

### Advances in environmental and occupational disorders

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As with the previous year, 2005 was a very active year for investigation of the effect of environmental agents on allergic disease, be they allergens, pollutants, bioaerosols, or occupationally encountered agents. There were a large number of articles on the prevalence of allergic disease in the United States, identification and characterization of a number of allergens, and the role of indoor allergens and potential mitigation of the effect of such allergens, as well as the hygiene hypothesis, air pollution, and the effect of these agents on airway disease. The *Journal of Allergy and Clinical Immunology* also saw very interesting case reports and mechanistic studies examining the causes of occupational immune-mediated disease. There were also reports on gene-environment interactions, highlighting the importance of such interactions in modulating the risk for development of allergic disease. That these interactions have proved to be remarkably complex comes as no surprise to the allergy and immunology community because allergists and immunologists have long appreciated the role of environmental influences on disease. (*J Allergy Clin Immunol* 2006;117:1367-73.)

**Key words:** Environment, allergens, asthma, occupational diseases, environmental controls

We review contributions to the *Journal of Allergy and Clinical Immunology* (JACI) that represent significant advances in 2005 to our understanding of environmental and occupational disorders (Table I).

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#### Abbreviations used

CBD: Chronic beryllium disease  
DEP: Diesel exhaust particle  
GSTM1: Glutathione-S-transferase M1  
JACI: *Journal of Allergy and Clinical Immunology*  
NHANES: National Health and Nutrition Examination Survey  
PM: Particulate matter  
SNP: Single nucleotide polymorphism

#### PREVALENCE

The National Center for Health Statistics estimated the prevalence of allergic sensitization in the United States.<sup>1</sup> The National Health and Nutrition Examination Survey (NHANES) III included 10,863 participants who underwent prick puncture skin testing to a number of indoor and outdoor allergens. The overall skin test reactivity to at least one indoor allergen was 43%. The overall prevalence of skin test reactivity to at least one outdoor allergen was 40%. The main finding was that 54% of the population had one or more positive skin test responses to common allergens, and positive test responses were higher in each decade of age compared with those in the NHANES II. An ongoing NHANES study will evaluate skin test reactions to allergens, total and allergen-specific IgE levels, and levels of indoor allergen exposure in the homes. We await these studies with interest.

Asthma-associated morbidity is increasing in the United States, especially in children residing in inner cities. The Inner City Asthma Consortium study<sup>2</sup> evaluated allergen sensitivities, exposures, and associated morbidity. The results suggest that cockroach allergen has a greater effect on asthma morbidity than house dust or pet allergen in these children. As with the NHANES study cited above,<sup>1</sup> pet exposure to cats or dogs was not a risk factor for the development of positive skin test responses.

Erwin et al<sup>3</sup> studied antibodies to cat and mite allergens and their relationship to wheezing in children. Children who had lived with a cat during their lifetimes were less likely to have IgE to cat; however, cat ownership had no effect on IgE antibody to mite. The results suggest that induction of tolerance to cat allergen is allergen specific but

**TABLE I.** Key advances

- Allergy is much more prevalent than generally thought (up to 54%).
- Important allergens are present in day-care centers, which are often not recognized as important sites of allergen exposure.
- Several new allergens have been identified and characterized.
- *Alternaria alternata* exposure, although high in the Midwest and South, occurs across the United States and inside homes, as well as outdoors.
- Allergen avoidance requires multifactorial interventions but is clinically effective.
- The effect of a specific genetic polymorphism of the CD14 gene promoter on response to endotoxin can vary based on environmental levels of endotoxin, highlighting the importance of gene-environment interactions.
- The GSTM1 gene modifies response to air pollutants and demonstrates the importance of antioxidant defenses in response to a broad range of pollutants.
- Public health measures can decrease pollutant-induced asthma exacerbations.

cannot be attributed to endotoxin or family choice of not having a cat. Furthermore, the results suggest that IgE antibody responses to cat are controlled not only in tolerant individuals but also in individuals who are sensitized to cat allergen. The authors conclude that the type of allergen and amount of exposure might contribute to tolerance and the induction of a T<sub>H</sub>2-modified (IgG<sub>4</sub>) response.

## ALLERGENS

Several new allergens have been identified, and their biologic effects have been evaluated, which can improve our diagnostic capabilities and understanding of allergic mechanisms. Barderas et al<sup>4</sup> reported the cloning and high-level expression of a major allergen from ash pollen, Fra e 1. Recombinant Fra e 1 is a glycoprotein of 145 amino acids that exhibits 80% to 90% homology with other members of the Oleaceae family. The recombinant allergen elicited positive skin test responses and basophil histamine release *in vitro*.

Wunschmann et al<sup>5</sup> evaluated the enzymatic activity of the cockroach allergen Bla g 2. Bla g 2 shares sequence homology with the aspartic proteinase family of proteolytic enzymes; however, Bla g 2 lacks proteolytic activity. The study showed that Bla g 2 does not possess enzymatic activity in standard aspartic proteinase assays; however, allergenicity was observed. Therefore in contrast to dust mite allergens that possess both enzymatic and allergenic potential, the allergenicity of Bla g 2 is not likely related to its proteolytic activity.

Hilger et al<sup>6</sup> reported the cloning and expression of a major allergen from the pigeon tick *Argas reflexus*, Arg r 1. The recombinant allergen is a member of the lipocalin family and was found to have immunoreactivity both *in vitro* and *in vivo*.

Boasen et al<sup>7</sup> examined potential mechanisms of Toll-like receptors in the innate immune response to house

dust mite extracts. House dust mite extracts activated mouse bone marrow–derived dendritic cells that produced IL-6 and IL-12 and increased the expression of CD40, CD80, CD86, and MHC II molecules. Correlations were seen between the relative bioactivity of the house dust mite extracts and their endotoxin levels. These studies show that Toll-like receptor signaling pathways play a central role in dendritic cell responses to noninfectious factors and might lead to further understanding of the mechanisms of atopic diseases.

House dust mite allergens were also the target of a study by Takai et al.<sup>8</sup> Recombinant proforms and the mature forms of Der p 1 and Der f 1 were compared. The recombinant mature forms exhibited similar molecular sizes, secondary structures, and allergenicities as the naturally occurring allergens. On the other hand, the proforms exhibited different secondary structures and less IgE activity than the mature forms. These studies might be helpful in understanding the basis for allergen sensitization and lead to more effective allergen vaccines.

The relationship between airborne allergens and food-related allergens were studied in 2 reports. In the first, Jahn-Schmid et al<sup>9</sup> evaluated individuals with birch pollen allergy who experienced the oral allergy syndrome. This study characterized the major T-cell epitopes of the major birch pollen allergen Bet v 1 and investigated involvement in the cellular cross-reactivity with related food allergens. Major allergens of the Apiaceae family, such as celery and carrot, as well as hazelnut, produced the most stimulation. Homologous proteins from the Rosaceae family, apple and cherry, were less stimulating, although these produced more symptoms in patients. These results show that the ingestion of pollen-related food with a strong T cell–activating capacity might amplify the allergic response at times when patients are not exposed to the pollen. Alternatively, ingestion could also possibly lead to tolerance.

In the study by Karisola et al,<sup>10</sup> the molecular basis of natural rubber latex allergy and reactions to foods was evaluated. Approximately 50% of patients with natural rubber latex allergy have reactions to avocados, banana, kiwi, and papaya and are sensitized to a 31-kd endochitinase protein. The N-terminal hevein-like domain (HLD) of these endochitinases was purified or produced from avocado, banana, latex, and wheat germ and tested for IgE reactivity. Isolated HLD molecules alone, but not when linked to endochitinases, seem to be responsible for the IgE-mediated clinical reactions in the latex-fruit syndrome.

## FUNGI

Several developments in the area of fungal allergy have provided new insights into exposures and the diagnosis of fungal sensitivity.<sup>11–13</sup> Salo et al<sup>11</sup> assayed house dust samples from homes in different locations throughout the United States for the concentration of *Alternaria alternata* antigens. *A. alternata* antigens were detected in 95% to 99% of the dust samples. Regional factors strongly

affected the levels (eg, concentrations were higher in the midwestern and southern homes). Concentrations were also significantly higher in older homes than newer homes and in homes in which a dehumidifier was used. The presence of a dog or cat was associated with higher concentrations in the living room floor and upholstery dust. Infrequent cleaning contributed to higher *A alternata* allergen levels in the floor and upholstery dust, especially in living rooms. Correspondingly, levels of *A alternata* antigen in beds were lower if the bedding was washed frequently. The authors acknowledge that one limitation of the study was the variability in *A alternata* exposure in different geographic locations because of the small number of homes in each area, which also did not allow for variations caused by different seasons of the year. These limitations are discussed in detail by Dreborg.<sup>14</sup>

An interesting study from Australia by Green et al<sup>12</sup> investigated the expression of allergens from airborne fungi. All air samples contained fungal hyphae that expressed soluble antigens in significantly higher concentrations than the conidia (spores) of well-characterized allergenic fungi. Fungal conidia of 10 genera that were previously uncharacterized as allergen sources also demonstrated IgE binding. These data implicate airborne hyphae, fragmented conidia, and the conidia of a much more diverse range of genera as airborne allergens than previously suspected.

Asturias et al<sup>13</sup> reported on the diagnosis of *A alternata* sensitization with both natural and recombinant Alt a 1 allergens. Specific IgE levels to natural Alt a 1 or recombinant Alt a 1 showed significant correlations and similar sensitivity and specificity. The authors conclude that Alt a 1 either in its natural or recombinant form is reliable for the diagnosis of *A alternata* sensitization and can induce a skin prick test reaction comparable with that produced by a commercially available *A alternata* extract.

## ALLERGEN AVOIDANCE

Review articles appeared dealing with allergen avoidance in asthma.<sup>15-17</sup> O'Connor<sup>15</sup> pointed out the uncertainties and controversies about which allergen avoidance interventions should be recommended to patients. There are several reasons why interventions might fail to be clinically efficacious. O'Connor lists appropriate interventions that might be useful in reducing asthma symptoms in individuals with existing asthma, and these appear to be quite reasonable.

As pointed out by Eggleston,<sup>17</sup> homes cannot be made allergen free, but exposure can be reduced. Once allergen levels have been reduced by appropriate measures, continuing efforts are necessary to maintain the reduced allergen levels. This review supplements that of O'Connor.<sup>15</sup>

An editorial by Tovey and Kemp<sup>16</sup> discussed environmental factors that influence asthma development. The editorial was directed at an article by Rautava et al,<sup>18</sup> in which it was observed that probiotics could be efficacious in the prevention of eczema in childhood, although not in

later life. Systemic influences on the immune system might lead to local modulations, and this needs further exploration. Further evidence on how interventions can be optimized is clearly needed.

Two articles explore the potential roles of allergen reduction that might have therapeutic consequences. Martyny et al<sup>19</sup> studied the ability of a sodium hypochlorite-containing spray to kill *Aspergillus fumigatus* and inhibit *A fumigatus* allergens. The use of sodium hypochlorite solutions on mold-contaminated surfaces can kill the fungus and modify its surface characteristics, as well as reduce allergen skin test reactivity. However, it should be pointed out that this applies only to surface contamination and not to fungi that have penetrated deeply into pore surfaces.

Cho et al<sup>20</sup> examined the effect of a combination of systemic corticosteroid therapy and allergen avoidance in reversing allergen-induced airway remodeling. In this animal model environmental control alone reduced airway inflammation, mucus expression, and some aspects of fibrosis, but the combination of exposure avoidance along with systemic corticosteroid therapy resulted in a much more complete reversal of airway remodeling. Clearly, further studies are needed in human subjects with asthma to determine whether environmental control measures in combination with inhaled corticosteroids can contribute to the reversal of this process.

## INDOOR ALLERGENS: NOVEL ASPECTS WITH IMPLICATIONS FOR AVOIDANCE

It is well known that indoor allergens derived from dogs, cats, house dust mites, and cockroaches play a significant role in modulating allergic disease in children. A number of reports in the 2005 JACI examined new patterns of sensitization or important novel allergens in the environment.

Immunologic patterns of sensitization to specific cockroach allergens were examined by Satinover et al.<sup>21</sup> These investigators used the purified German cockroach allergens Bla g 1, Bla g 2, Bla g 4, and Bla g 5 and the American cockroach allergen Per a 7 to assess levels of allergen-specific IgE and IgG levels. Per a 7, Bla g 2, Bla g 5, and the tropomyosin, Per a 7, are important specific antigens that might be targets for epidemiologic surveillance and therapeutic intervention for cockroach allergy.

As newly purified allergens are identified, there is often a lag in ability to easily assay these molecules. Erwin et al<sup>22</sup> reported that use of biotinylated allergens coupled with streptavidin-treated, high-capacity immunosorbent assays allowed for assessment of allergen-specific IgE directed against such allergens, allowing for more rapid investigation into IgE responses to newly identified agents.

Matsui et al<sup>23</sup> examined the home environments of school-age inner-city asthmatic subjects for levels of mouse (*Mus m 1*) allergen. This study demonstrates the importance of mouse allergens in the inner city. Factors linked to increased *Mus m 1* levels in these homes

included cracks or holes in the walls of the homes and evidence of exposed foods in the home.

Arbes et al<sup>24</sup> examined day-care settings for *A alternata*, Bla g 1 (cockroach), Fel d 1 (cat), Can f 1 (dog), Der p 1 (mite), Der f 1 (mite), and Mus m 1 (mouse). All of these allergens (except for *A alternata*) were found to be at greater than sensitization thresholds in specific centers. Higher levels of *A alternata*, Can f 1, and Fel d 1 were recovered from carpeted day-care centers, suggesting a potential environmental control strategy in this setting.

The majority of the reagents used for allergen assays are based on ELISA technology from a single source. Pate et al<sup>25</sup> compared the variability and reproducibility of several laboratories, assessing unknowns from the same stock of allergen using these assays. Although there was some variability between laboratories, the results were generally reliable between them. These results suggest that reagents are being developed that might allow more routine assessment of allergen levels in a number of environments.

## ENDOTOXIN AND THE HYGIENE HYPOTHESIS

Intense interest in the hygiene hypothesis remained evident in the JACI this year. The biologic complexity of the response to endotoxin was reviewed by Singh and Schwartz.<sup>26</sup> Although endotoxin is generally thought to promote T<sub>H</sub>1 responses and protect against allergic sensitization, a number of factors, including timing of exposure, degree of exposure, and genetic factors, all influence the ultimate phenotype of the endotoxin response.

The dichotomy of the effect of endotoxin exposure and the effect on allergy and asthma were demonstrated in articles that explored exposure to farm animals in both childhood and adult life. Adler et al<sup>27</sup> examined the prevalence of asthma in rural children from Wisconsin using survey questionnaires. They reported that farm residence within the first 5 years of life was associated with decreased occurrence of ever having asthma, although it seemed likely that this protective effect might be time limited. Portengen et al<sup>28</sup> examined health outcomes of endotoxin exposure in pig farmers. They found that endotoxin exposure was associated with decreased allergic sensitization, although it was not associated with increased symptoms in allergic farmers but was associated with increased airway reactivity.

There were also 3 very important articles examining the relationship between the influences of the -260 C-T single nucleotide polymorphism (SNP) of the CD14 gene promoter on allergic disease coupled with specific environmental exposures to endotoxin and on the expression of allergic disease. Eder et al<sup>29</sup> reported that the C allele for this SNP was associated with increased IgE levels in children exposed to domestic animals and decreased IgE levels in those with farm animal exposure. Zambelli-Weiner et al<sup>30</sup> observed in a population living in Barbados that the TT genotype for this SNP was

generally associated with decreased risk for asthma. However, when the population was further characterized on the basis of endotoxin found in house dust, this genotype was protective with low endotoxin exposure but might confer increased risk for asthma with high endotoxin exposure. Litonjua et al<sup>31</sup> examined the effect of this SNP in 2 cohorts of children on the development of eczema and found that the TT genotype was associated with increased IgE levels and occurrence of eczema, contrary to the protective effect of this genotype on allergic disease previously reported. Taken together, these reports demonstrate that environmental aspects of gene-environment interactions require much more attention to fully appreciate the biology of innate immune influences on allergy.

In assessing exposure to endotoxin and other microbial stimuli, many studies focus on measures made from floor dust samples or exposure to animals. However, many have argued that for airway disease, airborne levels of endotoxin are equally relevant. Platts-Mills et al<sup>32</sup> examined the relationship between dog and cat ownership and airborne levels of endotoxin in homes. There was no significant difference in endotoxin levels between homes without pets versus those with pets. However, in comparing houses with dogs versus cats, endotoxin levels were higher in houses occupied by a dog, with correlations between Can f 1 and endotoxin being significant, whereas there was no correlation between Fel d 1 and endotoxin. Rabinovitch et al<sup>33</sup> also used airborne measures of endotoxin to examine the relationship between endotoxin exposure and FEV<sub>1</sub> in children. They report a significant association between FEV<sub>1</sub> and endotoxin when using samples obtained from personal monitors as opposed to stationary monitors, which demonstrates the importance of accurate exposure assessment in determining the effect of endotoxin exposure on disease.

There were also reports assessing human response to inhalation challenge with endotoxin. Alexis et al<sup>34</sup> reported that 20,000 EU of endotoxin (a dose consistent with low-level occupational exposure or high-level domestic exposure) resulted in recruitment of cells with increased expression of CD80, CD86, and MHC class II molecules, suggesting increased antigen-presenting capability of airway monocytes, which might have significance regarding the effect of endotoxin in airway allergy. Michel et al<sup>35</sup> using a higher level of endotoxin, reported that CC16 (a Clara cell protein derived in the airway) was increased in serum of volunteers after challenge, although this could be inhibited by pretreatment with inhaled steroids. The authors suggest that serum CC16 levels might be useful as biomarkers for the effect of endotoxin on airway inflammation.

## OCCUPATIONAL DISEASES

There were 2 notable articles in the 2005 JACI that examined mechanisms of immune-modulated occupational disease. Chronic beryllium disease (CBD) is a T<sub>H</sub>1 granulomatous disease closely resembling sarcoidosis.

Pott et al<sup>36</sup> examined the amount of CD4<sup>+</sup> cells with increased IFN- $\gamma$  and IL-2 levels in beryllium-sensitized persons and patients with CBD. Beryllium-sensitized persons and patients with CBD had equivalent amounts of beryllium-induced lymphocyte proliferation. Using ELISPOT technology, the investigators found that both beryllium-sensitized persons and patients with CBD had increased IFN- $\gamma$  and IL-2 production from beryllium-stimulated PBMCs compared with that from control cells. However, the responses in the cells from patients with CBD were significantly increased over those seen in cells from those who were only sensitized. The ELISPOT-based assay was more sensitive in detecting sensitization. These observations advance the understanding of the evolution of beryllium sensitization to CBD and might lead to improved detection and monitoring assays for these disorders.

Johnson et al<sup>37</sup> studied the role of IL-1 in mediation of toluene diisocyanate-induced asthma in a mouse model using normal (wild-type) and IL-1 receptor knockout mice. Data from the study suggest that IL-1 signaling plays a central role in toluene diisocyanate-induced asthma.

Elliott et al<sup>38</sup> examined the progression of self-reported symptoms of animal allergy in laboratory workers either with physician-diagnosed allergy, receiving allergen immunotherapy, or with hay fever and found that these patients had a 7.34-fold increased risk of having laboratory animal allergy. Of note is the novel observation that female workers had a 3.4-fold increased risk of laboratory animal allergy compared with male workers.

Two case reports in the JACI served to illustrate the ongoing recognition of novel allergens and exposures that can induce occupational asthma. Alday et al<sup>39</sup> reported a case of IgE-mediated occupational asthma to *Angelim pedra* (a tree native to the Amazon basin harvested for its timber). Skin test responses to *Angelim pedra* were positive, and SDS-PAGE electrophoresis of *Angelim pedra* extracts revealed a 35-kd protein that immunoprecipitated IgE from this patient. Allergen-specific asthma was confirmed by means of demonstration of increased nonspecific airway reactivity and symptoms after challenge with *Angelim pedra* exposure. Yacoub et al<sup>40</sup> reported a case of nonatopic cyanoacrylate-induced asthma caused by avocational exposure. The patient had a classic late-phase reaction and increased sputum eosinophilia after cyanoacrylate challenge. Although this chemical is known to cause occupational asthma in the workplace, it has not been previously reported in those recreationally exposed.

## AIR POLLUTION

There were a number of reports that addressed various aspects of the effect of pollution on allergic and other diseases, including chronic obstructive pulmonary disease. Silkoff et al<sup>41</sup> examined patients with chronic obstructive pulmonary disease for the relationship between wintertime exacerbation of disease and particulate matter (PM) exposure, finding that such a relationship occurred

even with PM levels within the current US Environmental Protection Agency National Ambient Air Quality Standards. In a review of the effect of air pollution in children, Trasande and Thruston<sup>42</sup> discussed the effect of pollutants on immune development and the development of allergic disease. Several pollutants (NO<sub>2</sub>, O<sub>3</sub>, and PM components) are linked to asthma exacerbation and might contribute to asthma pathogenesis. Other morbidities associated with pollutants (especially PM) include fetal loss, growth delay, and development of leukemia and lymphoma. Both Silkoff et al<sup>41</sup> and Trasande and Thruston<sup>42</sup> placed emphasis on the need for public health policy changes as a primary method to influence pollutant-induced disease and the role that allergists can play in advocating for such policy changes.

Riedl and Diaz-Sanchez<sup>43</sup> reviewed the effect of diesel exhaust on allergic inflammation. This agent has effects on numerous components of the immune system, as well as epithelial cells. These effects skew immune function toward a T<sub>H</sub>2 phenotype. Animal and human studies demonstrate that diesel exhaust particles (DEPs) enhance recall response to allergens but also increase the development of IgE responses to neoantigens. The mechanism by which DEPs exert effects might be through metabolism of polyaromatic hydrocarbon components of DEPs. Phase II enzymes protect cells from the effect of polyaromatic hydrocarbon products, which, if left unchecked, activate mitogen-activated protein kinase and nuclear factor  $\kappa$ B, resulting in proinflammatory and allergic responses. Among the enzymes involved in phase II response to DEPs are nicotinamide adenine dinucleotide phosphate/oxidoreductase, glutathione-S-transferase M1 (GSTM1), and hemoxygenase 1. Genetic polymorphisms have been examined as risk factors for increased effects of DEPs on allergen-induced inflammation in human subjects, and those who are GSTM1 deficient demonstrate increased adjuvant effects of DEPs.

Another very important observation on the role of environmental agents in determining the way in which genetic factors might affect asthma was made by Meyers et al.<sup>44</sup> These investigators carried out a genome screen for the genetic associations among specific genetic loci, airway reactivity, and asthma. About half of the children examined lived with a smoker, and the other half did not. There was no difference in either asthma or airway reactivity in the 2 groups, and in both groups asthma was linked to the 3p chromosome. However, airway reactivity was linked to the 5q chromosome in only the smoke-exposed children, which again demonstrates the importance of gene-environment interactions.

In a review of epidemiologic and genetic risks associated with pollutant-induced asthma, Peden<sup>45</sup> outlined the effect of pollutants on airway and allergic diseases, as well as specific mitigations for these effects. It was noted that certain interventions decrease responses to either naturally occurring or experimental pollutant exposures. Vitamins E and C are effective in mitigating the effects of ozone, and nonsteroidal anti-inflammatory agents blunt the effect of ozone. Inhaled corticosteroids decrease

responses to ozone and endotoxin in asthmatic subjects. As with DEPs, the null variants of the GSTM1 gene increase the response to ozone. In studies of children exposed to pollutants with this genetic defect, use of antioxidant vitamins was very beneficial. Also noted in this review was the experience gained from changes in traffic patterns developed for the 1996 Olympic Games in Atlanta, Georgia. During that summer, asthma-induced visits to emergency departments, local ozone levels, and inner-city use of automobiles was decreased. Together, these data suggest that societal interventions might have an effect on pollutant-induced airway disease.

Consistent with these data are novel findings by Ryan et al,<sup>46</sup> who examined the influence of proximity to roadways as a factor in the evolution of wheezing episodes. They observed that infants living within 100 m of a roadway with stop-and-go bus and other vehicular traffic had a 2.5-fold increased risk of wheezing episodes relative to those living farther from the roadway.

Vandenberg<sup>47</sup> presented an editorial outlining the process by which the US Environmental Protection Agency reviews data in setting ambient air quality standards and the public health successes achieved by such regulation. Brisson et al<sup>48</sup> examined the role of the built environment on human health and asthma pathogenesis. It was noted that increases in automobile exhaust and obesity clearly point to ways in which the built environment might adversely affect asthma. Together, these data and the various reviews published in the 2005 JACI indicate that interventions to decrease fossil fuel use and improve the built environment could decrease morbidity associated with pollutant-triggered asthma.

## SUMMARY

As outlined above, the JACI saw significant contributions in publications related to the prevalence of allergic disease, identification of new allergens and characterization of known allergens, understanding of the effect of occupational and environmental agents on allergic disease, and appreciation for the role of allergen and pollutant avoidance in mitigating the effects of these agents in asthma and other diseases. Important contributions to this field were made in the form of instructive case reports, prospective research studies, and thoughtful reviews of the state of the science surrounding environmentally modulated allergic disease. We look forward to an equally active examination of environmental factors to be presented in the JACI in 2006 and invite those from within our specialty and from other disciplines to join in this endeavor.

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## Correction

With regard to the February 2006 article entitled “Position paper: The medical effects of mold exposure” (2006;117:326-34): Declaration of conflict of interest information was provided by the authors prior to publication but was inadvertently omitted at the time of publication. The following should have appeared in the footnote on page 326:

Disclosure of potential conflict of interest: R. Bush is an employee of the US Department of Veteran's Affairs and University of Wisconsin Medical Foundation and has received grant support from the US Department of Veterans Affairs and the National Institutes of Health. J. Portnoy has received grant support from Clorox Corporation. A. Saxon has served as an expert witness for the defense in mold litigation and has received compensation for this testimony. A. Terr has served as an expert witness in mold litigation and has received compensation for this testimony. R. Wood has declared that he has no conflict of interest.