Asthma and allergen exposure

People with asthma and persistent rhinitis are frequently allergic to ‘domestic’ allergens, commonly sourced from furred pets (cats, dogs), cockroaches (*P. americana* and *B. germanica*), mice, house dust mites and fungi. The allergen(s) dominant within any population vary with geography, climate, housing, social and individual factors. ‘Domestic’ exposure is usually perennial, and occurs in houses, schools, and on transport. Allergen exposure occurs via particles each having different characteristic distributions of size and location, generated by disturbance of reservoirs.

Asthma is a complex, variable and multi-factorial disease, and, as our understanding of its pathology changes, so too does our understanding of the role of chronic and acute allergen exposure. While acute exposure to some allergens (eg cat, dog, rat, mouse) will frequently precipitate asthma symptoms in sensitised subjects, this rare occurs following exposure to other allergens (eg cockroaches, mites or fungi). Instead, it is likely that chronic exposure has ‘subclinical’ and synergistic effects, evidenced by increased expression of inflammatory markers, airway hyper-responsiveness, and the risk of exacerbations associated with viral infections. Success of anti-IgE therapy indicates the importance of allergens.

This session will largely examine the role of domestic allergen avoidance in the management of established asthma (‘tertiary avoidance’). Overall, evidence that asthma or allergic sensitisation can be reduced or prevented by domestic allergen avoidance in infancy (‘primary avoidance’) is not conclusive or currently supported.

**The current guidelines for allergen avoidance in asthma management**

The current guidelines for the role of allergen avoidance in asthma management differ nationally and are not consistent. Briefly the US National Institutes of Health, National Heart Lung and Blood Institute 2007 (NHLBI), guidelines are broadly supportive, whereas the global (GINA) and UK (BTS) guidelines are not, while the Finnish guidelines advocate alternative approaches. The NHLBI report provides a summary of the evidence for ‘the strong association between sensitisation to allergens and asthma’ but does not provide a comprehensive comparison of the literature or refer to any of the several meta-analyses of interventions. Many of the 27 publications cited are early studies. The report advises that the first and most important step in controlling allergen-induced asthma is to advise patients to reduce exposure to relevant indoor and outdoor allergens to which the patient is sensitive, and notes that effective avoidance requires a multifaceted, comprehensive approach. Recommended measures include encasing mattresses and pillows, washing bedding weekly in hot water (130°F) and to consider reducing indoor humidity, removing carpets from bedrooms and those laid on concrete, avoid lying on soft furnishings and minimising the number of stuffed children’s toys and washing them weekly. The use of chemicals or air filters alone is not supported, and it advises that vacuum cleaners will remove allergen but not mites.

Both GINA (2009) and BTS guidelines note that evidence of measures to create low allergen domestic environments to reduce asthma symptoms is either inconsistent or inconclusive. While single interventions are generally ineffective, there is some support for individualised, home-based, comprehensive interventions. They question the cost effectiveness of avoidance and note the unsupportive findings of the Cochrane review on dust mite allergen avoidance have also been found by other reviews. They also note that many families are committed to reducing allergen exposure and if so, they may wish to consider a series of standard measures which are similar to NHLBI.

By contrast, Finnish Allergy program 2008-2018 only supports avoidance in ‘mandatory situations’ and instead promotes ‘allergy health’ and the strengthening of immune tolerance through diet (Baltic/Mediterranean), physical activity, a connection with nature, microbial exposures and immunotherapy. As yet, there is no supportive trial data.

(2) **Methods of reducing allergen exposure and evidence-based studies of their effectiveness**

Methods and evidence cannot be summarised in simple terms. The methods conventionally ‘recommended’ are provided in the NHLBI guidelines (above). Many of these were also utilised within the 54 studies in the Cochrane meta-analysis. Despite the limitations of the Cochrane meta-analysis, its core conclusion of no overall clinical benefit has had enormous global impact. The analysis also concluded it was “inherently implausible to suggest that complete removal of a major provoking agent would be ineffective”, implying that the methods were ineffective at sufficiently reducing exposure.

While the methods advocated by NHLBI may seem ‘logical’, in fact there is a little consistent experimental data showing that large and long term reductions in aeroallergen exposure can be obtained by bed encasing, carpet removal, hot (55°C) water laundry, air filtration, HEPA vacuuming or acaricides, either singly or in combination. While some methods may provide acute reductions in reservoir concentrations, this may not result in large reductions in aeroallergen exposures, or the reductions are maintained over time. The effect of a reduction at a single site also needs to be understood in terms of 24-hour exposure. The focus has been on differences between products, rather protocols sustaining long term reductions.
At present we do not have a clear idea of when and where people get most of their personal exposure to cockroach, mite, cat, mouse allergens over 24 hours in different populations, age and lifestyle groups. Our models have been based largely on assessing allergen content of a few reservoirs, rather than airborne exposure, which is more complex to measure. While the main site of mite exposure is conventionally thought to be the bed, the only published study of aeroallergen exposure over 24 hours found the bedroom exposures were lower than lounge/living room and school. We have data at this meeting (Abstract #3511) showing the bedroom as a minor contributor to mite total 24-hour exposure. In some communities, cat and mouse allergens have also been reported to be present in higher concentrations in schools than homes.

There is more recent evidence of clinical effective allergen avoidance from (1) studies which use multiple domestic interventions including those tailored to the individual, (2) a study using complex engineering to provide clean air to a dwelling, and (3) a study which used laminar, HEPA-filtered air delivered over the bed. Together these suggest effective avoidance needs to focus on reducing chronic aeroallergen exposure.

The title of this session is “Rethinking allergen avoidance” and the take home message is that there is good reason to think that, at least in some patients at some time, avoidance of domestic allergens may be practical and beneficial. However, to be more effective, the following uncertainties need resolution. (1) the best way to measure a person’s domestic exposure, (2) understand where and when most aeroallergen exposure occurs, (3) methods to reduce overall aeroallergen exposure, (4) bio/genetic markers to identify subjects in whom such avoidance should be attempted, (5) an understanding of the synergies, risks, benefits and cost-effectiveness of long term allergen avoidance strategies compared to pharmaceutical and other environmental and lifestyle approaches. (6) Approaches to improve compliance with recommendations.

(3) Discuss new strategies for allergen avoidance that take into account the complex interactions between allergens, the innate immune system and genetic markers.

Some complexities include: (1). The shape of dose response relationships between exposures for allergens and allergic sensitisation and asthma may be non-linear for some allergens (mite, cat, mouse, cockroach for outcome of sensitization), but linear for others (mouse for outcome of asthma morbidity). (2) The effects of high-dose tolerance, which may be at play when there is a non-linear relationship between allergen exposure and allergic disease as described above. (3). The periodicity, or degree of variability, of allergen exposure. (4) The effects of exposures to innate immune stimulants, other environmental factors (cigarette smoke exposure, volatile organic compounds, particulate matter, nitrogen dioxide, and endocrine regulators such as phthalates, tributyl tin, and triclosan), and micronutrient status. Intrinsic factors, such as genetic polymorphisms, that confer (or protect against) susceptibility to these environmental exposures.

REFERENCES


