AllergyWatch®

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

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NOVEL DATA FOR ATOPIC RISK FACTORS

Babies Exposed to Two or More Dogs or Cats Have Lower Childhood Sensitization Rates

A growing body of evidence suggests that being exposed to animals during infancy is associated with lower rates of allergic sensitization later in childhood. The relationship between exposure to dogs and cats during the first year of life and allergic sensitization at age 6 to 7 was assessed in a birth cohort of 835 healthy, full-term infants. The infants, all enrolled in a Michigan HMO, were born over a 2-year period. Four hundred seventy-four subjects had complete annual follow-up examinations through age 6 to 7 years, including skin-prick and specific IgE testing for common aeroallergens.

At follow-up, rates of skin-prick positivity were 33.6% for infants with no dog or cat exposure during the first year of life and 34.3% for those exposed to one dog or cat. In contrast, for infants exposed to two or more dogs or cats, the prevalence of positive skin-prick results decreased to 15.4%. Analysis of specific IgE results showed a similar pattern.

Both relationships remained significant after adjustment for a wide range of other factors, including serum IgE level in cord blood, sex, older siblings, parental smoking or asthma, dust mite allergen levels at home, and current dog or cat ownership. Adjusted odds ratios for subjects exposed to two or more dogs or cats during infancy were 0.23 for atopy on skin-prick testing and 0.33 for seroatopy on specific IgE measurement.

Babies exposed to more than one dog or cat during the first year of life are less likely to become sensitized to common aeroallergens at age 6 to 7, the results suggest. This is so regardless of current pet ownership and is consistent whether sensitization is assessed by skin-prick testing or specific IgE measurement.

COMMENT: *This paper adds to the growing lit-* ➤➤

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- Chest
- Clinical Experimental Allergy
- Allergy
- International Archives of Allergy and Immunology
- Annals of Internal Medicine
- Pediatrics
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erature showing that, at the age of 6 to 12 months, exposure to endotoxin, farm animals, other children, and indoor mammalian pets has a protective effect against the development of allergy. There is no evidence that exposure to dust mite allergen has any beneficial effect at any age, suggesting a distinction among allergens. A surprising finding is that exposure to cats or dogs reduces sensitivity to pollens and molds as well as animals. The questions about pets stay the same, but the answers keep changing.
S. M. F.
Ownby DR, Johnson CC, Peterson EL: Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age.
JAMA 288:963-972, 2002.

Maternal Asthma Affects Relationship between Cat Exposure and Wheezing

THE effects of paternal history of atopy on the association between exposure to pets and wheezing were evaluated in a cohort of 448 children with at least one atopic parent. The children were followed up through age 5, including exposure to household pets, symptoms of wheezing, and measurement of allergens in dust samples.

Wheezing was unrelated to dog exposure. The effects of cat exposure on wheezing were modified by history of atopy in the mother, but not the father. Among children exposed to a cat and to a Fel d 1 level of 8 μg/g or higher in early life, wheezing risk was increased for those with a maternal history of asthma, relative risk 2.4. However, for those with no maternal history of asthma, wheezing risk was reduced: relative risk 0.6. The effect of cat exposure on total serum IgE was similarly modified by maternal history of asthma.

Maternal history of atopy appears to influence the relationship between early exposure to cats and subsequent development of wheezing in children. Cat exposure increases the risk of wheezing only in children whose mothers have a history of asthma; otherwise, children exposed to cats are less likely to wheeze.

COMMENT: *In this still-evolving area related to the allergic repercussions of exposure to cat allergen in young children, parental history can affect the outcome between exposure to cat and wheezing. Among children whose mothers had no history of asthma, exposure to Fel d 1 at a minimum of 8 μg/g at age 2 to 3 months was associated with a reduced risk of wheezing between age 1 and 5 years. Similar exposure in children whose mothers had asthma was associated with an increased risk of wheezing at or after age 3. Paternal allergy status and dog allergen exposure had no effect on the relationship between childhood wheezing and cat exposure. The beat goes on! (See* AllergyWatch *July/Aug. 2001, p. 3.)*
E. J. B.
Celedón JC, Litonjua AA, Ryan L, et al: Exposure to cat allergen, maternal history of asthma, and wheezing in first 5 years of life.
Lancet 360:781-782, 2002.

Very High Exposure to Birch Pollen Leads to Increased Sensitization and Allergic Asthma Rates

THE effects of early allergen exposure on later childhood sensitization and atopic disease remain unclear. Studies of exposure to pets and mites during infancy have reached conflicting conclusions. In 1993, record-high levels of birch pollen were recorded in Stockholm–10-fold higher than the previous year and 50-fold higher than the subsequent year–providing a unique opportunity to study the effects of intense pollen exposure on subsequent rates of sensitization and atopic disease in children.

The study included 583 children of atopic parents born in Stockholm during the Spring of 1992, 1993, or 1994. At about 5 years of age, the children underwent skin-prick testing for inhalant and food allergens, as well as RAST for IgE antibodies against birth pollen and recombinant birch pollen allergen (rBet v 1).

Rates of sensitization to birch pollen were significantly higher for children born in 1993, who had high-dose exposure at age 0 to 3 months. Of this group, 17.8% had a positive skin-prick test for birch pollen, compared with 8.8% for those born in 1994 (odds ratio [OR] 2.4). Similar trends were noted for children born in 1992, who had high-dose exposure at age 12 to 15 months (OR 1.7). The RAST results also supported the effects of high-dose exposure on sensitization rates.

Rates of most atopic diseases were similar between the three birth years. However, those born in 1993 were more than twice as likely to develop allergic asthma caused by pollen or animal dander (OR 2.6). There was evidence of an interaction between high-dose exposure to birch and having a cat at home.

Early exposure to very high levels of birch pollen appears to increase the rate of sensitization to this allergen in later childhood. A dose-dependent effect is apparent on analysis of both skin-prick test and RAST results. The risk of allergic asthma also appears higher in children with intense, early exposure to birch pollen.

COMMENT: *There is intense interest and conflicting conclusions about the relationship between early-life exposures to allergens and the subsequent risk of allergic diseases. To the mix, add this study suggesting that exposure to higher levels of birch pollen or cat in early infancy was correlated with later development of sensitization to these allergens, as well as with allergen-specific allergic asthma. In this area, there are many more questions than answers.*
R. J. M.

Kihlström A, Lilja G, Pershagen G, Hedlin G: Exposure to birch pollen in infancy and development of atopic disease in childhood.
J Allergy Clin Immunol 110:78-84, 2002. ♦♦

Infections During Pregnancy Increase Rates of Childhood Allergic Diseases

SEVERAL studies have suggested that the rising incidence of allergic and asthmatic disease may be related to reductions in exposure to microbes during early childhood. However, little is known about the effects of microbial exposure during pregnancy on risk of childhood allergic diseases. This issue was addressed using information from a British population-based data base.

The birth cohort study included nearly 25,000 children enrolled in the West Midlands General Practice Database. Factors affecting microbial load during pregnancy were assessed, including diagnosed infections and maternal prescriptions for antibiotics. The impact of these factors on the incidence of asthma, eczema, and hay fever was examined using Cox regression analysis.

About one-third of the mothers received antibiotic prescriptions while pregnant. In this group, the incidence of childhood allergic diseases was significantly increased. Adjusted hazard ratios associated with exposure to more than two courses of antibiotics were 1.68 for asthma, 1.7 for eczema, and 1.56 for hay fever. Maternal diagnoses of infection during pregnancy were also associated with small increases in allergic disease risk.

As noted previously in the data base, strong birth order effects were apparent. Previous pregnancies not leading to live births had no protective effect against allergic diseases.

In utero exposure to antibiotics and maternal infections appear to increase the risk of childhood allergic diseases in dose-dependent fashion. The findings support previous studies linking infections during pregnancy to an increased risk of allergic disease, and thus are not consistent with the "hygiene hypothesis." The mechanism by which older siblings reduce the risk of allergic disease remains unexplained.

COMMENT: *One of the components of the hygiene hypothesis is the decreased numbers of infectious agents to which infants and small children are exposed. Interestingly, few studies have looked at the impact of in utero infection exposure in incidence of allergic disease. This study examined a data base of over 24,000 live births for the effect of in utero exposure to antimicrobials on allergic rhinitis, eczema, and asthma. In children exposed to antibiotics while in utero, the incidence of all three outcomes was slightly higher. Additionally, in utero infections with a variety of organisms also increased risk for allergic diseases. These data support the importance of the in utero fetal environment on risk of developing allergic diseases and the potential value of prenatal counseling, particularly for patients with genetic risks.*
G. D. M.

McKeever TM, Lewis SA, Smith C, Hubbard R: The importance of prenatal exposures on the development of allergic disease: a birth cohort study using the West Midlands General Practice Database.
Am J Respir Crit Care Med 166:827-832, 2002. ♦♦

GSTM1 Genotype Affects Susceptibility to Respiratory Effects of Maternal Smoking

ASTHMA is related to both environmental and genetic factors. The effects of in utero tobacco exposure may be modified by fetal defenses against tobacco smoke. These defenses may include the glutathione *S*-transferase M1 (GSTM1) enzyme product, which plays a role in detoxification of tobacco metabolic byproducts and reactive oxygen species. The GSTM1 genotype, in utero tobacco exposure, and exposure to environmental tobacco smoke (ETS) were evaluated as risk factors for childhood asthma and wheezing.

The study included 2,950 children attending fourth, seventh, or tenth grade at Southern California schools. Using buccal cell specimens, the investigators per- ➤➤

formed DNA tests for GSTM1 genotype, classified as GSTM1 null or GSTM1 (+). Asthma and wheezing and exposure to maternal smoking in utero and ETS at home were assessed by parental questionnaires.

About 16% of the children had a physician diagnosis of asthma, with 10% having active asthma. The frequency of the GSTM1 null genotype varied by ethnicity, being lowest for African-Americans and highest for non-Hispanic whites.

In utero exposure to maternal smoking influenced the rate of asthma and wheezing mainly in children with the GSTM1 null genotype. For in utero-exposed children with the null genotype, the odds ratio for current asthma was 1.7 while that for lifetime history of wheezing was 1.8. This group also showed significant increases in early-onset asthma, persistent asthma, exercise-induced wheezing, drug treatment for wheezing, and emergency department visits in the past year. None of the associations with in utero tobacco exposure held for children with the GSTM1 (+) genotype. Exposure to ETS was not a significant risk factor for asthma or wheezing.

The GSTM1 gene appears to modify the impact of fetal tobacco smoke exposure on risk of asthma and wheezing. Children with the GSTM1 null genotype may be more susceptible to the adverse respiratory effects of maternal smoking during pregnancy. This genotype--present in nearly half the population–could define an important target group for preventive measures.

COMMENT: *It is reasonably well appreciated that the incidence and severity of allergy and asthma are affected by a combination of genetic susceptibility and environmental exposures. Multiple environmental influences have been proposed as have various genotypes. This study looked to determine which children were at increased risk of developing asthma as a result of cigarette exposure both in utero and environmentally. Glutathione* S-*transferase M1 is involved in xenobiotic metabolism and antioxidant pathways and thus may well play a role in asthma susceptibility. When the investigators looked at GSTM1 expression, some subjects were positive while others were negative. The null subgroup had a statistically significant increase in asthma directly related to in utero cigarette smoke exposure. This included early onset of asthma, persistent asthma, asthma requiring medications, and even emergency room visits in the previous year. This study further supports the need to look at both genetic influences and environmental exposures when risks for asthma are investigated.*
G. D. M.

Gilliland FD, Li Y-F, Dubeau L, et al: Effects of glutathione S-*transferase M1, maternal smoking during pregnancy, and environmental tobacco smoke on asthma and wheezing in children.*
Am J Respir Crit Care Med 166:457-463, 2002. ♦♦

Cord Blood IgE Levels Are Correlated with Maternal Allergen Exposures

DEVELOPMENT of the fetal immune system may be influenced by maternal cytokines. Maternal-fetal interactions may include small amounts of antigens or related peptides crossing the placental barrier. Levels of IgE in neonatal cord blood (CB-IgE) were measured and correlated with dust levels of specific allergens in the mother's environment.

The analysis included 1,332 full-term, normal weight infants enrolled in an ongoing birth cohort study of factors affecting immune system development and childhood allergies. At birth, total IgE levels in cord blood were measured using the Pharmacia neonatal IgE kit, which has a 0.35 kU/L limit of detection. To rule out contamination by maternal blood, IgA levels were assayed as well. The CB-IgE results were correlated with levels of cat allergen, mite allergen, and endotoxin concentrations in dust samples from the mothers' mattresses.

The CB-IgE level was below the limit of detection in two-thirds of cases. Fourteen percent of infants had CB-IgE levels over 0.90 kU/L. In statistical analyses including nonparametric smoothing and adjustment for confounders, CB-IgE levels of 0.45 kU/L or higher were significantly associated with log-transformed exposures to all three biocontaminants. The associations were linear for cat allergen, inverse U-shaped for mite allergen, and U-shaped for endotoxin.

The study is the first to show that in utero exposures to common allergens and to endotoxin are significantly correlated with CB-IgE levels. The finding of elevated CB-IgE levels demonstrates prenatal stimulation of T-cell responses. The mechanism of such stimulation remains unclear, although exposure of the fetal GI tract via amniotic fluid is one possibility. The relationship between allergen exposure and elevated CB-IgE is independent of family history of atopy.

COMMENT: *With recent published studies suggesting that early allergen exposure may actually protect against the development of atopy, these investigators sought to correlate cord blood IgE levels with prenatal, in-house allergen exposures: specifically cat and house dust allergens, as well as endotoxin levels from mothers' mattresses. They demonstrated a definite statistical correlation between elevated CB-IgE and high levels of cat and medium levels of dust mite allergen in mothers' mattresses. Interestingly, there was an* inverse *relationship between CB-IgE and endotoxin levels. This suggests that prenatal exposure may have an impact on subsequent development of atopic diseases, as manifested by allergen-specific IgE production.*
G. D. M.

Heinrich J, Bolte G, Hölscher B, et al: Allergens and endotoxin on mothers' mattresses and total immunoglobulin E in cord blood of neonates.
Eur Respir J 20:617-623, 2002. ♦♦

Mail Irradiation Adversely Affects Allergen Extracts

IN the wake of last year's anthrax bioterrorism attacks, the U.S. Postal Service has been using electron beam radiation to sterilize mail in some areas. ➤➤

The effects of electron beam radiation of biologic products--particularly at the high doses used to sterilize microbial spores–are unknown. Allergen extracts are commonly shipped through the mail. This study examined the effects of electron beam irradiation on the composition and potency of allergen extracts.

The investigators prepared standardized or characterized preparations of common allergens, including timothy, perennial rye, dust mite, *Alternaria*, and ragweed mix. Vials of extract were prepared in standard containers and padded envelopes and sent through the mail for electron beam irradiation: two passes at doses of nearly 50 kGy. The effects on allergen content and potency were evaluated by SDS-PAGE, immunoblotting, and enzyme-linked immunosorbent assay (ELISA), compared with untreated allergen samples.

The irradiated specimens showed readily apparent changes, including discoloration of the glass vials and the extracts themselves. Some irradiated packages showed extract leakage, suggesting failure of the rubber stoppers. These changes were accompanied by significant changes in the composition and potency of the allergen extractions. The results of ELISA and immunoblotting suggested almost total loss of allergenic and antigenic epitopes on major and minor allergens, compared with the untreated specimens.

At levels used to sterilize mail, electron beam irradiation can cause significant degradation of allergenic proteins and loss of allergenicity. Although the use of electron beam irradiation to sterilize the mail is currently limited to certain areas of the United States, this could change in the future. Allergists sending or receiving allergen extracts through the mail should be aware of whether mail irradiation is being performed in their area.

COMMENT: *This is a wonderful study that has serious implications for today's allergy practice. Electron beam radiation, at significantly higher doses than usually used for foods, is being used by the U.S. Postal Service to "sterilize" mail in the Washington, D.C., area. Any allergen extract exposed to these doses loses its allergenicity. We need to be aware of electron beam radiation irradiation in our own locales, since so much of our allergenic extract is shipped through the mail. The fact that there was no change in protein content after irradiation continues to re-emphasize the case for using standardized extracts, rather than the old weight/volume or PNU labeling methods.*
S. M. F.

Katial RK, Grier TJ, Hazelhurst DM, et al: Deleterious effects of election beam radiation on allergen extracts. **J Allergy Clin Immunol** 110:215-219, 2002. ♦♦

Pimecrolimus Cream Reduces Flares in Infants with AD

TREATMENT for atopic dermatitis (AD) in infants generally consists of emollients for dry skin, with topical corticosteroids used to control disease flares. Pimecrolimus 1% cream (Elidel) is a selective, nonsteroid inhibitor of inflammatory cytokines, developed for use in treating inflammatory skin diseases. Previous studies have shown it to be of value in the treatment of AD. A trial of topical pimecrolimus for the long-term treatment of AD in infants is reported.

The multinational study included 251 infants from 41 centers with a clinical diagnosis of AD. The patients, mean age 12 months, were randomized in a 4:1 ratio to receive pimecrolimus 1% or vehicle cream. Caregivers were instructed to apply the cream to affected areas twice daily at the first signs or symptoms of AD. The goal was to prevent progression to flare; when flares occurred, they were treated with a corticosteroid cream. Both groups received emollients for dry skin. The incidence of AD flares was assessed at 6 months after the start of treatment.

In the pimecrolimus group, 68% of patients were free of flares through 6 months' follow-up, compared with 30% of patients in the control group. At 12 months, the figures were 57% vs 28%, respectively. Sixty-four percent of infants in the pimecrolimus group received no corticosteroid treatment during the study, compared with 35% of those in the vehicle group. Both treatments were well tolerated; more than one-fourth of patients in both groups had at least one skin infection at some time during the study. The rate of study discontinuation due to lack of efficacy was 9% in the pimecrolimus group, compared with 30% in the vehicle group.

In infants with AD, early treatment with pimecrolimus 1% cream can help prevent flares and reduce the need for corticosteroid treatment. Pimecrolimus provides good control of infantile AD, a group with few other treatment options. Because of its high lipophilicity and molecular weight, pimecrolimus has low systemic absorption.

COMMENT: *Infantile AD is a frequent frustration for patients and those who help manage their disease. In this non-U.S., well-controlled, double-blind study, infants treated with pimecrolimus bid had significant reduction in the incidence of flares with improvement in overall control of the AD, compared to patients receiving conventional therapy with emollients and topical corticosteroids. It was interesting that three times more patients dropped out of the study in the control group than in the pimecrolimus group because of unsatisfactory control of their AD. Although this study shows that regular treatment with pimecrolimus can be helpful over a 1-year period, will it continue to be disease-modifying as the children age?*
S. M. F.

Kapp A, Papp K, Bingham A, et al, for the Flare Reduction in Eczema with Elidel (infants) multicenter investigator study group: Long-term management of atopic dermatitis in infants with topic pimecrolimus, a nonsteroid anti-inflammatory drug. **J Allergy Clin Immunol** 110:277-284, 2002. ♦♦

Study Documents Low Rates of Anti-inflammatory Drug Use for Asthma

ANTI-inflammatory medications are a key part of current asthma management. However, several studies have documented suboptimal use of inhaled ➤➤

anti-inflammatory medications, along with several sociodemographic variables associated with low use of these medications. A large-scale study of the use of asthma medications in the United States is reported, including the impact of symptom severity and sociodemographic variables.

A nationwide, random-dial telephone survey was performed to identify households with adults and children with current, physician-diagnosed asthma who were either taking asthma medication or had experienced asthma symptoms within the past year. Of more than 42,000 households screened, 3,273 (7.8% of the total) met the inclusion criteria. Complete interviews were conducted with 2,509 patients with asthma, including the caregivers of 721 children less than 16 years old. Current use of anti-inflammatory medications was assessed, with stratification for asthma symptom severity.

Fifty-eight percent of the patients studied were less than 35 years old. Ninety percent of patients reported significant disease-related limitations in their lives, with most patients describing moderate to severe limitations. Just 20% of patients reported using anti-inflammatory medications within the past month. Of those reporting anti-inflammatory use, 73% were using inhaled corticosteroids; 19% were using cromolyn-nedocromil and 11% were using antileukotrienes.

On bivariate analysis, factors associated with lower use of anti-inflammatory medications included lower income, lower education, nonwhite race, and being unemployed. A multiple regression equation suggested that medication use was lower for current smokers, younger patients, and those using less than four canisters of reliever medication per year. Use of long-term asthma controller medications was low as well.

This nationwide study reports very low rates of anti-inflammatory drug use by patients with asthma. The results suggest that less than one-third of patients who should be using anti-inflammatory drugs are actually doing so. Patients with adverse socioeconomic factors are at particularly high risk of suboptimal medication use; these barriers should be addressed as part of future efforts to improve the use of proven asthma treatments.

COMMENT: *It is known that American physicians are less likely to prescribe inhaled corticosteroids for asthma than are physicians in some European countries. It is also known that patients don't always adhere to prescribed treatment regimens. This extensive (42,000 households) cross-sectional study found a distressing--but not entirely surprising–low rate of utilization of anti-inflammatory medications. This was so at all levels of severity, including a 22% rate for moderate persistent asthma. The study also discovered correlations between utilization and economic, educational, age, and racial variables.*
R. J. M.

Adams RJ, Fuhlbrigge A, Guilbert T, et al: Inadequate use of asthma medication in the United States: results of the Asthma in America national population survey.
J Allergy Clin Immunol 110:58-64, 2002.

♦♦

FDNY Study Describes "World Trade Center Cough"

IN responding to the World Trade Center collapse of September 11, 2001, the Fire Department of New York City (FDNY) mounted an intensive rescue and recovery effort. As a result, thousands of firefighters were exposed to high levels of respiratory irritants. A case series of persistent cough and bronchial responsiveness in 332 firefighters exposed to the World Trade Center site is reported.

The FDNY's Bureau of Health Services identified 332 firefighters who developed severe symptoms after working at the World Trade Center site. All affected firefighters had persistent cough and other symptoms necessitating medical leave of 4 weeks or longer. The investigators performed a comprehensive examination--including spirometry, airway responsiveness testing, and chest radiographs--in all symptomatic workers and in a group of firefighters without severe cough.

Exposure to the World Trade Center site was rated high for 1,636 firefighters who arrived at the site before the towers collapsed, moderate for 6,958 firefighters who arrived after the collapse but within 2 days, and low for 1,320 who arrived 3 to 7 days after the collapse. Rates of "World Trade Center cough" were 8% in the high-exposure group, 3% in the moderate-exposure group, and 1% in the low-exposure group. Clinical findings associated with World Trade Center cough included a productive cough with grayish to black sputum infiltrated with "pebbles or particles." Significant reductions in forced vital capacity and FEV_1 were noted as well. Other symptoms included dyspnea in 95% affected firefighters, gastroesophageal reflux disease in 87%, and nasal congestion in 54%.

In all exposure groups, only a minority of firefighters used respiratory protective devices. Of affected firefighters tested before treatment, 63% responded to a trial of bronchodilator therapy while 24% had bronchial hyperreactivity. Bronchial hyperreactivity was also common in exposed firefighters who did not develop respiratory symptoms.

For some firefighters working at the scene of the World Trade Center collapse, exposure to dust and other respiratory irritants led to a persistent cough with bronchial responsiveness. The greater the severity of exposure, the higher the likelihood of developing World Trade Center cough. The cough syndrome was associated with a very high rate of gastroesophageal reflux disease; some exposed firefighters developed bronchial responsiveness in the absence of persistent cough. The rates of similar respiratory symptoms in others exposed to the World Trade Center collapse are unknown.

COMMENT: *After the collapse of the World Trade Center, thousands of firefighters who had been exposed to the dust and vapors were systematically evaluated for respiratory disorders. All had had previous spirometry in a surveillance program, and pre-existing asthma was an exclusion criterion for firefighters. The investigators found a dose-related incidence of disabling cough (but no more than 8% of those exposed) and bronchial hyperreactivity. This may be a form of reactive airways dysfunction syndrome.*

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R. J. M.
Prezant DJ, Weiden M, Banauch GI, et al: Cough and bronchial responsiveness in firefighters at the World Trade Center site.
N Engl J Med 347:806-815, 2002. ♦♦

Italian Study Looks at Asthma Incidence and Remission from 1953 to 2000

VARIABLES affecting the incidence of asthma differ from those affecting asthma persistence. Information on the natural history of asthma from birth to adulthood could lend valuable insights into the meaning of the epidemiologic data on this disease. The incidence, persistence, and remission of asthma from birth to age 44 years were studied in a large, cross-sectional study.

The analysis included 18,873 young adults living in Northern or Central/Southern Italy. Subjects were asked if they had ever had asthma and how old they were at the time of their first asthma attack. The study covered the period from 1953 to 2000. The number of events was divided by the number of person-years at risk to calculate the lifetime incidence of asthma. Asthma remissions–defined as no treatment and no attacks within the past 24 months–were assessed in subjects with a lifetime history of asthma.

A total of 8.1% of respondents said they had had asthma at some time during their lives, with 91.3% of these reporting a physician diagnosis. The crude asthma incidence was 2.59/1,000 persons/y: 2.76/1,000/y in men vs 2.42/1,000/y in women. The incidence of asthma increased from 1.59/1,000/y for subjects born in 1953-58 to 4.73/1,000 for those born in 1974-79. The highest incidences of asthma were noted in boys under 10 years old (4.38/1,000/y) and in women aged 30 years or older (3.1/1,000/y).

Of 1,449 asthmatic subjects with complete information, 45.8% went into remission. The remission rate was somewhat higher in men than in women: 49.5% vs 41.6%. The chances of remission were especially high children less than 10 years old at onset: 62.8%, compared with 15.0% in those with onset at age 20 years or older. The remission rate was high in the first 4 to 7 years after onset, decreasing rapidly thereafter.

This large, population-based study reports an average asthma incidence rate of 2.6/1,000/y for persons aged 0 to 44 years between 1953 and 2000. Asthma incidence shows an age-specific U-shaped pattern, suggesting that early- and late-onset asthma are two distinct forms of the disease. Asthma prognosis is strongly affected by age at onset. However, more than one-third of asthma cases among young adults are in patients with early-onset asthma who do not recover.

COMMENT: *Asthma is a heterogeneous disorder, a fact underlined by the epidemiologic data in this large cross-sectional study of 19,000 subjects. Childhood asthma has many features that differ from adult-onset asthma. Age at onset of asthma is the main determinant of its prognosis. It would be fascinating to combine these population observations with an understanding of the genetic and biochemical pathophysiologies.*
R. J. M.
de Marco R, Locatelli F, Cerveri I, et al, for the Italian Study on Asthma in Young Adults study group: Incidence and remission of asthma: a retrospective study on the natural history of asthma in Italy.
J Allergy Clin Immunol 110:228-235, 2002.

High Rate of Lymphoproliferative Disorders in Patients with AAE Type 2

PATIENTS with acquired angioedema (AAE) type 2 have anti-C1 inhibitor antibodies. Unlike patients with AAE type 1, they are not considered at risk of lymphoproliferative disease. The clinical and immunologic findings of 19 patients with AAE type 2 are reported.

The patients, drawn from 6 academic hospitals, were 11 men and 8 women, median age 60 years. All had recurrent attacks of angioedema associated with the presence of acquired C1 inhibitor deficiency type 2. At the time their AAE was diagnosed, 63% of patients had a monoclonal gammopathy. In 11 of these 12 patients, the immunoglobulin peak was of the same heavy- and light-chain isotypes as those of the acquired anti-C1 inhibitor antibody. Three patients developed malignant lymphoproliferative disorders within 4 to 6 years after the onset of AAE.

This study finds lymphoproliferative disorders in nearly two-thirds of patients with AAE type 2. The distinction between AAE types 1 and 2 should be based not on the presence or absence of lymphoproliferation but rather by the presence of anti-C1 inhibitor antibodies in type 2.

COMMENT: *There are two forms of AAE. Type 1 occurs in patients with lymphoproliferative disorders with no detectable autoantibodies to C1 inhibitor. Type 2 is characterized by anti-C1 inhibitor antibodies that induce a non-functional, cleaved form of C1 inhibitor. These authors studied 19 patients with type 2 AAE at the point of diagnosis and during a 1- to 10-year follow-up. Sixty-three percent of these AAE patients had a monoclonal gammopathy at diagnosis, and 3 went on to develop a malignant lymphoproliferative disease. The clear message here is that all cases of AAE must be carefully evaluated and followed for a lymphoproliferative disorder.*
E. J. B.
Frémeaux-Bacchi V, Guinnepain M-T, Cacoub P, et al: Prevalence of monoclonal gammopathy in patients presenting with acquired angioedema type 2.
Am J Med 113:194-199, 2002. ♦♦

Patients Prefer Sensory Properties of Inhaled Triamcinolone

PATIENT acceptance of intranasal corticosteroids is affected not only by the drugs' efficacy and ➤➤

safety but also by factors such as ease of use and sensory qualities. The sensory properties of three widely used inhaled corticosteroid preparations were compared.

The randomized, double-blind crossover study included 95 patients with allergic rhinitis. The patients used a questionnaire to rate 14 sensory properties of three intranasal corticosteroid sprays: triamcinolone acetonide aqueous (TAA), fluticasone propionate (FP), and mometasone furoate (MF). The items rated included which product the patients would prefer to receive and how likely they would be to use it. The patients followed a washout protocol between each spray that included chewing crackers, rinsing the mouth, and sniffing wool.

Compared with MF, patients preferred TAA in terms of comfort of administration, irritation, odor strength and preference, nose/throat moistness, and taste mildness and preference. Compared with FP, TAA was preferred in terms of odor strength and preference, nose/throat moistness, and taste mildness. Two minutes after administration, patients reported TAA as having less aftertaste and causing less irritation than MF or FP. Patients said they would prefer to receive TAA and would be more compliant with TAA than with the other drugs.

Patients with allergic rhinitis prefer the sensory attributes of TAA nasal spray over those of MF or FP spray. Prescribing TAA may help to enhance patient compliance with inhaled corticosteroid therapy.

COMMENT: *Topical nasal corticosteroids are a proven, efficacious treatment for allergic rhinitis. Clinical effectiveness of a treatment depends on patient use, which is influenced by patient preference. Patient preference is a characteristic not usually assessed in clinical trials and is extremely important in compliance with nasal sprays. This blinded study uses a novel technique to neutralize smell and taste to facilitate comparison among the products. The study was funded by industry, but the techniques appear to negate bias, resulting in a useful clinical paper. To use or not to use…that is the question. To taste and smell the treatment or not to taste and smell the treatment…that appears to be the answer.*
D. K. L.

Bachert C, El-Akkad T: Patient preferences and sensory comparisons of three intranasal corticosteroids for the treatment of allergic rhinitis.
Ann Allergy Asthma Immunol 89:292-297, 2002. ♦♦

Cyclosporine Eyedrops Are Safe and Effective for Vernal Keratoconjunctivitis

VERNAL keratoconjunctivitis (VKC) is a chronic, sometimes severe, and potentially vision-threatening form of conjunctivitis occurring mainly in warm climates. Although topical corticosteroid therapy is effective, prolonged use may lead to complications. A controlled trial of cyclosporine eyedrops for children with VKC is reported.

The study included 24 consecutive children with VKC, 79% with mixed tarsal-limbal involvement. The disease was considered seasonal in two-thirds of patients and perennial in one-third. Patients were randomized to receive cyclosporine 2% eyedrops in one eye and vehicle drops in the other eye. Treatment continued for 2 weeks. Clinical signs and symptoms were assessed at baseline and at 2 weeks, 4 weeks, and 4 months after the start of treatment.

All subjective and objective variables decreased in the cyclosporine-treated eyes. In contrast, the placebo-treated eyes showed improvement only in the ocular signs of papillae and corneal infiltrates. Most of the benefit of cyclosporine eyedrops was realized within 2 weeks, although the treatment effect was maintained over the subsequent 3 months.

Cyclosporine eyedrops are an effective treatment for VKC in children. Ocular signs and symptoms improve significantly within 2 weeks, with no major side effects. This form of therapy may help to prevent complications related to prolonged VKC and topical corticosteroid use.

COMMENT: *Vernal conjunctivitis is often resistant to treatment. The double-blind study results demonstrate that this mucosal inflammatory disease may respond to topical cyclosporine, a select T-cell immunosuppressant. The results are similar to the experience with immunosuppressants in atopic dermatitis.*
D. K. L.

Pucci N, Novembre E, Cianferoni A, et al: Efficacy and safety of cyclosporine eyedrops in vernal keratoconjunctivitis.
Ann Allergy Asthma Immunol 89:298-303, 2002.

Montelukast Is Effective for Seasonal Allergic Rhinitis

IN addition to histamine, allergic rhinitis is affected by mediators including kinins, tryptase, prostaglandins, and leukotrienes, particularly the cysteinyl leukotrienes. Thus the leukotriene receptor antagonists might be helpful in the treatment of allergic rhinitis. This randomized, controlled trial assessed the efficacy and safety of montelukast for the treatment of seasonal allergic rhinitis.

The industry-sponsored trial included 1,302 healthy patients, 15 to 81 years of age, with seasonal allergic rhinitis. All had symptoms that worsened during the spring, when the study was performed. After a 3- to 5-day placebo run-in period, patients were randomized to receive montelukast 10 mg, loratadine 10 mg, or placebo. All treatments were taken once daily at bedtime for 2 weeks. Daytime and nighttime symptom scores were assessed, along with quality of life and safety and tolerability measures.

Compared with baseline, patients receiving montelukast or loratadine had greater symptomatic improvement than those receiving placebo. Daytime nasal symptom scores decreased by 0.37, 0.47, and 0.24, respectively. The active-treatment groups also had greater improvement in secondary outcome measures, including nighttime symptom scores and rhinoconjunctivitis quality of life score, compared with placebo. ➤➤

Adverse event rates were similar across groups.

Montelukast 10 mg/d is a safe and effective treatment for seasonal allergic rhinitis. During pollen season, this treatment is associated with significant reductions in daytime and nighttime symptom scores and in quality of life. This is the first large study to demonstrate the efficacy of montelukast monotherapy for seasonal allergic rhinitis.

COMMENT: *While neither drug exhibited dramatic efficacy relative to placebo, montelukast fared rather well against loratadine in this study. Given the overwhelming success enjoyed by loratadine over the years, montelukast may do well in the rhinitis market when it receives approval for use in allergic rhinitis. Demonstrating montelukast's efficacy as monotherapy for allergic rhinitis has an added practical relevance, because it will be an attractive option for patients with both asthma and rhinitis. Unfortunately, it will not likely suffice as monotherapy for moderate or severe forms of either disease.*
S. A. T.

Philip G, Malmstrom K, Hampel FC Jr: Montelukast for treating seasonal allergic rhinitis: a randomized, double-blind, placebo-controlled trial performed in the spring.
Clin Exp Allergy 32:1020-1028, 2002. ♦♦

Add-on Formoterol Therapy Is Safe and Effective in Children with Persistent Asthma

STUDIES in adult asthma patients show that adding a long-acting β_2-adrenoreceptor agonist to inhaled corticosteroid therapy improves lung function and reduces symptoms. However, no studies have assessed the long-term effectiveness of such add-on therapy in asthmatic children. A 1-year trial of inhaled formoterol for children with persistent asthma symptoms despite anti-inflammatory therapy is reported.

The multicenter trial included 518 children, aged 5 to 12 years, with persistent asthma despite recommended doses of sodium cromoglycate, nedocromil sodium, and/or inhaled corticosteroids. All patients were still taking inhaled salbutamol on a daily basis to control asthma symptoms. After a 2-week run-in period, children were randomized to receive 12 months of treatment with formoterol dry powder, 12 or 24 µg twice daily, or placebo. Both treatments were delivered by Aerolizer inhaler. All patients continued their anti-inflammatory treatment and had access to rescue medication with salbutamol. Efficacy assessments included spirometry, peak expiratory flow recordings, and symptom scores.

Both doses of formoterol were superior to placebo on analysis of area under the curve for FEV_1 after 3 and 12 months of treatment. The two active treatments also yielded similar improvements in morning and evening peak expiratory flow rates. Median symptom score and median nighttime dosage of rescue medication decreased significantly in patients receiving formoterol 24 µg, compared with significant increases in the placebo group. There was no significant difference in asthma exacerbation rate, about 40% in each group. However, patients in the formoterol groups had a higher number of serious adverse events and asthma hospitalizations, perhaps related to a higher rate of treatment discontinuation in the placebo group.

Add-on therapy with dry-powder formoterol improves pulmonary function and symptom status for children with persistent asthma despite anti-inflammatory therapy. Although long-term formoterol therapy appears safe and well tolerated, more study is needed to explore the possibility that this treatment may mask airway inflammation. Anti-inflammatory medication and disease monitoring must continue during β_2-adrenoreceptor agonist therapy.

COMMENT: *Long-acting β_2-agonists have greatly improved the lives of asthmatic patients. These data further support the safety and efficacy of a dry-powder formoterol preparation in children.*
A. M.

Bensch G, Berger WE, Blokhin BM, et al, on behalf of the International Study Group on Foradil Evaluation in Pediatric Asthma: One-year efficacy and safety of inhaled formoterol dry powder in children with persistent asthma.
Ann Allergy Asthma Immunol 89:180-190, 2002. ♦♦

Neocate is Safe for Infants Allergic to Cow's Milk Protein and Extensively Hydrolyzed Formula

INFANTS with hypersensitivity to cow's milk protein (CMP) are generally managed with the use of extensively hydrolyzed formula (EHF). However, additional alternatives are needed for children who are also allergic to EHF. The long-term use of an amino acid-based formula for children with EHF allergy was evaluated.

The study included 52 CMP-allergic infants who remained symptomatic despite elimination of CMP and replacement with soy and EHF. All were started on the amino acid-based formula Neocate. One month later, the children were re-challenged with the EHF they had been receiving previously. Other suspected food allergies were managed with skin-prick testing, elimination diet, and single-blind oral challenge.

Twenty-one infants were classified as "oligofood" allergic, with allergy to less than six foods, while 12 met Hill's criteria for multiple food allergy. The rest had isolated EHF allergy. Over a mean duration of 11.4 months, Neocate proved safe in all infants. The median age to CMP tolerance was 20.5 months, although 11 children were still CMP-intolerant by the end of the study. Time to CMP tolerance was shorter in infants with isolated EHF: 13.4 months, compared with 21.7 months in patients with oligofood allergy and 34.5 months in those with multiple food allergy. Duration of Neocate feeding was 7.1, 13.5, and 20.0 months, respectively.

An amino acid-based formula is safe for infants with allergy to both CMP and EHF. The outcome depends on the extensiveness of allergies at baseline. ➤➤

Compared to infants with isolated EHF allergy, those with multiple food allergy are diagnosed later and have a higher rate of atopic dermatitis.

COMMENT: *This short but valuable article from France confirms U.S. experiences with the use of Neocate in cow's milk-allergic (and hydrolyzed formula-allergic) children. Thirteen of the fifty-two infants developed multiple food allergies and required the amino acid-based formula for a median of 20.0 ± 11.8 months. It is comforting to find that these seriously allergic children grew normally on a restricted diet with Neocate.*
J. A. A.
De Boissieu D, Dupont C: Allergy to extensively hydrolyzed cow's milk proteins in infants: safety and duration of amino acid-based formula.
J Pediatr 141:271-273, 2002. ♦♦

Body Mass Index Linked to Methacholine AHR in Older Men

As the prevalence of asthma rises, so does the rate of obesity. Data from a long-term follow-up study were analyzed to determine the role of body mass index (BMI) in men who developed new airway hyperresponsiveness (AHR) to methacholine.

The study was based on the Normative Aging Study, a longitudinal study of aging initiated by the U.S. Veterans Administration in the 1960s. Since 1984, men participating in the study have undergone regular respiratory evaluations, including a questionnaire on respiratory symptoms and smoking, methacholine challenge testing, allergy skin tests, and serum IgE measurements. The investigators identified 61 men, mean age 62 years, with an initial negative methacholine challenge test who later developed methacholine AHR. Two hundred forty-four men with consistently negative methacholine challenges were studied as controls. Conditional logistic regression models were used to assess the effects of initial BMI and change in BMI on the development of AHR.

The models showed a nonlinear relationship between initial BMI and the development of AHR. Risk of AHR was greatest for men at the lowest and highest quintiles of initial BMI–odds ratio 7.0 and 10.0, respectively–compared with the middle quintiles. In contrast, an increase in BMI during follow-up increased the risk of AHR in linear fashion.

Body mass index significantly affects the risk of developing methacholine AHR in men. The results show a U-shaped relationship between initial BMI and AHR risk and a positive, linear association between change in BMI and subsequent development of AHR. The results may lend insight into the apparent relationship between obesity and asthma in developed countries.

COMMENT: *A number of studies have associated an increased prevalence of asthma with a rising trend in obesity. (See the NHANES III data reviewed in the May/June, 2002,* AllergyWatch.*) In the ongoing Normative Aging Study, 61 men with an initial negative methacholine challenge test and a subsequent positive test were studied. The results revealed that both low and high BMI were associated with the development of AHR. The key to understanding these observations may reside in dietary fat intake, which has been associated with both AHR and asthma. The obese state is associated with increased levels of circulating acute-phase reactants and proinflammatory cytokines, which may help explain these observations.*
E. J. B.
Litonjua AA, Sparrow D, Celedon JC, et al: Association of body mass index with the development of methacholine airway hyperresponsiveness in men: the normative aging study.
Thorax 57:581-585, 2002. ♦♦

Tetracycline Drugs Suppress IgE Production by Asthmatic PBMCs

PREVIOUS studies have suggested that the tetracycline drug minocycline has a corticosteroid-sparing effect in asthma. This in vitro study examines the effects of minocycline and doxycycline on IgE responses in peripheral blood mononuclear cells (PBMCs) from serum IgE-positive asthma patients.

The investigators obtained peripheral blood samples from 7 serum IgE-positive asthma patients and 7 IgE-negative nonasthmatic controls. Cell surface marker studies suggested comparable numbers of CD4+ T cells: 779/mm^3 in the asthma patients and 766/mm^3 in controls. Numbers of CD19+ cells were also similar: 239/mm^3 and 379/mm^3, respectively. However, the CD8+ T cell count was only 378/mm^3 in the asthmatic patients vs 568/mm^3 in controls.

When PBMCs from the two groups were cultured with an anti-CD40 monoclonal antibody or with recombinant human interleukin-4, IgE levels were virtually undetectable on days 0 and 3. However, by day 10, IgE levels in supernatants of asthmatic PBMCs had increased to 28 ng/mL, compared with no change in the control cultures. When minocycline or doxycycline was included in the asthmatic PBMC cultures, IgE production was reduced in dose-dependent fashion: by more than 80% at a concentration of 10 µg/mL. The tetracyclines had no effect on IgE levels in control PBMC cultures.

Tetracycline drugs suppress IgE production by PBMCs cultured from asthma patients. This IgE-suppressive effect may help to explain the corticosteroid-sparing effect of minocycline observed in asthma patients. The mechanism of tetracycline suppression of IgE responses remains to be explained.

COMMENT: *We have known for decades that macrolides have an anti-inflammatory effect in asthmatic patients. This in vitro study suggests that the tetracyclines may have a unique IgE-suppressive effect. Given the large number of adolescents taking tetracyclines for acne, further prospective studies of those with asthma should be revealing.*
A. M.
Smith-Norowitz TA, Bluth MA, Drew H, et al: Effect of minocycline and doxycycline on IgE responses.
Ann Allergy Asthma Immunol 89:172-179, 2002. ♦♦

Family Supports Genetic Background of Chronic Idiopathic Urticaria

THE pathogenesis of autoimmune disorders may involve genetic as well as environmental factors. Previous studies of patients with chronic idiopathic urticaria (CIU) have reported histamine-releasing properties attributable to circulating anti-IgE or anti-FcεRI IgG or to some unknown serum factor. These findings suggest that at least some cases of CIU may be autoimmune in nature. Familial patterns of CIU were investigated in a large clinical sample.

The analysis included 1,308 patients diagnosed with CIU over a 10-year period: 920 females and 388 males, all at least 12 years old. In interviews, 4% of patients reported at least one first-degree relative with CIU, compared with an expected prevalence of 0.1%. The 56 patients with a positive family history belonged to 42 distinct families. Twenty-three patients with a family history of CIU underwent an autologous serum skin test; the results were positive in all patients but one.

The relatives of patients with CIU have a much higher than expected prevalence of this disease. The results support the hypothesis that CIU has a genetic background. They also confirm the previously reported link between CIU and human leukocyte antigen DR4.

COMMENT: *Chronic idiopathic urticaria remains a diagnostic and treatment challenge for the allergist. The new findings suggest that an autoimmune haplotype may be associated with a familial form of this disorder. We are just beginning to understand why we've been so frustrated for so long!*
A. M.
Asero R: Chronic idiopathic urticaria: a family study.
Ann Allergy Asthma Immunol 89:195-196, 2002.

IL-4Rα Gene Polymorphism Interacts with Infection, Study Suggests

ATOPIC patients have allergen-induced Th2 responses leading to production of interleukin (IL)-4 and increased IgE levels. One study has reported a glutamine-to-arginine substitution at position 551 of the gene coding the IL-4Rα chain associated with atopy. However, other studies have failed to confirm this association. Interactions between the R_{551} mutation and environmental factors associated with atopy were investigated in a birth cohort study.

Genotyping for the R551 polymorphism was performed by heteroduplexing in 1,051 children, representing a random 10% sample of a U.K. birth cohort. Sixty percent of children were wild-type homozygotes while 34% were heterozygous and 6% homozygous for the R_{551} mutation.

The R_{551} mutation was significantly and positively associated with flexural eczema–a marker of atopic eczema–in children up to 6 months old with no history of antibiotic treatment. However, no such association was observed in children who had received antibiotics. The genotyping results were unrelated to the results of skin-prick testing or serum IgE levels at age 5 years.

The R_{551} of the IL-4Rα gene is associated with flexural edema in infants with no history of infection requiring antibiotic treatment. The results suggest that this mutation may induce a bias toward Th2 responses, but only early in life. In addition, such a bias may be expressed only if the child does not experience any infections leading to a Th1 response.

COMMENT: *We all agree that atopy is dependent both on genetic and environmental factors. The hygiene hypothesis offers a provocative explanation of a repeatedly observed epidemiologic association between atopy and a lack of exposure to infectious micro-organisms. This study goes one step further by providing evidence for an age-restricted interaction between a specific genetic polymorphism and lack of infectious exposures.*
S. A. T.
Callard RE, Hamvas R, Chatterton C, et al: An interaction between the IL-4Rα gene and infection is associated with atopic eczema in young children.
Clin Exp Allergy 32:990-993, 2002. ♦♦

Trial Confirms Effectiveness of SIT for Asthmatic Children

DESPITE a long history of clinical use, there is continued debate over the role of specific immunotherapy (SIT) for asthma in children. The results of SIT for pediatric asthma using a standardized house dust mite (HDM) extract were assessed in a prospective study.

The trial included 29 asthmatic children with monosensitization to HDM. After a 1-year run-in period, the patients were randomized to 3 years of SIT using standardized HDM extract or a control group. The two groups were matched for age, allergen sensitization, disease severity, lung function, and nonspecific bronchial reactivity (BHR). Outcome measures included skin-prick and methacholine challenge testing, as well as symptom status and respiratory function variables.

Children receiving SIT had significant reductions in asthmatic symptoms, drug use, and nonspecific BHR. There was no significant improvement in respiratory function. Children in the SIT group developed no new sensitivities during the study period.

This randomized, controlled trial confirms the effectiveness of SIT using standardized HDM extract in monosensitized asthmatic children. In this group of patients, SIT reduces asthma symptoms and BHR and may prevent the development of new allergic sensitization.

COMMENT: *These authors employed standardized HDM extract in a prospective study to assess the benefits of SIT in a randomized clinical trial over a 3-year treatment period in asthmatic children with monosensitization to HDM. Though the study is relatively small, the observations support SIT as effective in reducing symptoms and medication requirements, as well as in reducing nonspecific BHR. Early institution of SIT appeared to avert sensitization to new allergens.*
E. J. B. ➤➤

Pifferi M, Baldini G, Marrazzini G, et al: Benefits of immunotherapy with a standardized Dermatophagoides pteronyssinus *extract in asthmatic children: a three-year prospective study.*
Allergy 57:785-790, 2002. ♦♦

REVIEWS OF NOTE

Sicherer SH: Food allergy. **Lancet** 360:701-710, 2002.

COMMENT: *The author provides an excellent review on clinical research which has enhanced our understand of the clinical, epidemiological, and immunological aspects of food-allergic disorders. This is an indispensable resource for clinicians who see primarily adult patients and do not have the diverse exposure to adverse food reactions seen mostly in children.*
E. J. B.

Johansson SGO, Haahtela T, O'Byrne PM: Omalizumab and the immune system: an overview of preclinical and clinical data.
Ann Allergy Asthma Immunol 89:132-138, 2002.

COMMENT: *This succinct, four-page review provides an overview of the biology of IgE. This is followed by a discussion of the effects of anti-IgE, including a review of the clinical studies with omalizumab. A summary is provided of the safety data in recipients, including the absence of immune complex disease, complement activation, or increased parasite infection. The review is useful reading for clinicians as we anticipate the approval of anti-IgE for patient care.*
D. K. L.

Sutherland ER, Martin RJ: Distal lung inflammation in asthma.
Ann Allergy Asthma Immunol 89:119-124, 2002.

COMMENT: *This review summarize the evidence that the small airways--inner diameter of 2 mm or less--contribute to the abnormal pulmonary physiology of asthma. The authors describe a variety of human studies, both histologic and physiologic, showing inflammation of the small airways. A significant point is that the severity and characteristics of small airway inflammation may differ from those of large airway inflammation. The latter is primarily assessed by clinical and investigative tools such as spirometry, lavage studies, and sputum analysis. Thus the question of asthma control cannot be answered without assessment and treatment of the small airways. The authors review a variety of inhaled corticosteroids, emphasizing their particle size and airway distribution. The drug and delivery system combination will determine the airway size in which the drug will be deposited. Oral therapy may also have an advantage by reaching the small airway. These may be important points in selecting specific therapies for asthma.*
D. K. L.

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