Advances in environmental and occupational disorders in 2012

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The year 2012 produced a number of advances in our understanding of the effect of environmental factors on allergic diseases, identification of new allergens, immune mechanisms in host defense, factors involved in asthma severity, and therapeutic approaches. This review focuses on the articles published in the *Journal* in 2012 that enhance our knowledge base of environmental and occupational disorders. Identification of novel allergens can improve diagnostics, risk factor analysis can aid preventative approaches, and studies of genetic-environmental interactions and immune mechanisms will lead to better therapeutics. (J Allergy Clin Immunol 2013;131:668-74.)

Key words: *Allergens, pollens, fungi, pets, air pollution, risk factors, immune mechanisms, asthma, immunotherapy*

Abbreviations used
APC: Antigen-presenting cell
DC: Dendritic cell
FENO: Fraction of exhaled nitric oxide
HDE: House dust extract
iNOS: Inducible nitric oxide synthase
PM2.5: Particulate matter of less than 2.5 μm in diameter
PM10: Particulate matter of 2.5 to 10 μm in diameter
RR: Relative risk
SPT: Skin prick test
STAT: Signal transducer and activator of transcription

The *Journal of Allergy and Clinical Immunology* reported a number of advances in 2012 focused broadly on environmental and occupational factors that affect allergic disease. There were also a number of reports focused on food, insect, fungal, and pollen allergy and exposures to these agents. Environmental influences on atopy included the effect of global climate change on allergen exposure, the effect of pollutant exposure on both exacerbation and induction of asthma, and the relationship of rural and farm exposures on the development of asthma. Immunotherapy also received attention in 2012. Outlined below are the leading contributions to the *Journal* in these areas in 2012.

ALLERGENS: FOODS, DRUGS, AND "BUGS"

Food allergy prevalence in children is increasing, especially in Western industrialized countries. Lack[1] provided an updated review of risk factors that might be involved in this increase. Interestingly, geography can affect the prevalence of food allergy because of several factors, such as the levels of allergen exposure, differences in preparation and processing of allergens, and genetic differences within the population. Several genetic components play an important role in the development of food allergy. A family history of food allergy is well known to be associated with food allergy in children. Ethnicity is under investigation as well. Male sex (at least in childhood) imposes a higher risk (odds ratio, 1.87; 95% CI, 1.32-2.66) for the development of food allergy. Molecular biology studies indicate that genetic polymorphisms and specific gene mutations are associated with an increased risk of food allergy.

Changes in diet (eg, inadequate vitamin D, decreased antioxidants, and obesity) and environmental changes (hygiene hypothesis) might also enhance the development of food allergy. New evidence suggests that cutaneous exposure could be an important route of sensitization. Although oral exposure to food allergens early in life might induce tolerance, investigations to clarify the effects of early oral exposure in reducing food allergy are currently underway.

Identification of new allergen sources and characterization of allergens can lead to a better understanding of the mechanisms of allergic sensitization and improve diagnostic and therapeutic approaches for allergic disease. Latex glove sensitivity is well known. Nitrile gloves are a recommended alternative for use in latex-sensitive patients. Gonzalo-Garijo et al[2] reported on 5 hospital workers with latex sensitivity who had immediate reactions (urticaria and rhinitis) from certain nitrile gloves. The authors found that latex allergenic proteins were present in these gloves, whereas they were not present in other nitrile gloves. Manufacturers, physicians, and patients with latex allergy need to be aware of the possibility of latex-contaminated nitrile gloves.

In an interesting report, Santiago et al[3] found that there was immunologic (IgE) cross-reactivity between the cockroach allergen Bla g 5, a glutathione-S-transferase, and the glutathione-S-transferase of the filarial pathogen *Wuchereria bancrofti*. Human subjects infected with this organism and mice infected with the intestinal nematode *Heligmosomoides bakeri* had IgE antibodies that cross-react with Bla g 5. Molecular mimicry studies of parasites and environmental allergens can increase our understanding of the pathogenesis of allergic diseases.

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Korošec et al[4] reported that the sensitivity of an *in vitro* diagnostic test based on recombinant yellow jacket venom allergens was enhanced by the inclusion of the *Vespula* species recombinant allergens rVes v 1 to rVes v 5. Although the use of whole venom might be more sensitive (because all allergens are included) as a first-line test, the use of recombinant allergens from an insect venom can be useful in more specifically identifying the disease-causing (anaphylaxis) venom allergen.

The diagnosis and management of drug-induced allergic reactions are important parts of clinical practice. Mertes et al[5] identified a possible increased risk for hypersensitivity reactions (anaphylaxis and bronchospasm) induced by the use of methylene blue–treated fresh frozen plasma. Although the precise mechanism for these reactions is unknown, alterations in plasma proteins might be responsible.

Carboplatin and other platinum-based chemotherapeutic agents are often used in cancer treatment. Hypersensitivity reactions (urticaria and anaphylaxis) can occur. Skin testing might be useful in identifying patients who can benefit from desensitization protocols. Patil et al[6] evaluated 39 patients with carboplatin-induced reactions using skin testing. Twelve subjects converted from an initial negative skin test result to a positive skin test result after receiving carboplatin. Because converters are at risk for reactions, the authors suggest that repeat skin testing is necessary for assessing the risk of future reactions.

Aspirin-exacerbated respiratory disease can be improved by aspirin desensitization with subsequent chronic administration of aspirin. Gastrointestinal symptoms (abdominal pain and gastroesophageal reflux) are among the most common adverse effects of this procedure. Hoyte et al[7] reported on 3 patients who were believed to have had acute pancreatitis temporally associated with aspirin desensitization. In an editorial Stevenson et al[8] argued that the evidence for association between pancreatitis and aspirin desensitization was not convincing. However, Durrani and Kelly[9] reported a case in which the patient had normal pancreatic enzyme levels before aspirin desensitization but had abdominal symptoms and increased enzyme levels during the desensitization. Physicians with aspirin desensitization procedures should be aware of this possibility. Additional studies might clarify the issue.

POLLENS

Sensitization to pollen allergens is a major factor in seasonal allergic rhinitis. One of the most important allergens worldwide is grass pollen. In a birth cohort of German children enrolled in 1990, Hatzler et al[10] investigated the evolution of grass pollen sensitization at the molecular level in children and the predictive value of specific IgE responses in the development of seasonal allergic rhinitis. Yearly medical questionnaires were administered, and serum was collected at various age points from ages 1 to 13 years. Children with seasonal allergic rhinitis (170/820) at age 12 years initially had monomolecular/oligomolecular (to 8 purified *Phleum pratense* allergens) IgE responses. At age 3 years, serum specific IgE (≥0.35 kU/L) to *P pratense* predicted seasonal grass pollen–induced allergic rhinitis at age 12 years (positive predictive value, 60% [95% CI, 50% to 82%]; negative predictive value, 84% [95% CI, 80% to 87%]). As the children aged, the concentration and complexity (number of purified allergens involved) increased through a process known as "molecular spreading." Thus early identification of children who are at risk for allergic rhinitis can lead to improved preventive measures.

The increase in the Earth's surface temperature is in part due to the accumulation of anthropogenic gases, especially CO_2. This can affect rainfall, cause severe weather events, and prolong pollen seasons. CO_2 accumulation can directly affect plant physiologic parameters (pollen production). Ziska and Beggs[11] reviewed the potential effects of these climate changes on public health caused by increasing allergen exposure.

Pollen exposure can clearly affect symptoms in sensitized patients with allergic rhinoconjunctivitis and asthma. Caillaud et al[12] investigated the relationship between increasing atmospheric Poaceae pollen concentrations and their effect on nasal and ocular symptoms in allergic subjects. The authors found a sharp positive linear trend of increasing symptoms with increasing pollen levels (up to 80-90 grains/m^3), at which point symptoms reached a plateau. At the beginning of the pollen season, a priming effect was observed, as well as a nonspecific prepriming phenomenon.

The effects of pollen exposure on emergency department visits for asthma were evaluated by Darrow et al[13] in an Atlanta, Georgia, population. Poaceace (grass) and *Quercus* species (oak) pollens were associated with emergency department visits as the pollen concentrations increased in the environment. Oak pollen exposure was particularly important in children (5-17 years old).

These studies clearly show a cause-and-effect relationship between pollen exposure and symptoms of allergic disease. Climatic factors that enhance aeroallergen production and duration can result in increasing morbidity, especially in children.

FUNGI

Fungi play an important role in the pathogenesis of allergic diseases and can be a cause of infection in immunodeficient patients. Engelhardt and Grimbacher[14] reviewed the genetic defects involved in patients with chronic mucocutaneous candidiasis and hyper-IgE syndrome. Various mutations ultimately result in impaired IL-17 immunity, IL-22 immunity, or both. IL-17 and IL-22 have potent antifungal properties, particularly against *Candida* species. Understanding the genetic basis of these conditions might eventually lead to more effective therapies.

Fungal allergen exposure has been linked to the development and severity of asthma. Reponen et al[15] examined the relationship between indoor fungal exposure and the subsequent development of asthma at age 7 years in a birth cohort study of 289 children. Dust samples were collected from the children's homes at age 8 months. Samples were analyzed by using a DNA-based, mold-specific quantitative PCR technique to identify and quantify the presence of fungi in the homes. Asthma was diagnosed at age 7 years in 24% (69/289) of the children. An increased risk for asthma was associated with high scores on the Environmental Relative Moldiness Index, which is composed of concentrations of 36 molds (adjusted relative risk [RR] for 10-unit increase in Environmental Relative Moldiness Index score, 1.8; 95% CI, 1.5-2.2). Summation levels of the fungi *Aspergillus ochraceus*, *Apergillus unguis*, and *Penicillium variable* were associated with asthma at age 7 years (adjusted RR, 2.2; 95% CI, 1.8-2.7). The study adds to our knowledge of the association between