Allergy, environment and asthma

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Abstract
Clinical allergy represents the outcome of interactions between allergic sensitisation, trigger events (such as viral respiratory infections and pollution) and genetic components. Allergen avoidance can improve allergic symptoms to a certain extent but complete allergen avoidance is very difficult to achieve. In humans, allergen avoidance may delay the natural induction of allergen tolerance and increase the 'window of risk'. Controlled allergen exposure, especially oral or intranasal, can prevent allergy in animal models of allergy. Allergen exposure, ideally within a well-defined 'window of opportunity' could induce tolerance and may be protective against allergy. The immunological mechanisms that confer protection to allergy have to be identified in order to define the end-point that needs to be achieved in controlled allergen exposure interventions. Finally allergen desensitisation may hold promise.

Keywords: Allergy, asthma, environment, tolerance

Introduction

The prevalence of allergic diseases worldwide is increasing. World Allergy Organization (WAO) has suggested that 30-40% of the world's population is currently suffering from some forms of allergy such as asthma, drug and food allergy, anaphylaxis, rhinitis, eczema, urticaria and angioedema. The WAO estimates that 400 million people worldwide could have asthma by 2025; another 400 million suffer from rhinitis and up to 250 million people may have food allergies. There is an epidemic of allergic diseases especially amongst children.

Allergen avoidance

It is logical therefore to ask whether allergen avoidance can help stop the inexorable rise in prevalence of allergic diseases. Previous studies on relocating house dust mite (HDM) allergic children from sea level (where HDM is abundant) to the mountains (where the HDM is scarce) have shown encouraging results.¹,² There was a reduction in bronchial hyperresponsiveness when the children attended schools in Davos, Switzerland (1560 m) or Misurina, Italy (1756 m) compared to when they were in their home towns at sea level. Unfortunately any improvement gained from living in the mountains was lost soon after they returned home during their holidays.

This has important implications for Hong Kong as HDM allergy is very common and up to 75% of the population may be sensitised. However prospective studies in infants using anti-allergic pillows and HDM protective bed sheet covers had only a limited and minor short lasting benefit on wheezing, despite substantial reductions in HDM exposure.³ A Cochrane review showed that a monofaceted allergen avoidance intervention was ineffective for reducing odds for developing asthma in children.⁴ A multifaceted intervention of multiple food and respiratory allergens in the first 2-5 years of life resulted in a small but consistent decrease in the odds for having asthma at 5 years old, but any benefit was lost quite soon upon resumption of normal lifestyles.

The reason for these disappointing results may be due to the immense difficulty in removing ubiquitous respiratory and food allergens completely from the environment.⁵ Even stringent avoidance of eating egg by mothers during pregnancy was shown not to prevent egg sensitisation in their infants.⁶

Interactions between allergen, genes and environment

Allergy results from complex interplay between allergen...
exposure, environmental factors and genes (Figure 1). It is only when all three key elements are present in the same individual that there is a high risk of developing allergy. Thus it is not surprising that manipulating allergen exposure alone has only a limited effect.

The importance of genetic factors is illustrated well by the molecule filaggrin. Filaggrin is formed of repeated peptide subunits that are extensively cross-linked in the skin. When intact it is a scaffold for the attachment of lipids that make the skin impermeable to water and therefore water soluble allergens. If filaggrin has a genetic mutation that renders it dysfunctional the risk for developing eczema is greatly enhanced. The presence of the filaggrin mutation, exposure to cats at birth increased the risk of developing eczema.

The critical contribution of the environment is emphasized by the fact that onset of wheezing was predicted by the synergy between allergic sensitisation and lower respiratory tract infections (Figure 2). In addition the incidence and prevalence of asthma during infancy and childhood were increased with higher levels of the ambient pollutants NO₂, particulate matter <10 microns (PM₁₀) and PM <2.5 microns (PM₂.₅). Hospital admissions for asthma in children were also associated with elevated ambient NO₂, PM₁₀ and PM₂.₅. In Nicosia children who lived within 50 m (but not further) from heavily polluted roads had a significantly higher prevalence of wheezing. The fact that diesel exhaust particles might act as adjuvants promoting a TH2 immunological response could be a key mechanism in perpetuating allergic inflammation.

The Oxford Street experiment was especially germane, when asthmatic patients were invited to walk for several hours along Oxford Street in London, which was heavily polluted, and the results compared with those in subjects who walked around a part of Hyde Park, which prohibited cars and motorcycles. Respiratory symptom scores

![Figure 1. Allergy results from complex interactions between allergen exposure, environmental trigger factors and genetic components.](image)

![Figure 2. Late childhood wheezing is predicted by the synergy between allergic sensitisation and lower respiratory tract infections.](image)
during the Oxford Street walk were higher than those during the Hyde Park walk. The falls in FEV1 during the day were also greater in the high pollutant Oxford Street, especially in those with moderately severe asthma.

These epidemiological and real life experiments emphasize the important need to limit pollution for respiratory health, in addition to the many other well recognised health benefits from cleaner air.

**If the answer is not allergen avoidance, how may allergy be prevented?**

If allergen avoidance is not the panacea one might hope for preventing allergic diseases, is there an alternative solution? Recent data has suggested that instead of avoidance, early allergen exposure may protect against allergy by inducing specific tolerance. In contrast allergen avoidance may delay the natural induction of immunological tolerance and increase the window of risk. In support of this hypothesis, controlled oral or intranasal exposure to ovalbumin prevented subsequent allergic sensitisation by this protein due to induction of tolerance in a mouse model of asthma.11 In humans it is known that early introduction of egg protein in infancy is correlated with lower egg allergy12 and early consumption of peanuts in infancy is associated with a lower prevalence of peanut allergy.13 One way to induce tolerance is to undergo allergen-specific desensitisation and there are research studies testing whether early allergen immunotherapy may prevent subsequent development of allergic diseases.

**Conclusion**

Clinical allergy represents the outcome of interactions between allergic sensitisation; trigger events (such as infections and pollution); and genetic components. Allergen avoidance can improve allergic symptoms to a limited extent but complete allergen avoidance is very difficult to achieve. In humans allergen avoidance may delay the normal induction of immunological tolerance. In contrast allergen exposure during a window of opportunity could induce tolerance and protect against allergic sensitisation, as already demonstrated in animal models of asthma. Allergen desensitisation may hold promise in the future. The immunological mechanisms that confer protection to allergy have to be identified so that the end point that needs to be achieved in controlled allergen exposure interventions can be defined.

**References**


