The Role of Allergens in Asthma

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The etiology of asthma is not known. Acute and chronic asthma can be triggered by several factors, including allergen exposure, upper respiratory tract infections (particularly viruses), exposure to irritants such as cold air, cigarette smoke, and other air pollutants, exercise, nonsteroidal anti-inflammatory drugs, sulfites, and possibly emotional factors. While the exact role of allergen exposure in asthma is unknown, 75% to 85% of patients with asthma have positive immediate skin test reactions to common inhalant allergens. These and other observations demonstrate a strong and well-established association between asthma and allergic disease. These figures may overestimate the true role of allergen exposure, but indicate the need for evaluation of the role of allergen exposure in the diagnosis and treatment of asthma.

The extent to which allergy triggers asthma varies somewhat according to the age of the patient. In infants who have not yet become sensitized to aeroallergens, respiratory infections are more likely to initiate asthma. In children beyond infancy, allergy assumes importance not only in persistence and severity, but also possibly in the development of the disease. Studies have reported that the severity of childhood asthma correlates with the number of positive skin tests. Children who have multiple positive skin tests may have asthma symptoms on a daily rather than intermittent basis. Exposure to aeroallergens may be important in adults under age 30. Occupational exposure may also account for up to 2% of all asthma. In contrast to findings in children, the presence of allergen skin test reactivity in adults does not appear to be associated with increased severity of asthma.

Pathology of Asthma

Pathologically, asthma is an inflammatory disease of the airways. The inflammatory constituents include eosinophils, basophils, and lymphocytes. Bronchoprovocation with allergens has served as a useful model to study airway inflammation in asthma. Sensitized individuals who have undergone bronchial provocation have demonstrated both immediate bronchoconstrictor phase and late inflammatory phase reactions. Bronchoalveolar lavage studies have shown that allergic inflammation in the lung is associated with the release and generation of multiple inflammatory mediators derived principally from mast cells (histamine, prostaglandin D₂). Subsequent changes occur which include recruitment of inflammatory cells such as eosinophils, basophils, and lymphocytes into the lavage fluid, demonstrating the inflammatory character of the late response. The late-phase asthmatic response is associated with increased bronchial reactivity to nonallergic stimuli which can lead to asthma symptoms on exposure to irritants or with exercise.

Consequences of Allergen Exposure

Seasonal allergen exposure results in an enhanced early- and late-phase asthmatic response to provocation with inhaled allergen after the season. This effect was noted in patients who were not receiving steroids; the response could be blunted by corticosteroid treatment. Increased production of specific IgE antibodies may prime sensitized patients to become more responsive to inhaled allergens. Crimi et al. found that the frequency of late-phase allergic pulmonary responses to provocation challenge conducted during seasonal allergen exposure increased, suggesting that such exposure enhances the inflammatory changes in the airways of asthmatic individuals.

Seasonal allergen exposure not only enhances the response to inhaled allergens, but also enhances airway responsiveness to nonallergic stimuli.

![Diagram](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21648/)

**Figure 1.** Theoretical mechanism for the development of perennial allergen-induced asthma (Reproduced with permission).

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responsiveness to nonspecific stimuli such as methacholine and histamine.\textsuperscript{10,11,12} This increase in seasonal airway responsiveness to nonimmunologic stimuli can be inhibited by treatment with corticosteroids, suggesting that airway inflammation is responsible for this phenomenon.\textsuperscript{14}

Allergen exposure may precipitate sudden and severe life-threatening episodes of asthma. Of 59 patients presenting with acute asthma at an emergency room during the grass pollen season, 54 (92\%) had elevated levels of specific IgE antibody to grass pollen in their sera.\textsuperscript{15} Moreover, dust samples from the homes of 15 of these patients demonstrated very high levels of grass pollen (>10 μg of allergen per gram of dust).\textsuperscript{16} These results demonstrated that sensitized patients have an increased risk of developing acute asthma during a period of greater exposure. Evaluation of 102 emergency room patients demonstrated that in adults under 50 years of age, the prevalence of specific IgE antibodies to dust mites, cockroach, cat dander, grass, and ragweed pollen was 4 times greater in individuals with asthma than in a control population.\textsuperscript{18} Another study of 11 patients between ages 11 and 25 who experienced episodes of respiratory arrest (with 2 fatalities) indicated that these individuals had skin test reactivity to \textit{Alternaria alternata} and elevated specific IgE levels against this fungus.\textsuperscript{17}

Can IgE-mediated sensitivity cause asthma? Burrows et al\textsuperscript{18} investigated the association of self-reported asthma with serum IgE levels and skin test reactivity to a panel of Aeroallergens in 2,657 subjects. The prevalence of asthma was closely related to the serum IgE level when standardized for age and sex. Although no correlation was found between positive skin test reactivity to the battery of Aeroallergens used in the study and the presence of asthma, the linear relationship between serum IgE levels and the presence of asthma suggested that asthma may indeed have an allergic basis. The ability to develop IgE sensitivity appears to have a genetic basis, but early exposure to house dust mite allergens is an important determinant in the subsequent development of asthma.\textsuperscript{18} Sears et al\textsuperscript{18} found that sensitivities to dust mite and cat dander were highly associated risk factors for the development of asthma in children up to the age of 13.

\section*{OCCUPATIONAL ASTHMA}

Occupational asthma can occur in individuals exposed to organic dust. This is governed, in part, by the concentration of exposure and host susceptibility factors, although nonatopic individuals may become sensitized and ultimately develop asthma, ie, animal handlers and power plant workers along the Mississippi River.\textsuperscript{11} Epidemic asthma has occurred in situations in which air pollution caused by organic dust has led to sensitization and ultimately asthma attacks. This recently occurred in Barcelona, Spain, where the unloading of soybean shipments in the harbor caused community outbreaks of asthma due to the inhalation of soybean dust.\textsuperscript{19}

\section*{DIAGNOSIS}

Because allergen sensitivity may trigger as well as cause asthma, identification of the offending allergens is important for the proper diagnosis and management of the asthmatic patient. Detailed medical history, including evaluation of the home environment such as pets, indoor mold exposure, and conditions contributing to dust mite proliferation (high humidity and carpeted floors), should be taken. Occupational and recreational exposures are important factors for adults. Appropriate skin testing or \textit{in vitro} assays for specific IgE antibodies should be considered part of any evaluation. Correlation of positive skin tests with the medical history is necessary to establish a definitive diagnosis. \textit{In vitro} laboratory tests can be substituted for skin tests in some instances; however, the sensitivity of the laboratory tests is not as high, and the expense is often greater.

\section*{TREATMENT OF ALLERGEN-INDUCED ASTHMA}

Allergen avoidance is a fundamental part of the treatment for IgE-mediated asthma. Adults with dust mite sensitivity and asthma who were placed in controlled environments in which dust mite exposure was avoided showed improvement in symptoms, pulmonary function, and nonspecific bronchial reactivity, and were able to decrease medication use.\textsuperscript{20} Removal of pets from the residence of animal dander-sensitive individuals may result in symptomatic improvement, although airborne concentrations of cat antigen may remain in the environment for several months. Occupational exposures can be provided with protective garb and respirators to minimize exposure and risk of sensitization. Topical corticosteroid nasal sprays can reduce coughing, wheezing, and dyspnea in patients with allergic rhinitis, possibly by decreasing posterior nasal drainage.

Another beneficial technique is to stay in an air-conditioned environment and avoid outdoor aeroallergen exposure. Residential air cleaning devices used to treat allergic respiratory disease have not provided conclusive positive results.\textsuperscript{21} Control of indoor humidity by dehumidification to levels of less than 50 percent relative humidity is useful in reducing dust mite and mold spore exposure. Removal of carpets from bedrooms, covering mattresses and box springs with plastic, and washing bedding regularly in hot water have produced clinical improvement in dust mite-sensitive individuals.\textsuperscript{21} Tannic acid solutions sprayed on carpeting and upholstered furniture may inactivate dust mite and cat allergens. Acricides such as benzoic acid esters are available to reduce dust mite concentrations in house dust.\textsuperscript{21} Pet owners who refuse to part with cats may achieve some benefit by bathing the cat, removing indoor carpeting, and using a high-efficiency indoor air filter system.\textsuperscript{21} Techniques are also commercially available to quantitate indoor airborne allergen levels of dust mite and cat dander.

The role of immunotherapy in the treatment of asthma is controversial. Several placebo-controlled, double-blind studies have indicated beneficial effects from treatment with grass pollen, ragweed pollen, dust mite, cat dander, and the fungus \textit{Cladosporium herbarum}.\textsuperscript{22} Immunotherapy may be considered as an adjunct to pharmacotherapy for asthma in selected patients who demonstrate clear-cut exacerbation of their asthma during seasonal exposure to aeroallergens. Immunotherapy should not be used as an alternative to proper environmental controls in the treatment of animal dander sensitivity.

\section*{CONCLUSIONS}

In sensitive individuals, allergen exposure is capable of
inducing inflammatory reaction in the airways. Seasonal exposure to aeroallergens can result in increased nonspecific airway responsiveness, leading to chronic symptomatic asthma. Exposure to high levels of allergens such as dust mite in infancy may lead to sensitization and eventual development of asthma. Seasonal allergen exposure may precipitate acute, life-threatening attacks of asthma. An evaluation of IgE-mediated sensitivity should be conducted in all patients with asthma. When allergen exposure produces asthma symptoms, environmental control measures should be instituted and allergen exposure reduced. In selected patients, immunotherapy may be used as an adjunct to appropriate pharmacotherapy.

REFERENCES