UNIT NO. 5

ALLERGEN AVOIDANCE

Dr Tan Keng Leong

ABSTRACT

Allergy is a significant triggering factor in asthma and allergic rhinitis. Inhaled allergens and IgE-mediated allergic reactions play a central role in the pathogenesis of allergic asthma and allergic rhinitis. Allergen avoidance is recommended for the management of allergic asthma and allergic rhinitis by current guidelines. House-dust is the most prevalent sensitizing agent in Singapore. Effective allergen avoidance requires a multifaceted, comprehensive and sustained approach.

SFP2009; 35(2): 28-32

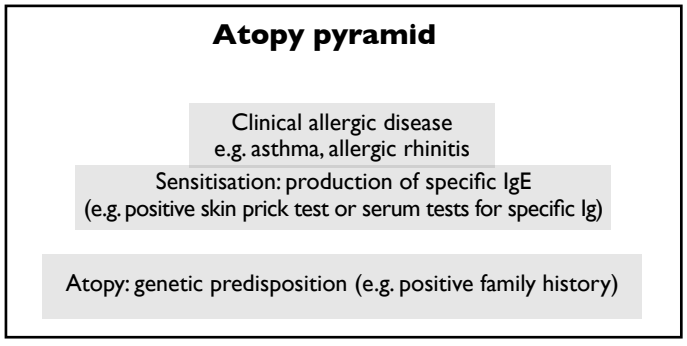
INTRODUCTION

Allergen avoidance is important in the management of allergic asthma and allergic rhinitis and is recommended for all patients by current guidelines. A primary objective for any physician treating patients with an allergic disease caused by or exacerbated by a specific allergen is to educate the patients on how to avoid the relevant allergens. By understanding the role that specific allergens play in causing symptoms and the allergen avoidance measures, they may gain control of their allergic disease, reduce symptoms and medication needs.

ATOPY AND ALLERGY

Individuals with a genetic predisposition to IgE-mediated type I hypersensitivity reactions after exposure to low doses of environmental allergens are described as atopic (allergy prone). This predisposition can be recognized based on a positive family history for allergic diseases or on the occurrence of an allergic sensitization or disease in a given individual.

Figure 1: The Atopy Pyramid



TAN KENG LEONG, Senior Consultant, Department of Respiratory and Critical Care Medicine and Director, Allergy Clinic, Singapore General Hospital

The definition of atopy describes a genotype; a predisposition to develop allergic diseases. Not all atopic individuals exhibit clinical disease. Individuals with a family history of atopy, who have an underlying genetic profile involving multiple genes, are at increased risk of IgE sensitization. Early signs of allergic disease (e.g. atopic eczema), and the presence of IgE antibodies specific to inhalant allergens, are important risk factors for the development of allergic respiratory diseases, such as allergic asthma or allergic rhinitis, later in life.

Allergic sensitization is defined as the production of specific IgE directed against an environmental allergen, which can be detected clinically by a positive skin prick test response to these allergens and/or elevated levels of allergen-specific IgE in the serum. Not every sensitized individual demonstrates a clinical disease.

ALLERGIC ASTHMA

Asthma is a chronic inflammatory disorder of the airways. Since Rackemann introduced the terms in 1918, asthma that can be shown to be related to hypersensitivity to a foreign substance has been described as "extrinsic"; otherwise, the disease has been classified as "intrinsic". The distinction between the allergic ("extrinsic") and nonallergic ("intrinsic") forms of asthma is usually based on the presence or absence of allergy skin-test reactivity to one or more aeroallergens considered capable of inducing the disease. Increased specific IgE is a characteristic feature of allergic asthma. Most children with asthma are atopic and IgE sensitization is common. Extrinsic asthma is the predominant form of the disease among children and young adults, and intrinsic asthma is considered to be more common among older subjects.

Immediate hypersensitivity to allergens is very common among children and young adults with asthma and rhinitis. Sensitization to one or more of the major indoor allergens (such as dust mite, cat, dog, or cockroach), combined with significant accumulation of relevant allergens in the house, has been consistently found to be the strongest risk factor for asthma in population, case control, and prospective studies.

Our current understanding of the process of sensitization indicates that there is a strong genetic predisposition to form IgE to allergenic proteins on airborne particles. In susceptible individuals, a cascade of events is subsequently triggered in which many inflammatory cells and mediators are implicated. The inflammatory cells involved in IgE-mediated inflammation in the lung are present in the airways and include mast cells, T lymphocytes and eosinophils. Upon IgE-dependent signaling and following allergen exposure, human mast cells in the lung

generate and release a wide variety of inflammatory mediators. These mediators play an important role in the allergen-mediated early response and also facilitate the development of the late response and, subsequently more chronic inflammatory reactions.

Eosinophilic asthma

Airway inflammation is the primary cause of asthma symptoms, exacerbations, reversible airflow limitation, airway hyperresponsiveness and remodeling (which is thought to lead to the development of chronic airflow limitation). Asthma is phenotypically heterogeneous, and studies have provided evidence of different patterns of inflammatory cell involvement in allergic and nonallergic asthma. Airway inflammation may be measured in induced sputum cell counts. Sputum cell counts demonstrate different types of inflammation due to different causes. These are:

(i) eosinophilic (due to inhaled allergens or chemical sensitisers to which the patient is allergic or sensitised, or to inadequate steroid treatment),

(ii) neutrophilic (which can be trivial and non-specific or more intense due to viral or bacterial infections),

(iii) eosinophilic and neutrophilic, or

(iv) neither.

Eosinophilic asthma represents a distinct disease phenotype which is characterized by the presence of airway eosinophilia (as classified by induced sputum eosinophil count criteria) and a favorable response to adequate steroid treatment. On the other hand, non-eosinophilic asthma (absence of induced sputum evidence of eosinophilic airway inflammation) is associated with poor response to inhaled corticosteroids.

ALLERGIC RHINITIS

The historical view of allergic asthma and allergic rhinitis as distinct and separate entities is being displaced by current view that they represent two manifestations of inflammation involving one common airway. The mucosal surfaces of both nasal and bronchial airways are exposed to the same environmental stimuli and respond to these in a similar fashion. The submucosal environment however is different in the two organ systems, which predefines the spectrum of clinical symptoms. The shared cell types, mediators and pathways in the allergic cascade that characterizes these diseases, however supports this approach.

Allergic rhinitis, like allergic asthma, is characterized by mucosal inflammation and hyperresponsiveness. As in asthma, the allergens responsible are inhaled (aeroallergens). Because the offending allergens are the same, environmental control for allergic rhinitis is identical to that recommended for the management of allergic asthma. Outdoor allergens, such as plant pollens (e.g. ragweed, grasses, and weeds) and molds (e.g. Alternaria) typically cause seasonal rhinitis, whereas indoor allergens such as house dust mite, cockroach, and pet danders cause perennial symptoms. In subtropical and tropical climates, where seasons are less distinct, the differentiation between seasonal and perennial patterns of disease is of less value.

COMMON ALLERGENS

The important allergens are those that are inhaled. Indoor aeroallergens are associated with asthma prevalence, severity and exacerbation while outdoor allergens are associated with asthma exacerbation. Food allergens are not a common precipitant of asthma symptoms.

House-dust mite is the most common sensitizing agent in Singapore. Hundreds of varieties of dust mite exist. House-dust mite tends to colonize beds, upholstered furniture and carpets. Their growth is dependent on humidity and human skin scales, which serves as their food. Mite allergen accumulation is in the form of fecal particles.

PREVALENCE AND DISTRIBUTION OF ALLERGENS

Blomia tropicalis is the most prevalent species of house-dust mite in Singapore. Their densities were found to be highest in living room carpets and mattresses in the bedrooms. There was no significant seasonal variation in dust-mite allergen levels in the homes over a one-year period. The absence of seasonality in mite allergen levels is consistent with the tropical climate and high humidity (64-96%) all year round in Singapore.

Local studies indicate that although public places are contaminated with common indoor allergens, the home constitutes a major reservoir of these allergens. As such, homes should be the target of allergen avoidance measures. Major cat and dog allergens were found to be well distributed and not confined to homes with pets. This passively transferred allergen may become airborne and cause symptoms. Allergenic material from cat (Fel d1), a water-soluble protein produced in sebaceous, salivary and anal glands, is sticky and may be transported for long distances on cat dander to homes and buildings without cats.

PREVALENCE OF SENSITISATION TO ALLERGENS

Locally, asthma and/or allergic rhinitis patients were found to be highly sensitized to the local dust-mite fauna. The sensitization rates among patients with asthma and/or allergic rhinitis in Singapore (in the order of importance) were found to be as follows: Blomia tropicalis dust mite (96.2%), D. pteronyssinus dust mite (93.4%), D. farinae dust mite (92.3%), three other species of dust mites (A. malaysiensis 78.2%, S. brasiliensis

71.6%, T. putrescentiae 71.3%), bird's feathers (canary feathers 69.9%), two species of cockroach (P. Americana 59.5%, B. germanica 56.4%), mosquito (Aedes sp 46.4%), dog dander (34.3%), cat hair (29.1%) and three species of indoor fungi (Aspergillus fumigatus 20.8%, Penicillium notatum 18%, Candida albicans 9.3%).

The allergenic extracts of the local mite fauna should therefore be included in the diagnostic panel for the evaluation of allergic disorders in our local practice.

ALLERGENS AND ASTHMA EXACERBATION

Immediate hypersensitivity to indoor allergens is known to be associated with allergic asthma. Inhalant exposure to seasonal outdoor fungal spores and to indoor allergens has been implicated in fatal exacerbations of asthma. Amongst asthmatics, exposure to the allergens to which they are sensitive has been shown to increase asthma symptoms and precipitate asthma exacerbations. Reducing exposure to these allergens improves the control of asthma and reduces medication needs.

EVALUATION

The clinician should evaluate the potential role of allergens, particularly indoor inhalant allergens. The patient's medical history often helps in the identification of allergen exposures that may worsen his asthma. Sensitivity to seasonal allergens should be assessed from the patient's history. Working asthmatics should be queried about the possible occupational exposures. The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects in the management of occupational asthma. When occupational asthma is suspected, a referral to the specialist is indicated.

Skin testing or in vitro testing (specific IgE antibodies to allergen) is used to determine sensitivity to perennial indoor inhalant allergens to which the patient is exposed. A positive alone does not determine whether the specific IgE is responsible for the patient's symptoms. Hence, patients should be tested only for sensitivity to the allergens to which they may be exposed. It is important to determine the clinical significance and relevance of positive allergy tests in the context of the patient's medical history.

ALLERGENS EXPOSURE CONTROL

Allergen avoidance measures must be allergen specific. The patient should be given advice to reduce exposure to the relevant indoor or outdoor allergens to which he is sensitive. Although allergen avoidance is always recommended by guidelines for the management of allergic asthma and allergic rhinitis, it is seldom completely effective in clinical practice. The clinical benefit for the effectiveness of allergen avoidance measures has been difficult to be demonstrated in clinical studies. In many published house-dust mite avoidance studies, the measures taken were inadequate and did not achieve a reduction in mite exposure by more than 95%. In general, effective allergen avoidance requires a multifaceted, comprehensive approach. Single allergen avoidance steps are generally ineffective in reducing the allergen load sufficiently to lead to clinical improvement.

Table 1: Effectiveness of Avoidance Measures for Some Indoor Allergens

Effectiveness of Avoidance Measures for Some Indoor Allergens*

Measure	Evidence of effect on allergen levels	Evidence of clinical benefit
House dust mites		
Encase bedding in impermeable covers	Some	None (adults) Some (children)
Wash bedding in the hot cycle (55-60°C)	Some	None
Replace carpets with hard flooring	Some	None
Acaricides and/or tannic acid	Weak	None
Minimize objects that accumulate dust	None	None
Vacuum cleaners with integral HEPA filter and double-thickness bags	Weak	None
Remove, hot wash, or freeze soft toys	None	None
Pets		
Remove cat/dog from the home	Weak	None
Keep pet from main living areas/bedrooms	Weak	None
HEPA-filter air cleaners	Some	None
Wash pet	Weak	None
Replace carpets with hard flooring	None	None
Vacuum cleaners with integral HEPA filter and double-thickness bags	None	None

* *Adapted from* Custovic A. Wijk RG. The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA(2)LEN). *Allergy* 2005;60(9):1112-1115.

Woodcock et al (2003) showed that using allergen-impermeable encasements as a single measure to avoid exposure to dust mite allergens was ineffective for adults. A number of trials have shown a reduction in dust mite allergens when allergen-impermeable encasements were used, but did not show clinical improvements (Oosting et al 2002, Rijssenbeek-Nouwens et al 2002, van Strien et al 2003). When there is a reduction in allergen in a study but no improvement in health, this may be due to other sources of allergen from schools or occupational settings (Oosting et al 2002). Clinical benefit usually required three to six months of sustained allergen avoidance interventions in clinical studies.

House-dust mite

Avoidance measures for house-dust mite should focus mainly on the bedroom as homes constitute a major reservoir of allergen and as patients spends the most time in the bedroom. Recommended

measures to control house-dust mite allergen include the following: encase mattress in an allergen-impermeable cover, encase pillow in an allergen-impermeable cover, wash pillow, bed sheets and blanket in hot water (55-60ºC) at least once weekly. A temperature of >55ºC is necessary for killing house-dust mites.

In bedding or toys that cannot be washed, drying bedding in a clothes drier on a hot setting, and freezing toys may be pursued. Prolonged exposure to dry heat or freezing can kill house-dust mites but does not remove allergen as in washing. Removal of carpeting, stuffed animals and curtains, may also be pursued. Because house-dust mites do not drink and rely on absorption of humidity from the atmosphere, reducing humidity below 50% has also been recommended.

Acaricides (pesticide developed specifically for mites) has a short lived effect and temporarily reduce the number of mites in furnishings but this has not been shown to be associated with clinical improvement. Air cleaners are usually not effective in reducing dust mite antigen, because the antigen is large and heavy and rarely airborne.

Animal dander

The most effective measure to control animal dander allergens is to persuade patients not to keep animals in the home. Deep cleaning strategies will only work if the source of the allergen (the pet) is removed, although cat allergen (Fel d1) tends to remain in the building for at least six months. Patients who are allergic to cat or dog allergens should also be informed about the relevance of passively transferred allergen. Bathing cat weekly was previously thought to be an effective method but is difficult to perform in an adult cat. Recent studies have shown that cat allergen in the air returns to prebath levels as quickly as 24 hours later. A hypoallergenic cat has been developed by breeding cats naturally deficient in the primary antigenic protein Fel d1 and is commercially available.

Cockroach

For cockroach antigen, current recommendations include placing multiple baited traps or poisons, eliminating food sources and removing cockroach debris. Air filtration is not effective as cockroach antigen is heavy and does not remain airborne.

Indoor mold

Burr et al (2007) described the first randomised controlled trial to demonstrate improvement in asthma and allergic rhinitis symptoms and reduction in medication needs with eradication of mold from home of asthmatics. In the treated households, all visible mold was removed by the application of detergent and surfactant with fungicide and installation of ceiling ventilation fan. Practical measures to reduce mold growth include prevention of wet areas on walls and carpets and elimination of household plants, which are a common reservoir for mold growth.

Outdoor allergens (grass, weed and tree pollen, seasonal mold spores)

Patients who are sensitive to seasonal outdoor allergens are recommended to stay indoors with windows closed during peak allergen exposure periods.

Environmental tobacco smoke and drugs

Amongst asthmatics, exposure to tobacco smoke is associated with increased symptoms, decreased lung function and greater use of health services. Asthmatics should be advised not to smoke or be exposed to environmental tobacco smoke.

Adults with asthma, nasal polyps and a history of sensitivity to aspirin or NSAIDs should be counselled regarding the risk of severe and fatal exacerbations from using these drugs.

REFERENCES

1. Berry M, Morgan A, Shaw DE et al. Pathological features and inhaled corticosteroid response of eosin ophilic and non-eosinophilic asthma. Thorax 2007; 62: 1043-9.
2. Pizzichini MM. Is sputum eosinophilia a good or poor predictor of benefit from inhaled corticosteroid therapy in asthma? Eur Respir J 2002; 20:1359-61.
3. Global initiative for asthma. Global strategy for asthma management and prevention (updated 2008).
4. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Asthma Education and Prevention Program. National Heart, Lung, and Blood Institute. US Department of Health and Human Services 2007.
5. A Custovic, RG van Wijk. The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA2LEN). Allergy 2005; 60: 1112-5.
6. L Zhang, FT Chew, SY Goh et al. Prevalence and distribution of indoor allergens in Singapore. Clinical and Experimental Allergy 1997; 27:876-85.
7. FT Chew, L Zhang, TM Ho et al. House dust mite fauna of tropical Singapore. Clinical and Experimental Allergy 1999; 29: 201-6.
8. FT Chew, SH Lim, DYT Goh et al. Sensitisation to local dust-mite fauna in Singapore. Allergy 1999; 54: 1150-9.
9. Woodcock A, Forster L, Matthews E et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. New England Journal of Medicine 2003; 349(3): 225-36.
10. Oosting AJ, de Bruin-Weller MS, Terreehorst I et al. Effect of mattress encasings on atopic dermatitis outcome measures in a double-blind, placebo-controlled study: the Dutch mite avoidance study. Journal of Allergy and Clinical Immunology 2002; 110(3): 500-6.
11. Rijssenbeek-Nouwens LH, Oosting AJ, de Bruin-Weller MS et al. Clinical evaluation of the effect of anti-allergic mattress covers in patients with moderate to severe asthma and house dust mite allergy: a randomized double blind placebo controlled trial. Thorax 2002; 57(9): 784-90.
12. van Strien RT, Koopman LP, Kerkhof M et al. Mattress encasings and mite allergen levels in the prevention and incidence of asthma and mite allergy study. Clinical and Experimental Allergy 2003; 33(4): 490-5.
13. Burr ML, Matthews IP, Arthur RA et al. Effects on patients with asthma of eradicating visible indoor mold: a randomized controlled trial. Thorax 2007; 62: 766-71.
14. Ferguson BJ. Environmental controls of allergies. Otolaryngol Clin N Am 2008; 41: 411-7.

LEARNING POINTS

- **Allergen exposure has been shown to increase symptoms of allergic asthma and allergic rhinitis and precipitate exacerbations of asthma and allergic rhinitis.**
- **Allergen avoidance is important in the management of allergic asthma and allergic rhinitis and is recommended for all patients by current guidelines.**
- **Patients should be tested only for sensitivity to the allergens to which they may be exposed.**
- **The clinical significance and relevance of positive allergy skin testing or in vitro allergy test should be interpreted in the context of the patient's medical history.**
- **Single allergen avoidance steps are generally ineffective.**
- **Effective allergen avoidance requires a multifaceted, comprehensive approach.**
- **Clinical benefit usually required 3 to 6 months of sustained allergen avoidance interventions.**
- **House-dust mite is the most common sensitizing agent in Singapore.**
- **Avoidance measures for house-dust mite should focus mainly on the bedroom.**