Environmental and Occupational Asthma*
Exposure Assessment

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ELISA = enzyme-linked immunosorbent assay; PTFE = polytetrafluoroethylene; RAST = radioallergosorbent test

The investigation of allergic lung diseases has focused on the nature of the response. As a consequence, knowledge of the physiology, pathology, cellular and molecular biology of these diseases, and in particular of asthma, is now considerable. In contrast, studies of the exposures that initiate and provoke asthma and hypersensitivity pneumonitis have been far less productive and our understanding of them correspondingly less. Two of the several reasons for this paucity of knowledge seem particularly relevant. First, although most environmental allergens have long been associated as frequent causes of asthma, the importance of specific occupational causes has been recognized only more recently. A disease that occurs in only a minority of the general population exposed to common environmental allergens can perhaps be attributed to individual susceptibility; occupational causes, on the other hand, focus attention on exposure and the means to control it in order to prevent further cases. Second, exposure assessment requires the means to measure the concentration of allergen in air. It is only in the past decade that the development of specific immunoassays has made such measurements possible.

Why Measure Airborne Allergen Concentration?

There are 3 major reasons to measure airborne allergen levels both in the general environment (outdoors and indoors) and at work:

1. To examine variability in allergen exposure and its determinants;
2. To evaluate the effectiveness of interventions particularly in the workplace, aimed at reducing allergen exposure;
3. To examine exposure–response relationships in allergic lung disease.

Methods for Measurement of Allergens in Air

Prior to the development of immunoassays, 3 methods were used to estimate the concentration of allergen in an air sample: (1) counting the morphologically identifiable particles (eg, pollen grains and mold spores) under a microscope, (2) culture of bacteria and fungi, and (3) assay of chemicals such as isocyanates and acid anhydrides. Both counting and culturing airborne particles have their limitations: many allergenic proteins (eg, rat urine proteins) are not associated with morphologically distinct particles, and microbes that flourish best in culture are not necessarily those present in the highest concentration in air. With the development of immunoassays the quantification of airborne allergens took several steps toward that achieved by assays for airborne chemicals.

Measurement of airborne allergen concentration is not in principle different from methods developed by industrial hygienists to measure the concentration of dust particles in air. There are 3 important steps:

1. A known volume of air is sampled and the airborne particles retained on a filter sheet;
2. The soluble allergens are extracted from the filter sheet;
3. The amount of retained allergen is assayed by immunoassay.

The major limitation of the technique has been the sensitivity of immunoassays to measure the (usually) small concentration of allergens in air; several refinements to each stage have been described since the initial report of the first of an immunochemical assay by Agarwal et al in 1981.1

In the early studies air samples were obtained by the use of a high volume area sampler with a flow rate of 1,400 L/min. This ensured a sufficient volume of air for outdoor sampling, but indoors the devices could, in a short time, clean the air sampled and consequently underestimate the concentration of allergen in air. High volume samplers are noisy and poorly tolerated indoors (by both mice and men). Improvements in the methods of allergen extraction and assay have considerably reduced the volume of sampled air required and, for laboratory animal urine proteins, sample volumes of between 120 and 240 L contain sufficient allergenic protein to assay.2 This has allowed personal samplers with flow rates of 2 L/min to be used. Substitution of the hydrophobic PTFE filter for glass fiber, the addition of Tween to the extraction buffer, and the development of more sensitive immunoassays have all contributed to the reduction in the air sample volume required.

Two types of immunoassay have been used—inhibition assays (RAST and ELISA) and direct immunoassays. Both types of methods are based on the comparison of specific immunoglobulin binding by the soluble material extracted from the filter with a reference allergen source. Accurate quantification requires purified allergen as the standard and the same specificities in the binding immunoglobulins used. With few exceptions (eg, assay of antigen P1 with monoclonal antibodies), these strict criteria have not been met. However, the use of a semipurified standard with a pool of human or

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animal sera containing antibody of similar specificities allows comparisons to be made and sensible estimates of airborne allergen concentration to be made.

Applications

The majority of studies reported to date have examined the variation in airborne concentrations and the factors determining this. Agarwal et al found that the concentrations of ragweed AgE and Alternaria Alt 1 correlated closely with changes in the counts of morphologically identifiable ragweed pollen and Alternaria spore counts. In a subsequent study, Agarwal et al estimated the concentration of airborne AgE in a laboratory by RAST inhibition immunoassay. Airborne allergen concentration varied between 1.8 and 825 ng/m³ and was influenced by both animal density and level of work activity. Similarly, Price and Longbottom found that the airborne concentration of mouse, rat, and rabbit allergens was increased by greater animal density and by greater work activity, such as cleaning an animal room or animal handling. Edwards et al. showed that increasing the ventilation rate and the humidity in an animal laboratory appreciably reduced the concentration of rat urine protein in air.

Few studies have examined exposure–response relationships or evaluated outcome after intervention. In an important study, Reed et al. using a human IgG inhibition immunoassay, measured the concentration of humidifier antigen in a humidified building where several of the work force had developed hypersensitivity pneumonitis. They identified humidifier antigen in air and demonstrated that after the introduction of measures designed to reduce microbial growth in the humidifier, antigen level fell over the subsequent 6 months both in work areas and in the humidifier air ducts. The antigen concentration, which before these measures were instituted were reported to be between 0.5 and 15 µg/m³, after remedial measures fell to levels consistently below 0.001 µg/m³. Examination of the changes in antigen content in relation to the development of IgG antibody to humidifier antigens and the provocation of symptoms led the authors to suggest 0.05 µg/m³ as a level below which initiation of sensitization did not occur.

In a study of baker workers, Musk et al. found that the prevalence of work-related respiratory symptoms and airway hyperresponsiveness was greater in those who had ever worked in the more dusty conditions (category 6 or greater in a ranking of perceived dustiness of 0 to 10). Of those working currently conditions designated as in category 6 or higher, the concentration of airborne flour protein was 10 µg/m³ or greater in 18 of 37 air samples, compared to only one of 28 air samples in those working in conditions designated as category 5 or lower.

The application of these longitudinal study techniques may provide sufficient knowledge of exposure–response relationships for airborne allergens and asthma in the workplace that scientifically based control measures can be implemented that will significantly reduce the incidence of disease.

References


2108 Workshop on Environmental and Occupational Asthma

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