MC, Catena E, on behalf of the Italian Study Group: Low-dose budesonide with the addition of an increased dose during exacerbations is effective in long-term asthma control. **Chest** 117:440-446, 2000. ♦♦

Chronic *Chlamydia pneumoniae* Infection Is Not a Risk Factor for Respiratory Disease

INFECTION with *Chlamydia pneumoniae* can cause acute upper and lower respiratory disease. The finding of high levels of IgG antibodies against *C. pneumoniae* in patients with acute asthma exacerbations suggests that these infections may trigger bronchospasm in some patients. The relationship between *Chlamydia pneumoniae* serologic status and respiratory disease was studied in a population-based cohort of 1,773 Welsh men. Plasma samples were tested for IgG and IgA antibodies to *C. pneumoniae*. The subjects were followed up 5 years for lung function results; "chronic nonspecific lung disease" (CNSLD), assessed according to the use of certain respiratory medications; and death from respiratory causes.

Thirty-six percent of the sample had circulating IgG antibodies against *C. pneumoniae* at titers of 1:16 or higher. Of these, 56% had detectable IgA antibodies as well. Neither antibody titer was related to the risk of respiratory death. Although men with elevated IgG or IgA titers were more likely to have CNSLD at baseline, the difference was not significant. The *C. pneumoniae* antibody titers were also unrelated to pulmonary function measures. The rate of decline in FEV_1 was nonsignificantly slower in men without detectable IgG antibodies, while the opposite was true for IgA antibodies.

These population-based data suggest that chronic infection with *C. pneumoniae* is not a significant risk factor for respiratory disease, including progressive airflow obstruction. The study has limited power to detect an effect on respiratory mortality, and did not assess the role of acute *C. pneumoniae* infection in short-term exacerbations of chronic obstructive pulmonary disease. IgA antibodies to *C. pneumoniae* likely represent an impaired response to chronic *C. pneumoniae* infection.

COMMENT: *There was no association between IgA or IgG antibody to* Chlamydia pneumoniae *and the prevalence or incidence of "chronic nonspecific lung disease" or decline in lung function with time. Individuals with CNSLD were identified as those using medications commonly prescribed for chronic bronchitis, asthma, and emphysema. These findings suggest that* C. pneumoniae *does not play a role in persistent or progressive airflow obstruction, although infection with this organism may cause acute exacerbation of asthma and COPD.*
J. R. B.
Strachan DP, Carrington D, Mendall M, et al: Chlamydia pneumoniae *serology, lung function decline, and treatment for respiratory disease.*
Am J Respir Crit Care Med 161:493-497, 2000. ♦♦

Montelukast Does Not Cause Churg-Strauss Syndrome

IN a previous report, the authors described 8 asthma patients in whom manifestations of Churg-Strauss syndrome (CSS) appeared after treatment with the leukotriene receptor antagonist zafirlukast. The findings suggested that the emergence of CSS was not caused by zafirlukast, but rather from an existing systemic eosinophilic disorder, unmasked by withdrawal of corticosteroids. Of the dozens of cases of vasculitis related to zafirlukast reported to the Food and Drug Administration, nearly all have occurred after corticosteroid withdrawal. The emergence of CSS was studied in 4 patients receiving montelukast, a newer leukotriene receptor antagonist with a different molecular structure.

The patients were 3 women and 1 man, age range 25 to 63 years. All began treatment with montelukast to control asthma, which allowed discontinuation of oral or high-dose inhaled corticosteroids. All patients developed signs of CSS, such as rash, eosinophilia, and neuropathy. In each case, the symptoms of CSS resolved or lessened after discontinuation of montelukast and resumption of corticosteroid therapy. Similar symptoms developed after tapering of oral or high-dose inhaled corticosteroids in 2 asthma patients who were not taking montelukast.

In these cases, the emergence of CSS might have been caused by treatment with montelukast. However, it seems more likely that the CSS symptoms reflect unmasking of an underlying vasculitic syndrome, which may occur not only with leukotriene modifiers but with other medications that reduce the need for systemic steroids. Based on data from a large British data base, the investigators estimate the incidence of CSS at 6 to 18 cases per million patients with asthma per year.

COMMENT: *Churg-Strauss vasculitis has now been reported in rare patients taking each of the three approved leukotriene-modifier agents. It is still not clear whether* ➤➤

any of these cases was caused by the drug(s). The authors estimate the incidence of CSS in patients being treated with zafirlukast or montelukast, and argue that it is comparable to the incidence in the overall asthma population.
S. A. T.
Wechsler ME, Finn D, Gunwardena D, et al: Churg-Strauss syndrome in patients receiving montelukast as treatment for asthma. **Chest** 117:708-713, 2000. ♦♦

Steroids Inhibit ICAM-1 Upregulation in Response to Rhinovirus

RHINOVIRUSES are a major cause of asthma exacerbations, though the mechanism of this effect is unclear. Previous studies have shown that rhinovirus infection causes increased surface expression of intercellular adhesion molecule-1 (ICAM-1) on bronchial and pulmonary epithelial cells, a change that involves activation of nuclear factor-κB. This study evaluated the effects of various corticosteroids on the rhinovirus-induced increase in ICAM-1 surface expression.

Cultured primary bronchial or transformed respiratory epithelial cells were pretreated with hydrocortisone, dexamethasone, or mometasone furoate, then infected with rhinovirus type 16. Flow cytometric analysis showed that corticosteroid pretreatment inhibited the up-regulation of ICAM-1 surface expression in both types of cells. The inhibitory response was dose dependent, and similar for all three types of corticosteroids; 50% inhibitory concentrations were 10^{-10} mol/L for hydrocortisone and 10^{-11} mol/L for both dexamethasone and mometasone furoate.

This in vitro study suggests that corticosteroids inhibit the rhinovirus-induced increase in surface expression of ICAM-1 in primary bronchial epithelial cells and type II respiratory epithelial cells. Corticosteroids inhibit several different phenomena involved in rhinovirus-induced inflammation. However, the new findings indicate that ICAM-1 plays a critical role in the inflammatory response to rhinovirus, and that inhibition of ICAM-1 expression is a key mechanism by which corticosteroid treatment controls virus-induced asthma exacerbations.

COMMENT: *Rhinoviruses exacerbate asthma. The receptor for rhinoviruses on respiratory epithelium is ICAM-1, the same proinflammatory molecule that binds leukocytes to the airway. Rhinovirus infection upregulates ICAM-1 on respiratory epithelial cells, an effect inhibited in vitro by corticosteroid pretreatment. Is this the main mechanism of action of corticosteroids in asthma?*
R. J. M.
Papi A, Papadopoulos NG, Degitz K, et al: Corticosteroids inhibit rhinovirus-induced intercellular adhesion molecule-1 up-regulation and promoter activation on respiratory epithelial cells.
J Allergy Clin Immunol 105:318-326, 2000. ♦♦

Aerosol Measles Vaccination Is Effective

SCHOOL-age children typically receive a second, "booster" dose of measles vaccine. Previous reports have described the use of aerosol vaccine administrations, suggesting that the immunogenic response is at least as good as with percutaneously administered vaccine. This randomized trial compared the serologic response to aerosol vs subcutaneous measles vaccination in 4,327 South African schoolchildren, aged 5 to 14 years. The children were randomized to receive standard doses of the Edmonston-Zagreb measles vaccine by either the aerosol or subcutaneous route, or the subcutaneous Schwartz vaccine. (Another group was assigned to receive aerosol Schwartz vaccine, but this route proved ineffective.) Before vaccination and 1 month and 1 year afterward, blood samples were collected for measurement of antibody titers.

Complete antibody titer measurements were available for 992 children. At 1 year, the rate of seronegative results was 3.6% for children receiving Edmonston-Zagreb vaccine by aerosol, compared with 8.6% for those receiving the subcutaneous Edmonston-Zagreb vaccine and 13.9% for those receiving the Schwartz subcutaneous vaccine. One-month seroconversion rates were 84.7%, 78.8%, and 62.6%, respectively. None of the children had any serious side effects. A rash developed within 2 weeks after vaccination in about 5% of each group.

This study demonstrates the effectiveness and acceptability of aerosol measles vaccine administration to school-aged children. The serologic response to aerosol Edmonston-Zagreb vaccine is better than that to subcutaneous Edmonston-Zagreb or Schwartz vaccine. Aerosol vaccination can be performed using currently available devices, is well suited to mass vaccination programs, and avoids the infection risk associated with needles. The aerosol route of vaccination could be a useful tool in measles eradication efforts.

COMMENT: *These investigators randomly compared 4,327 schoolchildren (aged 5 to 14 years) who received measles vaccine either by subcutaneous route or by aerosol. There were no serious side effects, and about 5% of children in each group had a rash within 2 weeks of vaccination. The response to vaccination was better after standard-potency vaccine delivered by aerosol than vaccine given subcutaneously.*
E. J. B.
Dilraj A, Cutts FT, de Castro JF, et al: Response to different measles vaccine strains given by aerosol and subcutaneous routes to schoolchildren: a randomised trial.
Lancet 355:798-803, 2000. ♦♦

New Drug Reduces Severity of Acute Influenza

INFLUENZA is a major cause of respiratory illness, and carries a substantial rate of complications resulting in hospitalization and death. Effective drugs for the treatment of influenza A are available, but have ➤➤

significant adverse effects; there are no effective drugs against influenza B. The potent, specific influenza neuraminidase inhibitor oseltamivir carboxylate inhibits replication of influenza A and B viruses in vitro. A randomized, controlled, multicenter trial was performed to evaluate oseltamivir for safety and efficacy in the treatment of acute influenza.

Six hundred twenty-nine previously healthy, nonimmunized adults were enrolled in the study within 36 hours after developing symptoms of influenza, including a temperature of 38° C or higher. They were randomized to receive oseltamivir 75 or 150 mg/d or placebo for 5 days. Laboratory studies confirmed influenza infection in 374 patients.

Both doses of oseltamivir significantly reduced the duration of illness compared with placebo—from a median of about 100 to about 70 hours. Severity of illness scores, duration of fever, and time to resume usual activities were also significantly reduced with oseltamivir. Bronchitis, sinusitis, and other secondary infections occurred in 7% of patients receiving oseltamivir vs 15% of those receiving placebo. Virologic studies showed a similarly rapid decline in viral shedding in all three groups. Drug susceptibility studies identified a virus with altered neuraminidase susceptibility to oseltamivir in 1 patient treated with the 75 mg dose.

Oseltamivir effectively reduces the duration and severity of acute influenza infection in appropriately selected adult patients. Treatment may also reduce the risk of complications. Neuraminidase inhibitors offer an expanded spectrum of anti-influenza activity, compared with existing M2 inhibitors. Emergence of resistant viruses is a potential concern.

COMMENT: *This report provides pivotal efficacy data for oseltamivir, an oral therapy of acute influenza. The duration and severity of illness were reduced by 30% to 40%, cough by 40%, and average number of days with more than mild symptoms by 1 day. Subjects with chronic diseases—this presumably included asthma—were excluded. Thus the clinician has available a therapy that will mitigate influenza symptoms, but the value of this therapy in high-risk populations has not been assessed. The importance of influenza in aggravating asthma elevates the significance of this paper, despite the relatively modest clinical improvement demonstrated.*
D. K. L.

Treanor JJ, Hayden FG, Vrooman PS, et al: Efficacy and safety of the oral neuraminidase inhibitor oseltamivir in treating acute influenza: a randomized controlled trial. **JAMA** 283:1016-1024, 2000. ♦♦

Eosinophilia Associated with Wheezing After RSV Bronchiolitis in Infants

INFANTS who develop respiratory syncytial virus (RSV) bronchiolitis are at risk of persistent wheezing. However, it is unclear whether the bronchiolitis leads to airway changes and thus to asthma, or whether it merely reflects a predisposition to asthma during infancy and childhood. There are few data on risk factors for persistent wheezing.

Forty-three infants with acute RSV bronchiolitis were retrospectively studied. Peripheral blood eosinophil count was measured at the time of hospitalization. At age 7 years, the children were assessed for reports of wheezing and asthma. At follow-up, 15 of the children had persistent wheezing. At the time of bronchiolitis, the median eosinophil count was 98 cells/mm^3 in infants who developed persistent wheezing vs 0 cells in those with no recurrent wheezing or no wheezing past 3 years of age. Initial eosinophilia was the only factor significantly related to wheezing at age 7 years, after adjustment for family history of asthma, sex, and exposure to passive cigarette smoke. Eosinophilia had a 56% positive predictive value for wheezing at age 7.

Among infants with RSV bronchiolitis, those with peripheral blood eosinophilia are more likely to develop persistent wheezing. It is unclear how eosinophilia comes to be maintained in this subset of infants with bronchiolitis, although some immunologic mechanism already appears to be in place. Increased secretion of interleukins-4 and -5 may play a role.

COMMENT: *For years, pediatricians have been arguing about whether wheezing triggered by RSV infection occurs because a patient has asthma to begin with or whether the RSV causes lung damage that leads to asthma. This article looks for predictors of subsequent wheezing by looking at factors that can be measured at the time of the first wheezing event and whether those same patients are still wheezing 7 years later. The only factor that predicted subsequent wheezing response was eosinophilia. Since eosinophilia is an immunologic response to the infection that is specific to certain patients, the authors offer this as evidence that the patients were predisposed to have asthma before they were infected by RSV and therefore the virus doesn't cause the asthma. Because the mechanism of the eosinophilia in predisposed individuals is still unknown, the debate is likely to continue.*
J. M. P.

Ehlenfield DR, Cameron K, Welliver RC: Eosinophilia at the time of respiratory syncytial virus bronchiolitis predicts childhood reactive airway disease.
Pediatrics 105:79-83, 2000. ♦♦

Isolated Late Reactions to Skin Testing Are Common in Children

SOMETIMES children show a cutaneous reaction several hours after allergen skin testing, despite having no immediate reaction. Few studies have addressed such isolated late reactions (ILRs). The parents of 50 children undergoing routine, clinically indicated skin testing examined the skin test site 6 hours later. All children had a positive histamine control with 1 or more negative immediate reactions to allergen skin testing.

Eighteen children (36%) had a total of 40 ILRs measuring 5 mm or larger after skin prick testing. ➤➤

Twenty percent of the ILRs were associated with cockroach antigen, but many other allergens were implicated as well. The children did not consistently have symptoms when exposed to the allergens causing their ILRs, although all patients with ILRs to indoor allergens reported symptoms year round. The occurrence of ILRs was unrelated to age, sex, or asthma diagnosis. There was no pruritus, wheal-and-flare formation, or other signs of mast cell degranulation before the ILRs appeared.

Thirty-six percent of children undergoing routine skin testing for allergy show ILRs. The mechanism of ILRs is unknown; an Arthus or type 3 hypersensitivity reaction is possible. The clinical significance of these common but little-studied reactions requires further evaluation.

COMMENT: *Many allergists rely on intradermal skin testing as a basis of allergic disease diagnosis and treatment. Although the late-phase response is clearly important in the pathophysiology of allergic airways disease, this study and others have failed to determine the clinical relevance of isolated delayed reactions to intradermal testing.*
A. M.
Lierl MB: Isolated late cutaneous reactions to allergen skin testing in children.
Ann Allergy Asthma Immunol 84:294-298, 2000. ♦♦

Factors Associated with High-Severity Asthma Identified

THE 1990s saw an increase in the number of children with asthma and the number of children dying from asthma. However, the number of hospitalizations for childhood asthma decreased. Data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample were analyzed to examine trends in asthma severity during the 1990s. The analysis included data on 29,077 children with asthma admitted to 746 hospitals during 1990 and 33,443 patients admitted to 811 hospitals during 1995. Severity of illness was assessed using the All Patient Refined-Diagnosis Related Groups. In addition to patterns of asthma severity, the study evaluated patient and hospital factors associated with high-severity and the effects of severity on cost and length of stay.

Respiratory distress and respiratory failure were the diagnoses most frequently associated with high-severity asthma. High-severity asthma accounted for 4.2% of cases in 1990 and 4.6% in 1995, a nonsignificant rise. Rates of high-severity asthma were highest for males and for patients aged 13 years or older, and for urban teaching hospitals vs nonteaching hospitals. Rates of high-severity asthma were higher for hospitals in the western, southern, and northern United States than for those in the northeast. The median length of stay for high-severity asthma was unchanged from 1990 to 1995, compared with a decrease in length of stay for medium-severity asthma.

The proportion of asthmatic children with high-severity disease did not increase during the first half of the 1990s, a time when the overall number of children with asthma increased. The rate of high-severity disease is significantly affected by patient age, sex, region, and hospital type. Secondary diagnoses in hospital discharge data do not necessarily reflect hypoxemia.

COMMENT: *Accurate epidemiologic data on pediatric asthma are needed to verify changes occurring in the prevalence and severity of the condition. This study analyzed data from the National Inpatient Sample to assess differences in severity and hospitalizations in children from 1990 to 1995. Although there were no significant differences in numbers or severity of children hospitalized between 1990 and 1995, the authors found certain regional differences: more severe asthma in the western, southern, and north-central United States; in urban teaching hospitals; among girls; and among the lowest-income families. These data should help direct programs to groups with high-severity asthma*
M. S. B.
Meurer JR, George V, Subichin S, et al: Asthma severity among children hospitalized in 1990 and 1995.
Arch Pediatr Adolesc Med 154:143-149, 2000. ♦♦

Gastric Reflux Affects Arousals in Sleep Apnea

PREVIOUS studies have established a strong association between gastroesophageal reflux (GER) and obstructive sleep apnea (OSA). The association may have to do with shared risk factors, such as obesity and alcohol use, or with laryngeal inflammation caused by acid reflux. The relationship between GER and OSA was studied in 63 patients with sleep apnea, defined as an apnea-hypopnea index (AHI) of 15.0 or higher, and 41 controls with an AHI of less than 5.0. Esophageal pH monitoring studies performed at the same time as polysomnography found more GER events in OSA patients. The mean number of reflux episodes per 8 hours was 155 in the OSA group, compared with just 23 in controls. In the OSA group, 53% of reflux episodes were temporally associated with apneas or hypopneas. However, only 47% of apneas and 44% of arousals were temporally associated with acid reflux events.

Two treatment trials were performed to see if treatment for OSA affected GER characteristics, and vice versa. Nasal continuous positive airway pressure had a nonspecific effect, reducing GER parameters in patients with or without OSA. Antireflux therapy reduced nighttime arousals in patients with OSA, but did not affect the AHI.

The rate of GER is elevated in patients with confirmed OSA, compared to matched controls without OSA. Reflux is nonspecifically reduced by nasal continuous positive airway pressure, whether or not the patient has OSA. The pathogenetic contribution of sleep apneas to GER is unknown. Acid reflux may contribute to arousals in patients with OSA, but does not appear to play a role in the pathogenesis of apneas.

COMMENT: *These authors studied the preva-* ➤➤

lence of significant gastroesophageal reflux (GER) in patients with obstructive sleep apnea (OSA), seeking to determine whether therapy for OSA altered GER parameters and vice versa. Patients with GER have more frequent and prolonged OSA than matched controls. Reflux is temporally related to 40% to 50% of arousals and apneas. Nasal continuous positive airway pressure reduces GER parameters in patients with and without OSA. The role of OSA in the pathogenesis of GER remains uncertain. However, GER may be involved in the pathogenesis of arousals in patients with OSA. Whether this is a vagal reflex or direct microaspiration is unknown.

E. J. B.

Ing A, Ngu MC, Breslin ABX: Obstructive sleep apnea and gastroesophageal reflux.

Am J Med 108:120S-125S, 2000. ♦♦

Serologic Markers of *Chlamydia* Linked to Asthma

SOME cases of asthma are designated "asthma associated with infection" (AAWI), because they first appear after an episode of acute bronchitis or pneumonia. Both of these respiratory diseases can be caused by *Chlamydia pneumoniae*, which has previously been associated with asthma. Serologic testing for IgA antibodies against *C. pneumoniae* may help to identify persistent chlamydial infection in patients with asthma. This study evaluated specific serologic markers of *C. pneumoniae* for their association with AAWI.

The study included 164 outpatients with asthma, mean age 44 years. Sixty-eight had AAWI, with initial asthmatic symptoms developing after an acute respiratory illness. The remaining patients had other forms of asthma; also studied were 16 patients with acute bronchitis but without asthma and 44 healthy controls. All subjects were tested for serologic markers of *C. pneumoniae*, including species-specific IgG, IgA, and IgE antibodies and the genus-specific chlamydial heat shock protein 60 (CHSP60) antibody. Subjects positive for CHSP60 underwent immunoblotting for C. *pneumoniae*-specific IgE antibodies.

The rate of IgG seroreactivity was 93% to 94% among patients with AAWI or acute bronchitis, compared with 61% to 84% for controls. Rates of IgA seroreactivity were 69% to 75% vs 31% to 43%, respectively. Nineteen percent of the AAWI group had CHSP60 antibodies, compared with 3% of other patients. Five of the 13 AAWI patients who were positive for CHSP60 also had IgE antibodies against *C. pneumoniae*. Follow-up studies showed that positivity for IgG, IgA, and CHSP60 persisted over time.

Patients with acute bronchitis and AAWI have increased rates of seropositivity for *C. pneumoniae* antibodies. The findings support the use of specific IgA antibodies as serologic markers of persistent chlamydial infection. Rates of CHSP60 seroreactivity are relatively lower—this marker is strongly associated with the presence of *C. pneumoniae*-specific IgE.

COMMENT: *Infectious triggers of asthma are usually assumed to be viral. This article adds data to support a role of chronic* Chlamydia pneumoniae *infection in asthma exacerbations. The limitation of serologic testing in distinguishing previous infection from active, chronic infection was partially addressed by using IgA specific for* C. pneumoniae *and antibodies specific for CHSP60. Identification of active chlamydial infection in symptomatic asthma may be important since potential treatment is available.*

D. K. L.

Hahn DL, Peeling RW, Dillon E, Saikku P: Serologic markers for Chlamydia pneumoniae *in asthma.*

Ann Allergy Asthma Immunol 84:227-233, 2000. ♦♦

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