AllergyWatch®

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

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Facts Are Stubborn Things!

QUESTIONS remain about the role of exposure to allergens during infancy in the later development of sensitization and allergic disease. Studies of the contributions of pet and mite allergens have yielded conflicting results. This prospective study examined the effects of allergen exposure at age 3 months on the presence of asthma at age 4 years.

The birth cohort study included 1,127 Dutch children. Of these, 464 had atopic mothers and were considered high risk. At age 3 months, mattress dust samples were collected to assess exposure to house dust mite, cat, and dog allergens. Specific IgE levels and allergic symptoms were evaluated at age 4 years. The effects of allergen exposure on the development of sensitization, wheezing, and asthma were tested.

Of 365 children with complete data on sensitization, specific IgE to mite allergen was detected in 14%, to cat allergen in 7%, and to dog allergen in 4%. Most children had complete data on clinical outcomes--26% had early transient wheezing, 11% had persistent wheezing, and 4% had physician-diagnosed asthma.

Children exposed to dust mite and cat allergen at age 3 months were more likely to be sensitized to those allergens at age 4 years. Exposure to cat allergen during infancy was linked to an increased rate of persistent wheezing at age 4, an association of borderline significance. Exposure to dog allergen was associated with persistent wheezing, but only among children with nonatopic mothers. None of the three allergen exposures was related to asthma.

Infants exposed to mite and cat allergen are more likely to be sensitized to these allergens at age 4. The relationship of early exposure to allergic respiratory symptoms is less clear, although early cat allergen exposure seems to increase the risk of persistent wheezing. The clinical effects of other exposures may depend on history of maternal atopy. Further follow-up of the birth cohort is planned.

COMMENT: *The "hygiene hypothesis" suggests that exposure to animals in infancy may afford protec-*➤➤

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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

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tion against the development of asthma. This report analyzed data from 1,127 four- year-olds from a prospective birth cohort of over 4,000 children. Environmental allergens were measured at 3 months of age. It was not surprising that early exposure to dust mite and cat allergens was associated with sensitization to those allergens at 4 years of age. Early exposure to cat allergen also led to wheezing. Dog exposure was also associated with development of wheezing, but only in children with non-allergic mothers. This study proposes that early exposure to environmental allergens can have a significant impact in the development of allergies and allergic airway disease in childhood.
S. M. F.
Brussee JE, Smit HA, van Strien RT, et al: Allergen exposure in infancy and the development of sensitization, wheeze, and asthma at 4 years.
J Allergy Clin Immunol. 2005;115:946-952. ♦♦

Love and a Cough Cannot Be Hid

ALTHOUGH vaccination has reduced the incidence of pertussis disease, *Bordetella pertussis* continues to circulate in the population. Many cases of prolonged cough illness in adolescents and adults may actually be caused by unrecognized *B. pertussis* infection. Published studies of the epidemiology of pertussis disease and *B. pertussis* infection were reviewed and analyzed.

Reported cases of pertussis in have increased steadily since 1984, continuing in the same cyclical pattern of epidemics--peaking every 2 to 5 years--as in the prevaccine era. Increased awareness is one factor, but reductions in the efficacy of the pertussis vaccines used are another likely contributor to this problem.

Studies of adolescents with prolonged cough illness in have suggested that 13% to 20% of such cases result from *B. pertussis* infection. Five U.S. studies examining changes in *B. pertussis* antibody levels have reported infection rates of 1% to 8%, with a median of 2.2%. The rate of cough illness caused by *B. pertussis* infection among U.S. adolescents and adults is estimated at 370 to 1,500 per 100,000 population, or between 800,000 and 3.3 million cases per year.

The rising rate of pertussis disease in the United States appears to reflect increased awareness and the use of less effective vaccines. Infection with *B. pertussis* is a common cause of prolonged cough in adolescents and adults; neither vaccination nor infection provides lasting immunity. The use of acellular pertussis booster immunizations for adults and adolescents probably provides the best chance to eliminate endemic *B. pertussis* from the population.

COMMENT: *Cough, cough, cough…this past winter was a bad year for "prolonged cough illness" in my community! Dr. Cherry's analysis of both pertussis disease and infection over the past 15 years in the United State is very timely, since some of these cough problems have been proven to be caused by pertussis infection. I now understand that immunity is short-lived to natural pertussis infections, and that immunization immunity has waned since 1980. This has led the adolescent and adult population to become increasingly susceptible to pertussis illness, which is endemic in our communities.*
J. A. A.
Cherry JD: The epidemiology of pertussis: a comparison of the epidemiology of the disease pertussis with the epidemiology of Bordetella pertussis *infection.*
Pediatrics. 2005;115:1422-1427. ♦♦

RSV Comes in Extra-Large Too

RESPIRATORY syncytial virus (RSV) is the main cause of pediatric lower respiratory tract infections, but is also a known cause of illness in the elderly population. An adult RSV vaccine has been proposed. More data on the epidemiology and clinical effects of this virus among community-dwelling elderly are needed.

This prospective study evaluated the disease burden of RSV over four consecutive winters in one U.S. city. Three prospective cohorts were defined: 608 healthy elderly subjects, 540 "high-risk" adults with congestive heart failure or congestive heart disease, and 1,388 patients hospitalized for cardiopulmonary illnesses. In all three groups, average age was 70 years or older. The disease burden of RSV was evaluated through culture, reverse-transcriptase polymerase chain reaction, and serologic studies. The same techniques were used to test for influenza A virus.

Rates of RSV activity were relatively stable across the four study years, ranging from 3% to 7% among healthy elderly subjects and 4% to 10% in the high-risk group. In contrast, influenza A and B virus involvement varied substantially by year. In the healthy elderly group, infection with RSV was less likely than influenza A to lead to a doctor's office visit. There was no such difference in health care utilization within the high-risk group. For hospitalized patients, RSV and influenza A virus had a similar impact in terms of length of stay, ICU utilization, and mortality risk. Overall, RSV was estimated to be responsible for about 11% of hospital admissions for both pneumonia and COPD, 5% for congestive heart failure, and 7% for asthma.

For both healthy elderly and high-risk adults, the clinical impact of RSV infection appears comparable to that of influenza A virus. The annual rate of RSV infection averages about 5.5% per year--relatively stable across years and approximately double the rate of influenza A virus infection. The findings support further research into development of an adult RSV vaccine.

COMMENT: *Everyone knows that influenza A is a serious respiratory pathogen for older adults. This study demonstrates that, over a 4-year span, RSV caused twice as many lower respiratory tract infections as influenza A in ambulatory older adults, and equivalent numbers in older adults who required hospitalization. RSV awareness is not just for pediatricians.*
R. J. M.

Falsey AR, Hennessey PA, Formica MA, et al: Respiratory syncytial virus infection in elderly and high-risk adults.
N Engl J Med. 2005;352:1749-1759. ♦♦

A New "Sed Rate" for Asthma

ASTHMA treatment guidelines call for use of the lowest possible dose of inhaled corticosteroids to achieve disease control, based on symptoms and pulmonary function tests. The fraction of nitric oxide in exhaled air (FE_{NO}) is a potentially useful alternative measure of disease control. A FE_{NO}-based approach to adjustment of inhaled corticosteroid dose was tested.

The study included 97 asthmatic patients on regular inhaled corticosteroid therapy. Patients were assigned to have their fluticasone dose adjusted according to an algorithm based on FE_{NO} or on the Global Initiative for Asthma (GIA) 2002 criteria. In the FE_{NO} algorithm, the cutoff point for dose adjustment was 15 ppb of nitric oxide at an exhaled flow rate of 250 mL/sec. After dose optimization in the first phase of the study, patients were followed up for 12 months.

Final mean fluticasone dose was 370 µg/d in patients assigned to the FE_{NO} algorithm, compared with 641 µg/d for those assigned to the GIA algorithm. Asthma exacerbation rates were 0.49 and 0.90 episode per patient per year, respectively, although the difference was not significant. Oral prednisone use, pulmonary function measures, sputum eosinophil count, and other disease control markers were not significantly different between groups.

Use of a FE_{NO}-based algorithm to assess disease control can significantly reduce inhaled corticosteroid dose for asthmatic patients. This study finds a 40% dose reduction with no significant impact on clinical outcomes. Using exhaled nitric oxide to monitor asthma control may help to reduce the long-term risk of corticosteroid side effects.

COMMENT: *It is widely considered desirable to individualize doses of inhaled corticosteroids in asthmatics by "stepping down" to the lowest dose that maintains control. But how to assess "control"? This study compares the utility of two sets of criteria: exhaled nitric oxide levels or the published 2002 GIA algorithm. The FE_{NO} strategy maintained similar clinical outcomes using 40% lower fluticasone doses. Exhaled nitric oxide may become the "sed rate" for asthma, and may allow lower steroid doses.*
R. J. M.

Smith AD, Cowan JO, Brassett KP, et al: Use of exhaled nitric oxide measurements to guide treatment in chronic asthma.
N Engl J Med. 2005;352:2163-2173. ♦♦

Can eNO Replace Methacholine?

METHACHOLINE and other challenge tests are widely used for asthma diagnosis. Exhaled nitric oxide (eNO), as a marker of inflammation, is increased in patients with even mild asthma. Measurement of eNO was compared with standard bronchial provocation tests for the diagnosis of asthma.

The study included 85 patients referred for evaluation of possible asthma. All patients had had nonspecific respiratory symptoms, mainly cough or dyspnea, for at least 3 months. All had normal baseline spirometry results. The patients underwent measurement of eNO followed by methacholine, exercise, and adenosine 5'-monphosphate (AMP) challenge tests in random, blinded fashion. The test results were compared with clinical asthma status at 24 months' follow-up. ➤➤

Forty patients received a definitive diagnosis of asthma. Receiver operating characteristic curve analysis yielded an area under the curve of 0.896 for eNO, compared with 0.924 for methacholine challenge, 0.781 for exercise challenge, and 0.939 for AMP. An eNO value of greater than 7 ppb at a flow rate of 250 mL/s was optimal for differentiating between patients with vs without asthma: sensitivity 82.5%, specificity 88.9%, and positive and negative predictive value 89.1% and 85.4%, respectively.

Exhaled NO measurement is a potentially useful test for asthma diagnosis. It combines good diagnostic performance--similar to that of methacholine and other challenge tests--with safety and ease of use.

COMMENT: *We have all had patients in whom methacholine challenge is difficult to administer with accuracy. This is particularly true in patients with suspected vocal cord dysfunction, cough variant asthma, pertussis syndrome, etc. These authors show that measurement of eNO can be employed as a safe and rapid test for the diagnosis of asthma. They report that a cut-off value of NO over 7 ppb at a flow rate of 250 mL/s provided a sensitivity of 82.5% and a specificity of 88.9%. This was equivalent to methacholine challenge.*
E. J. B.

Berkman N, Avital A, Breuer E, et al: Exhaled nitric oxide in the diagnosis of asthma: comparison with bronchial provocation tests.
Thorax. 2005;60:383-388. ♦♦

Out, Damned Spot!

FOR patients with pet allergies, removing pets from the home is a standard recommendation. However, few studies have documented the clinical benefits of pet removal. This Japanese study compared clinical outcomes for pet-allergic patients who did and did not remove pets from the home.

The observational study included 20 patients with newly diagnosed asthma related to pet allergies. All had furred pets at home--most commonly hamsters, as well as cats, dogs, and ferrets. After baseline diagnostic tests, patients were advised to remove pets from the home. The results of follow-up tests were compared for 10 patients who complied with advice to remove the pets and 10 who refused.

The two groups were similar in terms of sensitization to pet allergens, although those who kept their pets were more likely to be sensitized to house dust mite, cedar and grass pollens, mold, and cockroach. At 10 months' follow-up, methacholine PC_{20} increased by 5.9-fold among the patients who removed pets from the home, compared to a 2.3-fold increase among patients who kept their pets.

None of the patients who removed pets were taking inhaled corticosteroids at follow-up, compared with 9 of those who kept their pets. The need for follow-up visits and other medications was also lower in the removal group. Patients who removed their pets had a significant increase in FEV_1--there was no difference compared to patients who kept their pets. Airway inflammatory markers also remained similar between groups.

In patients with pet-allergic asthma, removing pets from the home is associated with a significant reduction in airway hyperresponsiveness, compared to patients who insist on keeping their pets. Pet removal is also associated with a reduced need for inhaled corticosteroids, among other clinical benefits.

COMMENT: *One of the most frustrating discussions in everyday practice concerns the removal of the pet from the home of a pet-allergic patient. This study, however, reiterates the importance of such discussions. In the group of patients that complied with removal of the pet from the home, substantial clinical benefit was obtained. These patients had improvement in bronchial hyperresponsiveness and were able to achieve asthma control without the use of inhaled corticosteroids. I recommend keeping this study in the allergist's office, as more and more patients are motivated to decrease their overall disease and medication burdens. This study, though small, can be used as evidence to substantiate the benefit of removing pets from the home.*
T. L. H.

Shirai T, Matsui T, Suzuki K, Chida K: Effect of pet removal on pet allergic asthma.
Chest. 2005;127:1565-1571. ♦♦

Being Overweight Takes Your Breath Away

OBESITY has been linked to increased risks of wheezing and airway hyperresponsiveness, suggesting an effect on airway caliber. However, this factor cannot completely account for the excess rates and symptoms of asthma observed in obese patients. The effects of obesity on airway caliber, lung volumes, and other factors were evaluated.

The study included a random sample of 276 young adults, aged 28 to 30 years. This narrow age range was selected to avoid the confounding effects of age on lung elasticity. All subjects underwent evaluation of wheezing, airway hyperresponsiveness (AHR), functional residual capacity (FRC), and airway conductance (Gaw). After initial adjustment for smoking and asthma, multiple linear regression was performed to analyze relationships between weight and FRC and between body mass index (BMI) and Gaw.

Airway hyperresponsiveness was detected in 9.8% of subjects. Mean BMI did not differ between subjects with and without wheezing, AHR, or asthma. In both men and women, body weight was independently related to FRC--for each 1 kg increase in weight, FRC decreased by 30 mL in men and 20 mL in women. There was also a significant, inverse correlation between BMI and Gaw in men--FRC decreased by 0.017 L/s/cm H_2O per 1 kg/m^2 increase in BMI. The relationship between Gaw and BMI was much weaker in women.

Body mass index is significantly related to lung volume and airway caliber in young adults. As BMI increases, airway caliber is narrower than can be explained by changes in lung volume alone. Thus ➤➤

overweight and obesity may be associated with specific airway functional or structural changes.

COMMENT: *Many clinicians report increased asthma activity in obese patients, but it is not always clear whether the airway restriction is inflammatory or mechanical. This valuable study examines the question in terms of FRC and Gaw as a function of weight and BMI, respectively. The results show that obesity predisposes to reduced lung volume with airway narrowing. Interestingly, there is a greater association in males; the mechanism of this difference is unclear. The implication is that weight loss could have a positive clinical effect in asthma by improving the lung volume.*
G. D. M.
King GG, Brown NJ, Diba C, et al: The effects of body weight on airway caliber.
Eur Respir J. 2005;25:896-901. ♦♦

Let Us Not Forget Pneumovax

FOR people with risk factors such as chronic obstructive pulmonary disease, pneumococcal vaccination reduces morbidity from invasive pneumococcal disease. The risk of pneumococcal disease associated with asthma is unknown; current vaccination guidelines specifically exclude asthma patients. The asthma-related risk of invasive pneumococcal disease was assessed in a Medicaid population.

The nested case-control study included patients enrolled in the Tennessee Medicaid program (TennCare), aged 2 to 49 years, who lived in an area covered by a laboratory-based surveillance program. A total of 635 cases with invasive pneumococcal diseases--53.5% male, mean age 28.5 years--were matched to 6,350 controls. TennCare data were used to assess the presence of medical conditions carrying a high risk of pneumococcal disease. Data on medical diagnoses or use of anti-asthma medications were used to determine the presence of asthma. Patients with hospitalizations or emergency department visits for asthma, use of rescue medications or long-term oral corticosteroids, or three or more β-agonist prescriptions in the previous year were considered to have "high-risk" asthma.

Asthma was present in 18.0% of cases with invasive pneumococcal disease compared with 8.1% of controls. The asthma-associated increase in risk was significant: adjusted odds ratio 2.4. Annual incidence of invasive pneumococcal disease increased from 1.2 episodes/100,000 population for nonasthmatic enrollees, to 2.3 episodes/100,000 for those with "low-risk" asthma, to 4.2 episodes/100,000 for those with "high-risk" asthma.

Risk of invasive pneumococcal disease is significantly increased for patients with asthma. This risk is more than doubled for asthma patients overall, and quadrupled for "high-risk" asthma patients. Pneumococcal vaccine should be considered for patients with asthma.

COMMENT: *Invasive pneumococcal infections have been shown to be associated with COPD and diabetes. This study shows for the first time that asthma confers a similar risk. Guidelines from NIH and CDC do not currently specify asthmatics for pneumococcal vaccination. Maybe they should.*
R. J. M.
Talbot TR, Hartert TV, Mitchel E, et al: Asthma as a risk factor for invasive pneumococcal disease.
N Engl J Med. 2005;352:2082-2090. ♦♦

"I Only Smoke Outside"...Yeah, Sure!

ENVIRONMENTAL tobacco smoke (ETS) has serious adverse effects on children's respiratory health, yet there is no validated method of screening for ETS exposure in the pediatrician's office. A brief screening questionnaire for pediatric ETS exposure was assessed, including comparison with children's hair cotinine levels.

A convenience sample of 291 children attending a primary care center were included in the study. The study questionnaire asked for information on the parents' smoking status, number of cigarettes smoked, and locations of smoking. The responses were compared with the children's hair cotinine level, an accurate indicator of long-term exposure to ETS.

Forty-one percent of the caregivers (mainly mothers) reported smoking, mean 10.9 cigarettes/d. Twenty percent of the smokers said they smoked outdoors exclusively. Hair cotinine levels suggested high exposure to ETS in 43% of children (cotinine value over 0.7 ng/mg) and medium exposure in another 23% (cotinine value 0.3 to 0.7 ng/mg). Maternal, but not paternal, smoking was significantly associated with the children's hair cotinine levels. African-American children were more likely to be in the medium- or high-exposure group.

Other factors affecting ETS exposure included living in a household with other smokers and where smoking occurred indoors. Hair cotinine levels were not significantly different for children of smokers who reported smoking outdoors exclusively vs those who said they smoked indoors. The mothers' reported number of cigarettes smoked was also unrelated to the children's hair cotinine levels.

A simple questionnaire can aid in assessing children's exposure to ETS. Maternal smoking is strongly related to higher ETS exposure, regardless of mothers' reports of smoking outdoors only or amount smoked. For nonsmoking mothers, other important questions include whether the child is exposed to other smokers and whether they smoke indoors.

COMMENT: *Did you ever wonder how to interpret an answer to a question on smoking such as, "Yes, I smoke, but only outside"? This excellent study from Toronto used hair cotinine levels from children to validate a screening questionnaire for potential childhood exposure to tobacco smoke. There was no difference in cotinine levels between children whose mothers reported smoking "only out of doors" vs those whose mothers admitted smoking indoors. Neither was there any correlation with the number of cigarettes that the mothers reported smoking!* ➤➤

J. A. A.
Groner JA, Hoshaw-Woodard S, Koren G, et al: Screening for children's exposure to environmental tobacco smoke in a pediatric primary care setting.
Arch Pediatr Adolesc Med. 2005;159:450-455. ♦♦

Here Today...Not Gone Tomorrow

EXPOSURE to maternal smoking during gestation appears to be an independent risk factor for childhood asthma. Questions remain about this relationship, including the impact of the mother's smoking pattern and the benefits of smoking cessation. These issues were addressed in a case-control study including detailed information on in utero tobacco smoke exposure.

The analysis included 338 children with asthma diagnosed before age 5, along with 570 control children countermatched for maternal smoking during pregnancy. The mothers provided detailed information on their smoking habits during pregnancy and other potential asthma risk factors. Possible effects of the maternal grandmother's smoking during the mother's gestation were evaluated as well.

Children exposed to maternal smoking during pregnancy were at significantly increased risk of childhood asthma, odds ratio (OR) 1.5. In utero exposure was also associated with an increased risk of persistent asthma, OR 1.5. Smoking throughout pregnancy was associated with an OR of 1.6--little different from the risk associated with any smoking during pregnancy. In contrast, asthma risk was not significantly increased for children whose mothers quit smoking before they became pregnant, OR 0.9.

Few mothers quit smoking during pregnancy. If the maternal grandmother smoked during the mother's pregnancy, asthma risk was significantly increased for the grandchildren: OR 2.1.

Children whose mothers smoke during pregnancy are at increased risk of developing asthma by age 5. This is so regardless of the amount smoked during pregnancy. For mothers who quit smoking before pregnancy, risk appears similar to that of never-smokers.

COMMENT: *Several studies have linked in utero tobacco exposure to the development of asthma in childhood. This study revisits that link. It not only demonstrates an increased risk of development of asthma but also suggests that this relationship is not dose-dependent. Asthma risk did not increase as the smoking intensity increased during pregnancy. Furthermore, mothers who quit smoking prior to conception showed no increased risk of asthma in their children. This information should be discussed with patients during family planning and used to encourage cessation of tobacco use before pregnancy. It serves as more evidence that, once a woman is pregnant, any tobacco use is too much.*
T. L. H.
Li Y-F, Langholz B, Salam MT, Gilliland FD: Maternal and grandmaternal smoking patterns are associated with early childhood asthma.
Chest. 2005;127:1232-1241. ♦♦

Too Little, Too Much, Too Many Questions....

TREATMENT guidelines recommend daily anti-inflammatory therapy for patients with mild persistent asthma. However, many patients use their controller medications only intermittently, perhaps because they perceive daily treatment as unnecessary. This study compared the effects of daily vs symptom-based corticosteroid treatment in patients with mild persistent asthma.

The randomized, controlled trial included 225 adult patients with mild persistent asthma. All were instructed in a symptom-based action plan, consisting of budesonide 800 µg twice daily or prednisone 0.5 mg/kg/d if asthma symptoms got worse. In addition, two groups were randomized to receive twice-daily treatment with inhaled budesonide 200 µg or oral zafirlukast 20 mg, with corresponding oral or inhaled placebos. Patients in the intermittent-treatment group received both oral and inhaled placebos--the symptom-based plan was their only active treatment. One hundred ninety-nine patients completed the 1-year study.

Patients in the intermittent-treatment group averaged just one-half week of budesonide treatment during the study year. The three groups had comparable increases in morning peak expiratory flow and similar exacerbation rates. Several outcomes were superior for patients taking daily inhaled budesonide, including prebronchodilator FEV_1, bronchial reactivity, sputum eosinophil percentage, exhaled nitric oxide, asthma control score, and symptom-free days. Postbronchodilator FEV_1 and quality of life were not significantly different, however. There were no outcome differences between the intermittent-only and daily zafirlukast groups.

For adult patients with mild persistent asthma, a symptom-based plan of intermittent therapy yields outcomes similar to those of daily inhaled budesonide or oral zafirlukast. Regular budesonide therapy is associated with greater improvement in airway inflammatory markers. Further research is needed to evaluate this "as-needed" approach to asthma treatment.

COMMENT: *This study is generating controversy because it challenges the notion that mild persistent asthma should always be treated with daily controller medication. Over 1 year, measuring only what are considered short-term outcomes, the study found that intermittent anti-inflammatory therapy had results similar to continuous therapy. What it could not measure was whether long-term adverse outcomes were prevented. There was also no comparison of allergic and nonallergic subgroups.*
R. J. M.
Boushey HA, Sorkness CA, King TS, et al: Daily versus as-needed corticosteroids for mild persistent asthma.
N Engl J Med. 2005;352:1519-1528. ♦♦

Too Little, Too Much, Just Right!

GROWING up on a farm-- particularly early exposure to livestock--seems to reduce the risk of allergic sensitization. Exposure to bacterial endotoxin may be a key factor. Adult farmers were studied to analyze relationships between endotoxin exposure level, atopic sensitization, and respiratory health outcomes.

The case-control study included 162 Dutch pig farmers, 81 with and 81 without respiratory symptoms. Personal dust samples were analyzed to measure endotoxin exposure. Allergen-specific IgE, lung function, and airway hyperresponsiveness were assessed.

Seventeen percent of the farmers had specific IgE to at least one common allergen, most frequently house dust mite or grass pollen. For farmers with endotoxin exposure of 75 ng/m^3 or less, sensitization rates were significantly reduced--odds ratio 0.03 per 2-fold increase in endotoxin level. At higher endotoxin exposure levels, the relationship with sensitization was nonsignificant.

Endotoxin exposure was unrelated to total serum IgE. However, among sensitized farmers, endotoxin exposure was a risk factor for airway hyperresponsiveness and reduced lung function.

Adult pig farmers have a low rate of atopic sensitization. Exposure to endotoxin seems to have a protective effect, up to a level of 75 ng/m^3. However, in sensitized individuals, endotoxin exposure is a risk factor for adverse respiratory health effects.

COMMENT: *These Dutch researchers found that an inverse relationship between endotoxin exposure and sensitization to common allergens in pig farmers. Although endotoxin exposure did not affect total IgE levels, there was reduced sensitivity to dust mite, grass and birch pollen, and cat allergens. A critical threshold of 75 ng/m^3 was apparent for endotoxin exposure. Above this level there was no additional protection from allergic sensitization, but farmers exposed to higher levels were at increased risk for airway hyperresponsiveness and lower lung function. The moral of the story could be that working on a dirty pig farm might protect against certain allergies. However, if it's too dirty, other airway problems may result.*
S. M. F.

Portengen L, Preller L, Tielen M, et al: Endotoxin exposure and atopic sensitization in adult pig farmers. **J Allergy Clin Immunol**. 2005;115:797-802. ♦♦

Irony: Mold Inhibits Allergy!

ALLERGIC diseases are less common in children who grow up on a farm, perhaps reflecting exposure to endotoxin. A lower prevalence of allergy has also been reported in children of families that follow an anthroposophic lifestyle, who have limited exposure to antibiotics and immunizations. This study examined exposure to other bacterial and fungal components in farm and anthroposophic families.

Dust samples were collected from the homes of 229 farm children; 122 children attending Rudolf Steiner schools, whose families followed an anthroposophic lifestyle; and 67 control children from five European countries. The dust samples were analyzed for endotoxin and other microbial components.

Samples from the homes of farm children showed significantly increased levels of endotoxin, fungal extracellular polysaccharides, and mold β(1,3)-glucans. Levels of these components were 1.2 to 3.2 times higher than in samples from control homes. Samples from the homes of Steiner school children had elevated levels of the same microbial components, though not as high as in the farm families--1.1 to 1.6 times higher than in control samples.

The between-group differences were relatively stable across countries, despite variations in the mean values measured. The differences remained significant after adjustment for home- and family-related variables.

Children living on farms are exposed to higher levels of other mold components, as well as endotoxin. These exposures also appear relatively higher for children following an anthroposophic lifestyle. A future study will assess the implications of these exposures for allergic disease outcomes.

COMMENT: *Prior studies have demonstrated that growing up on a farm and the Steiner lifestyle (restricted use of antibiotics and immunizations) are associated with a lower prevalence of allergic disease in childhood. These different lifestyles are difficult to reconcile with the hygiene hypothesis. Mattress and living room dust were collected and studied from farm and Steiner children and respective reference children. Levels of endotoxin, glucans and fungal extracellular polysaccharides were highest in samples from farm children, but Steiner children also had higher levels than reference children, although less pronounced. Is it possible that exposure to mold components may be protective against atopy and allergy as is suggested for endotoxin? This is an ironic twist on all of the recent media hype related to "toxic mold", but must await further definitive studies.*
E. J. B.

Schram D, Doekes G, Boeve M, et al: Bacterial and fungal components in house dust of farm children, Rudolf Steiner school children and reference children: the PARSIFAL Study.
Allergy *2005;60:611-618.* ♦♦

Don't Judge a Book by Its Cover

INHALED corticosteroid (ICS) therapy has been linked a dose-related increase in fracture risk. However, recent studies have suggested that patients with obstructive airway disease (OAD) have reduced bone mineral density, independent of their use of ICS. The association between OAD severity and fracture risk was evaluated.

The study included 108,754 adult patients with osteoporotic fractures, identified from the U.K. General Practice Database. Each case was matched to a control with no history of fracture. Fracture risk was significantly elevated in patients with OAD--crude odds ratios (ORs) were 1.28 for asthma, 1.61 for chronic obstructive pulmonary disease, and 1.72 for both diag- ➤➤

noses. Markers of more severe OAD tended to be associated with increased fracture risk, such as OAD exacerbations, OR 2.02; and body mass index under 20, OR 2.54.

The fracture risk associated with more severe OAD was unrelated to ICS use. Among patients with more severe OAD, adjusted OR for osteoporotic fracture was 1.48 for inhaled corticosteroid users and 1.47 for nonusers.

Patients with more severe OAD are at increased risk of osteoporotic fractures, whether or not they receive ICS therapy. The mechanism of this association remains unclear, but it must be taken into account when assessing the fracture risk associated with ICS use.

COMMENT: *Concern and controversy remain regarding the systemic risks of ICS in asthma. Growth retardation and osteoporosis are two of the most commonly discussed manifestations. This paper supports the idea that it is as much the severity of disease as the use of ICS that promotes osteoporosis. It remains unclear whether this is related to the use of higher doses of ICS or greater use of systemic corticosteroids in patients with more severe disease. What does seem apparent is the need to account for disease severity in any interpretation of osteoporosis risk with ICS in asthma.*
G. D. M.

de Vries F, van Staa TP, Bracke MSGM, et al: Severity of obstructive airway disease and risk of osteoporotic fracture.
Eur Respir J. 2005;25:879-884. ♦♦

All Nasal Polyps Are Not Created Equal

PATIENTS with cystic fibrosis (CF) have a high rate of nasal polyps, with or without chronic rhinosinusitis. The pathogenesis of CF-related nasal polyps remains unclear, including the role of CF-specific sinonasal pathogens. This study compared the expression of innate markers and inflammatory mediators in specimens of nasal polyps from CF and non-CF patients.

The study included surgical specimens of sinonasal tissue from two groups of patients with nasal polyps: 14 with and 15 without CF. Specimens of normal nasal mucosa were studied as controls. Various markers of innate upper airway defense and inflammatory signaling were compared between groups.

Specimens from CF patients showed significantly higher mRNA expression of human β defensins, compared with non-CF or control specimens. Expression of toll-like receptor (TLR) 2 was also higher in the CF group. In contrast, specimens from non-CF patients showed higher macrophage mannose receptor expression than either CF or control specimens. There were no significant differences in TLR 4 expression.

Eighty percent of nasal polyp specimens from non-CF patients showed measurable interleukin-5, compared with none of the CF or control specimens. Expression of myeloperoxidase and interleukin-8 were significantly elevated in CF specimens, while eosinophil cationic protein, eotaxin, and IgE were higher in non-CF specimens.

Inflammatory mediators and innate markers differ significantly in nasal polyp specimens from patients with vs without CF. The observed differences suggest that, despite their clinical appearance, nasal polyps may represent distinct diseases in CF vs non-CF patients. More research is needed to explore the correlations between innate markers and inflammatory markers in both diseases.

COMMENT: *Although the inflammatory cell composition of nasal polyps of CF patients has been known to be somewhat different than polyps from non-CF patients, this study also identified significant differences in markers of innate immunity. The authors speculate that the correlations between markers of innate and specific immunity within CF vs non-CF polyps suggests that these arms of the immune system may be more closely linked than previously thought.*
S. A. T.

Claeys S, Van Hoecke H, Holtappels G, et al: Nasal polyps in patients with and without cystic fibrosis: a differentiation by innate markers and inflammatory mediators.
Clin Exp Allergy. 2005;35:467-472. ♦♦

Rhinovirus Hangs on Longer than We Thought

RHINOVIRUS is the main cause of asthma exacerbations in children, followed by respiratory syncytial virus (RSV). The influence of these viruses on the severity of asthma attacks is unknown, as is the significance of their persistence after symptoms resolve. The prevalence and persistence of rhinovirus and RSV infection were evaluated in children with asthma exacerbations.

The study included 50 children, mean age 7.4 years, seen at an emergency department for severe acute asthma. Nasal aspirates were obtained for assessment of rhinovirus and RSV RNA. Skin prick tests were performed as well. Forty-one patients were re-evaluated at 6 weeks and 16 at 6 months.

Nearly three-fourths of the children were atopic. At the time of the attacks, polymerase chain reaction assays detected rhinovirus RNA in 82% of patients and RSV RNA in 12%. Six-week follow-up studies still showed rhinovirus RNA in 44% of children. At 6 months, rhinovirus RNA was detected in 25% of the patients with asthma exacerbations, compared with 22% of a control group of children with stable asthma.

Peak expiratory flow in the emergency department was 63.4% of predicted. This value was not significantly different between patients with rhinovirus RNA, RSV RNA, or neither infection. On regression analysis, the extent of reduction in peak expiratory flow was significantly related to persistence of rhinovirus RNA, but not to the results of skin prick testing.

Over 80% of children have detectable rhinovirus RNA at the time of asthma exacerbations, while over 40% have persistent rhinovirus RNA at 6 weeks' follow-up. Persistence of rhinovirus RNA and severity of asthma are associated with more severe asthma attacks. ➤➤

COMMENT: *We have known for years that rhinovirus infections are strongly associated with asthma exacerbations requiring emergency department treatment, though the effects of persistent rhinovirus infection are unknown. This pediatric study reported an association between lower lung function and the continued presence of rhinovirus RNA 6 weeks after an ED visit for asthma. Perhaps susceptibility to rhinovirus infections is an important determinant of asthma severity.*
S. A. T.

Kling S, Donninger H, Williams Z, et al: Persistence of rhinovirus RNA after asthma exacerbation in children.
Clin Exp Allergy. 2005;35:672-678. ♦♦

A Moment's Insight Is Worth a Life's Experience

RAPID desensitization protocols can render patients temporarily unresponsive to medications to which they have previously had allergic reactions. The molecular mechanisms of this effect are unknown, although mast cells seem to play a role. A mouse model was used to demonstrate the role of signal transducer and activator of transcription 6 (STAT6) in the process of IgE-antigen desensitization.

The study used mouse bone marrow-derived mast cells from wild-type and STAT6-null mice. Cells were sensitized using dinitrophenyl (DNP) or trinitrophenyl (TNP) IgE, then activated with DNP/TNP-human serum albumin. Desensitization was carried out by regular administration of DNP/TNP-human serum albumin at suboptimal doses.

Wild-type cells were successfully desensitized, as evidenced by their nonresponse to an optimal dose of antigen. Desensitization was most effectively carried out with a 5-minute duration of antigen exposure. Desensitization was not reversed by resensitization with DNP-IgE, but the desensitized cells responded to calcium ionophore and phorbol myristate acetate. In contrast, cells from STAT6-null mice could not be desensitized using the suboptimal-dose protocol.

The study model demonstrates desensitization of mouse bone marrow-derived mast cells via rapid administration of suboptimal doses of antigen. Desensitization produces an early alteration in the high-affinity IgE receptor-dependent signaling pathway. The finding that desensitization cannot be achieved in cells from STAT6-null mice suggests that STAT6 plays at least an indirect role in the inhibitory process.

COMMENT: *Scientific confirmation of well-founded, empirical observations brings enormous satisfaction to the clinician. Admittedly, humans are not mice or rats, though we sometimes act the part. This murine study offers unique insights into the process of desensitization, including the importance of a target dose that is less than the therapeutic dose, the critical issue of time between densitization doses, and the surprising role of STAT6. All of those desensitization protocols we use for hospital consults are beginning to make more sense.*
D. K. L.

Morales AR, Shah N, Castells M: Antigen-IgE desensitization in signal transducer and activator of transcription 6-deficient mast cells by suboptimal doses of antigen.
Ann Allergy Asthma Immunol. 2005;94:575-580. ♦♦

Of Mice and Men

VARIOUS indoor allergens contribute to childhood allergic asthma, but little is known about the possible role of mouse allergen. Mouse exposure was evaluated as a risk factor for wheezing in infancy.

The analysis included 498 children with at least one parent having a history of asthma or allergies. The presence of mice in the home was reported by the parents of 26.5% of children. The rate of wheeze developing in the first year of life was 39.6%.

Mouse allergen was detected in 31.6% of available kitchen dust samples and 33.3% of living room dust samples. On multivariate analysis, parental report of mice in the home was significantly associated with wheezing in the first year of life, odds ratio (OR) 1.83. Other independent variables were low birth weight, OR 1.77; lower respiratory tract illness, OR 5.59; high levels of endotoxin exposure at age 2 to 3 months, OR 2.32; and high exposure to cockroach allergen at age 2 to 3 months, OR 1.83.

Mouse exposure is a risk factor for wheezing during infancy in children with a family history of allergy or asthma. The effects of mouse allergen on the later risks of allergic sensitization and asthma remain to be determined.

COMMENT: *The mouse now appears to be another member of the indoor allergen ensemble. The more we look the more we find. Thus it may not be surprising that subjects we think are allergic are sometimes negative with testing. We should continuously reconsider how many allergens are relevant for testing and not become complacent in our ignorance of the indoor environment.*
D. K. L.

Phipatanakul W, Celedón JC, Sredl DL, et al: Mouse exposure and wheeze in the first year of life.
Ann Allergy Asthma Immunol. 2005;94:593-599. ♦♦

Mechanisms in Airway Thickening

THICKENING of the airway wall plays a physiologic role in asthma. An imbalance between tissue inhibitor of metalloproteinase-1 (TIMP-1) and matrix metalloproteinase-9 (MMP-9) may be linked to chronic airflow obstruction. This study assessed the relationship of sputum TIMP-1 and MMP-9 to airway wall thickening in asthma patients.

The study included 26 outpatients with stable asthma. Sputum MMP-9 and TIMP-1 levels and their molar ratio were significantly correlated with CT measures of airway wall thickness. In particular, high absolute ➤➤

TIMP-1 values or high TIMP-1 relative to MMP-9 was associated with thickening of the airway wall. The MMP-9/TIMP-1 ratio was also related to lung function variables reflecting airflow obstruction, particularly postbronchodilator values reflecting "irreversible" changes in pulmonary function.

High levels of TIMP-1 may contribute to airway wall thickening and chronic airflow obstruction in patients with asthma. More study will be needed to clarify the mechanisms responsible for maintaining the balance between TIMP-1 and MMP-9, and to identify therapeutic approaches to altering this balance.

COMMENT: *We have all read with interest the emerging story of the gene encoding a disintegrin and metalloprotease (ADAM) 33. It has been observed that infants born to asthmatic parents in the United Kingdom show positive associations between single nucleotide polymorphisms of ADAM 33 and increased airway resistance. These authors have shown an association between excess TIMP-1 and whole airway wall thickening assessed by CT scanning. What needs to be addressed in future are the regulatory mechanisms responsible for the balance between MMP-9 and TIMP-1 and the means of altering them therapeutically.*
E. J. B.
Matsumoto H, Niimi A, Takemura M, et al: Relationship of airway wall thickening to an imbalance between matrix metalloproteinase-9 and its inhibitor in asthma.
Thorax. 2005;60:277-281. ♦♦

The More the Merrier

A MAINTENANCE dose of 100 µg is typically used in Hymenoptera venom immunotherapy. Patients not achieving full protection with the conventional dose may respond to a 200 µg dose. This retrospective study compared immunologic responses to 100 and 200 µg monthly maintenance doses of Hymenoptera venom immunotherapy.

The analysis included 22 patients, mean age 39 years, receiving *Vespula* venom immunotherapy. After initial rush immunotherapy, 13 patients remained on the initial 100 µg maintenance dose while 9 were switched to a 200 µg dose. The two groups had similar levels of venom-specific IgE antibody, measured before the start of immunotherapy. Skin test results were similar as well. After immunotherapy, both immunologic test results decreased significantly in patients receiving the 200 µg dose, compared with no significant change in the conventional dose group. No severe systemic reactions occurred in either group.

For patients receiving Hymenoptera venom immunotherapy, doubling the conventional maintenance dose leads to significantly greater reductions in venom-specific IgE levels and skin test sensitivity. Although the clinical implications remain to be clarified, a 200 µg monthly maintenance dose may reduce the duration of immunotherapy.

COMMENT: It has become increasingly clear that all immunotherapy is associated with a dose-dependent effect on success. While the conventional venom maintenance dose of 100 µg is safe and effective in most patients, it appears that doubling the dose may be necessary and more effective.
A. M.
Glérant J-C, Martinez P, Guillaume C, et al: Comparison of 2 maintenance doses (100 µg vs 200 µg) in Hymenoptera venom immunotherapy: influence of the maintenance dose on the immunologic response. Ann **Allergy Asthma Immunol**. 2005;94:451-456. ♦♦

For IM Injection, Women May Need a Longer Needle

THE standard recommendation for patient self-treatment of anaphylaxis is the use of an autoinjector to deliver intramuscular epinephrine into the anterolateral thigh. The widely used EpiPen autoinjector has a needle length of 1.43 cm. The adequacy of this needle length to reach the thigh muscle was compared for women vs men.

The study included thigh CT scans, performed for medical indications, of 50 men and 50 women. All body mass index categories from underwent to obese were represented. The mean measured distance from skin to muscle was 1.48 cm for women vs 0.66 cm for men, reflecting the deeper subcutaneous fat pad in women. The between-sex difference remained significant after adjustment for body mass index.

The standard EpiPen needle length would not reach the thigh muscle in 42% of women vs 2% of men. Even based on liberal assumptions for injection pressure and tissue compression, the muscle would not be reached in 28% of women.

The 1.43 cm EpiPen needle is not long enough to reach the thigh muscle in many women. Physicians should be aware that the EpiPen will deliver epinephrine into the subcutaneous tissue, rather than muscle, in many women and in some obese men.

COMMENT: *This study is a practical look at a practical question. We need to reach a little deeper when women are treated with IM epinephrine. The possibility of missing the muscle in 28% to 44% of women is of some concern. Another issue, not addressed by this study, is that many times the epinephrine is administered through clothing. EpiPen is a reasonable outpatient device, but consider using the "big one" when selecting a needle for epinephrine in the office.*
D. K. L.
Song TT, Nelson MR, Chang JH, et al: Adequacy of the epinephrine autoinjector needle length in delivering epinephrine to the intramuscular tissues.
Ann Allergy Asthma Immunol. 2005;94:539-542. ♦♦

Don't Panic!

PSYCHOLOGIC factors may play a role in asthma. Previous studies have suggested that asthma patients may be at increased risk of panic, with smoking being a possible shared risk factor. This community-based cohort study examined associations between asthma and panic in young adults.

A sample of 591 young men and women, stratified to overrepresent risk factors for psychiatric disorders, were interviewed in 1979 at age 19 and in 1999 at age 40. Asthma and panic disorder had similar 20-year cumulative prevalences of 7.3% and 7.8%, respectively. For any panic--including panic disorder and panic attacks--20-year cumulative prevalence was 20.5%. There was a stronger cross-sectional association between asthma and panic disorder, odds ratio (OR) 4.0; than between asthma and any panic, OR 2.1.

With adjustment for potential confounders, active asthma was a significant predictor of later panic disorder, OR 4.5. In addition, panic disorder was a significant predictor of later asthma, OR 6.3. Asthma also predicted the occurrence of any panic, OR 2.7. The associations were stronger in smokers and in women. Important confounding factors included smoking, anxiety during early childhood, and family history of allergy.

This long-term follow-up study demonstrates consistent associations between asthma and panic. Longitudinal associations tend to be stronger than concurrent associations, but the relationships are bidirectional in nature. Smoking and familial factors, including early-childhood anxiety, seem to play a role.

COMMENT: *There is a revival of interest in the relationships between asthma and psychologic factors that could exacerbate or maybe even cause asthma. Various psychologic disorders such as anxiety and depression have been linked to asthma activity. It is also known that asthma patients can panic during acute episodes of dyspnea. However, the etiologic relationships between asthma and panic have not been thoroughly studied. This interesting paper shows a compelling relationship between panic, panic disorders, and asthma. Risk is highest in smokers, patients with history of early childhood anxiety, and those with a family history of allergy. Such associations may be extended to determine whether the incidence of asthma can be influenced by early intervention to manage the incidence and severity of panic episodes in patients at risk (ie, positive family history).*
G. D. M.
Hassler G, Gergen PJ, Kleinbaum DG, et al: Asthma and panic in young adults a 20-year prospective community study.
Am J Respir Crit Care Med. 2005;171:1224-1230. ♦♦

Unique Therapy for SAR

NEW treatments with new mechanisms of action are needed to address the problem of seasonal allergic rhinitis (SAR). R112 is a newly developed inhibitor of Syk kinase, a transducer of signaling via the mast cell FcεR receptor. Intranasal R112 was evaluated for safety and efficacy in reducing symptoms of SAR.

The trial, conducted at park sites in Atlanta and San Diego, included 319 patients with spring SAR. On two study days, the subjects were randomized to receive treatment with intranasal R112, 3 mg per nostril every 4 hours; or placebo. Symptoms were evaluations using the Global Symptom Complex (GSC) score.

On both days, patients receiving R112 had greater reductions in GSC score than those receiving placebo. Despite differences in pollen counts, outcomes were similar at the two study sites. R112 improved all symptoms included in the GSC--stuffy nose, itchy nose, sneezing, and runny nose. Improvements were noted within 45 minutes after R112 treatment and persisted for longer than 4 hours.

Intranasal treatment with the Syk kinase inhibitor R112 provides rapid and long-lasting improvement in symptoms of SAR. Further study is needed to evaluate this novel treatment for a highly prevalent clinical problem.

COMMENT: *As we learn more about the mechanisms of the allergic cascade, researchers are developing more products that target specific inflammatory mediators to help patients with allergic disease. Syk kinase is an intracellular protein tyrosine kinase that plays a key role in mast cell and basophil activation. The new agent R112 inhibits Syk kinase and therefore reduces the release of histamine, other pro-inflammatory mediators, cytokines and lipid-derived mediators that play a critical role in the allergic cascade. Using intranasal R112 proved to be efficacious for springtime SAR within 45 minutes in this two-location park study. It would have been interesting to see the data for each site, since the pollen counts in Atlanta were more than 10 times greater than in San Diego. This agent could become another therapeutic option for our patients suffering with SAR.*
S. M. F.
Meltzer E, Berkowitz R, Grossbard E: An intranasal Syk-kinase inhibitor (R112) improves the symptoms of seasonal allergic rhinitis in a park environment.
J Allergy Clin Immunol. 2005;15:791-796. ♦♦

Mapping the Bronchi in Fatal Asthma

IN patients with asthma, inflammatory cells are found in both the small and large airways. Inflammation in the distal portions of the lung is thought to play an important pathophysiologic role. This study sought to map inflammatory activity throughout the respiratory system in patients who died of asthma.

The study included 20 subjects who died of status asthmaticus and 10 controls who died of nonpulmonary causes. The presence and locations of eosinophils, neutrophils, mast cells, and lymphocytes were mapped from the upper airways to the lung parenchyma. In all locations, eosinophil content was significantly higher in cases of fatal asthma. Subjects who died of asthma ➤➤

also had increased mast cell content in the outer area of large airways, in the small membranous bronchioles, and in the peribronchiolar parenchyma. Fatal asthma was also associated with increased CD3+, CD4+, and CD20+ cells in the intrapulmonary airways, including a significant correlation between the CD4+ content of the nasal mucosa and larger airways. Neutrophils were increased only in the peribronchiolar parenchyma.

Eosinophilic inflammation is found throughout the airways and lungs of subjects dying of asthma. However, the major inflammatory changes of fatal asthma are found in the outer wall of the small membranous bronchioles. The periphery of the lung seems to play a critical role in fatal asthma.

COMMENT: *The location of the inflammatory response in the asthmatic airway is now recognized to include both central and peripheral airways. Before this study, the distribution of inflammatory cell types for the entire respiratory tract has not been described. Among subjects with fatal asthma, eosinophils were prevalent at all levels of the airway, including the trachea. These data will serve as a useful reference for future studies attempting to better characterize asthma.*
S. A. T.

de Magalhães Simões S, dos Santos MA, da Silva Oliveira M, et al: Inflammatory cell mapping of the respiratory tract in fatal asthma.
Clin Exp Allergy. 2005;35:602-611. ♦♦

ALLERGY AND IMMUNOLOGY REVIEWS OF NOTE

COMMENT: *Although fortunately a rare occurrence in daily practice, these potentially fatal musculocutaneous eruptions with or without systemic involvement are likely to cause considerable angst in the allergist called as a consultant. This superb review would serve as an excellent primer on the latest approaches to these conditions.*
A. M.

Letko E, Papaliodis DN, Papaliodis GN, et al: Stevens-Johnson syndrome and toxic epidermal necrolysis: a review of the literature.
Ann Allergy Asthma Immunol 94:419-435,2005. ♦♦

COMMENT: *This excellent review summarizes the mechanisms underlying cystic fibrosis (CF), the outcomes relating to the absence of a functioning CF transmembrane conductance regulator, and the current treatments to correct these abnormalities.*
R. J. M.

Rowe SM, Miller S, Sorscher EJ: Mechanisms of disease: cystic fibrosis.
N Engl J Med. 2005;352:1992-2001. ♦♦

COMMENT: *This executive summary offers a unique opportunity to learn how our colleagues on the opposite side of the pond view the epidemiology, diagnosis and treatment of rhinosinusitis and nasal polyposis.*
E. J. B.

Fokkens W, Lund V, Bachert C, et al: EAACI position paper on rhinosinusitis and nasal polyps: executive summary.
Allergy. 2005;60:583-601. ♦♦

COMMENT: *This is an excellent review of the immunologic properties of the 13 officially accepted latex allergens.*
S. A. T.

Wagner S, Breiteneder H: Hevea brasiliensis *latex allergens: current panel and clinical relevance.* Int Arch **Allergy Immunol**. 2005;136:90-97. ♦♦

COMMENT: *The definition and treatment options of mild asthma are the focus of this single-author review. The choice of therapeutic options in mild asthma is complicated by the inconclusive data regarding the long-term effects of therapy and the natural history of mild asthma. Current guidelines do not help resolve these issue, so reviews such as this help provide a perspective from which to evaluate published data and clinical experience.*
D. K. L.

Irani A-M: The challenge of mild persistent asthma.
Ann Allergy Asthma Immunol. 2005;94:517-527. ♦♦

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