

Healthed The General Practice Education Day



House dust mite allergy, rhinitis and asthma.

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DHS

- Than-you for inviting me
- Clinical Immunologist
- No conflicts of interest



Topics

- House dust mite biology
- House dust mite allergy in rhinitis and asthma
- Diagnosis of allergy
- Treatment of allergic rhinitis

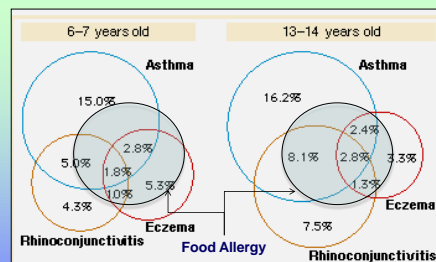
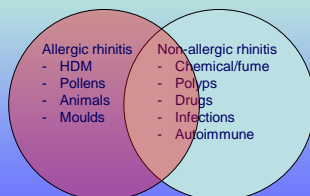


Figure 2: Venn diagrams showing the interrelation between wheeze, eczema and rhinitis in the previous 12 months in Australian schoolchildren. Values shown are the percentage of the total sample.

Colin F Robertson, Maria F Dalton, MJA 1998; 168: 434-438



Rhinitis



Allergic rhinitis

- | Seasonal AR – allergy caused by season allergens more often outdoor allergens, e.g. grass and tree pollen
- | Perennial AR – allergy caused by perennial allergens more often indoor allergens, e.g. dust mite, pet dander, but sometimes also pollens in QLD
- | Intermittent vs Persistent
- | Mild, Moderate or Severe

PAR, perennial allergic rhinitis
SAR, seasonal allergic rhinitis

Bousquet J, et al. J Allergy Clin Immunol 2001;108:S147



New AR classification:

<p>Intermittent</p> <ul style="list-style-type: none"> . < 4 days per week . <u>or</u> < 4 weeks 	<p>Persistent</p> <ul style="list-style-type: none"> . ≥ 4 days per week . <u>and</u> ≥ 4 weeks
<p>Mild</p> <ul style="list-style-type: none"> normal sleep & no impairment of daily activities, sport, leisure & normal work and school & no troublesome symptoms 	<p>Moderate-severe</p> <p><i>one or more items</i></p> <ul style="list-style-type: none"> . abnormal sleep . impairment of daily activities, sport, leisure . abnormal work and school . troublesome symptoms

1999 WHO ARIA recommendations:


- Depending on the subdivision and severity of AR, a stepwise therapeutic approach has been proposed
- The treatment of AR combines:
 - allergen avoidance (when possible)
 - pharmacotherapy
 - immunotherapy
 - education
- Patients with persistent AR should be evaluated for asthma by history, chest examination and, if possible and when necessary, the assessment of airflow obstruction before and after bronchodilator
- Patients with asthma should be appropriately evaluated (history and physical examination) for rhinitis
- A combined strategy should ideally be used to treat the upper and lower airway diseases in terms of efficacy and safety

Allergy diagnosis in rhinitis and asthma

- Detection of allergen specific IgE



Skin prick allergy test.



"RAST" test → solid matrix fluorescent enzyme immunoassay

Specific IgE / RAST

Pathology request

Patient details: Mr Snuffie Upagus DOB

Test: Specific IgE / RAST – house dust mite; grass pollen mix; alternaria (or cat/dog if patient has a pet)

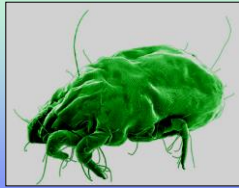
Requestor: Dr A. Llergy

Aeroallergens:

- House dust mite
- Grass pollens
- Moulds
- Cockroach
- Weed pollens
- Tree pollens
- Animal dander (cat > dog)
- Other airborne allergens
- The presence of 100 mites per gram of house dust is sufficient to sensitize an infant. For around 500 mites sensitized patient shows a greater risk of developing asthma at a later date. The higher the number of mites in dust, the earlier the first episode of wheezing.

House dust mite

- Many species
 - *Dermatophagoides pteronyssinus*
 - *Dermatophagoides farinae*
 - *Blomia tropicalis*
 - *Lepidoglyphus destructor*
 - *Euroglyphus destructor*
- Warmth - 25° C
- Humidity – 70-90%
- Dust
- Bedding, clothes, curtains, soft toys, flooring – carpet
- Mite allergens (proteases) are present in mite bodies, secreta, excreta – highest concentration in faecal particles



Links between allergic rhinitis and asthma

- Anatomical – “one airway”
- Epidemiological
 - Co-existent disease
 - AR is a risk factor for later asthma development
- Mucosal allergen exposure – allergic inflammation has a systemic component:
 - *Non-asthmatic atopic subjects with rhinitis show increased eosinophilic infiltration of the bronchial mucosa*
 - *Endobronchial challenge can produce nasal as well as bronchial symptoms*
 - *Nasal allergen challenge can induce bronchial inflammation*

Links between allergic rhinitis and asthma

- Possible effects of impaired nasal air conditioning in AR on lower airway function
- Treatment of AR has shown to reduce asthma morbidity in large (n=20 000) combined retrospective cohort studies.

Treatment of allergic rhinitis

- Allergen avoidance measures
- Antihistamines
 - Oral
 - Intranasal
- Corticosteroids
 - Intranasal
 - Oral / systemic
- Leukotriene antagonists
- Immunotherapy (allergen desensitisation)
 - Subcutaneous
 - Sublingual

Stepwise progression in treatment of A.R.

	Mild	Moderate	Severe
Allergen avoidance	★	★	★
Antihistamine	★	★	★
Intranasal corticosteroids		★	★
Specific Immunotherapy		★	★

Allergen avoidance measures:

- Bedding covers
- Flooring modification
- Removal of soft toys
- Washing linen at > 55°C
- Acaricide sprays
- Air filtration
- Stay indoors on high pollen count days
- Avoid animal exposure / pet ownership

Cochrane Systemic Review 2010: Dust mite control -
It probably helps if a systematic approach is undertaken.

Anti-histamines (H1)

- Non-sedating (2nd generation) antihistamines
 - Safe. No or minimal CP450 effect / non-cardiotoxic.
 - Effective in mild – moderate AR, good data.

- Loratidine
- Desloratidine
- Cetrizine
- Fexofenadine
- etc

}

Oral. Little to suggest benefit of one over another. Some patients benefit from cycling.

- Azelastine

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Nasal antihistamine spray

Corticosteroids

- Corticosteroids are the most potent pharmacological agents (i.e. excluding immunotherapy) for treatment of AR
- Oral corticosteroids may be used infrequently and short term for severe obstructive symptoms
- Intranasal corticosteroids (INC) provide the best risk/benefit ratio
- Care with HPA axis suppression with intranasal corticosteroids added to pulmonary inhaled steroids in children (although studies indicate safety)
- In moderate to severe A.R. some patients will not obtain control even with combinations of antihistamines and INC.

Leukotriene antagonists

- Block effects of leukotrienes at the cysteinyl leukotriene 1 (CysLTR1) receptor
 - Montelukast (*Singulair*)
- Effective in:
 - Allergic rhinitis
 - Asthma
 - Asthma and allergic rhinitis
- In Australia available on the PBS for treatment of asthma
- Non-PBS relatively inexpensive

Immunotherapy

- Previously "desensitisation", now "allergen immunotherapy" is preferred term
- Induction of tolerance to previously symptom inducing allergens through induction of non-allergic immunological changes:
 - T regulatory cells
 - IgG4 up regulation
 - IgE down regulation
- Proven benefit in:
 - Allergic rhinitis and allergic asthma – large numbers of RCTs demonstrating benefit
 - Benefits include symptom control and reduction in concomitant medication use

ACARIZAX: clinically proven effectiveness in both AR and AA¹⁻⁴

Phase II EEC trial (Nolte) ¹	Phase III AR trial (Demoly) ²	Phase III AA trial (Virchow) ³
<ul style="list-style-type: none"> • Population HDM AR ± asthma in an EEC 	<ul style="list-style-type: none"> • Population HDM AR ± asthma 	<ul style="list-style-type: none"> • Population HDM AR + HDM AA
<ul style="list-style-type: none"> • Primary endpoint outcome Efficacy by 8 weeks and nasal symptoms (TNSS) reduced by 49% at 24 weeks (p<0.001 vs placebo) 	<ul style="list-style-type: none"> • Primary endpoint outcome Reduced rhinitis symptoms and medication use during last 8 weeks of treatment (p=0.001, vs placebo), with treatment effect seen from Week 14 	<ul style="list-style-type: none"> • Primary endpoint outcome 34% reduced moderate or severe asthma exacerbation risk (p=0.017, vs placebo during the ICS withdrawal period)

AA - Allergy Asthma; AR - Allergic Rhinitis; EEC - Environmental Exposure Chamber; HDM - House Dust Mite; ICS - Inhaled Corticosteroids
 TNSS - total nasal symptom score
 References: 1. Nolle H et al. J Allergy Clin Immunol 2015; 135:1494-501 | 2. Demoly P et al. J Allergy Clin Immunol 2016; 137:444-52
 3. Virchow JC et al. JAMA 2016; 315:1715-25 | 4. ACARIZAX Product Information, 1 August 2016.

Indications for immunotherapy:

- Patients with allergic rhinitis / allergic asthma with specific IgE sensitisation
- Incomplete symptom relief from allergen avoidance / antihistamine / intranasal corticosteroid treatment
- Patients who wish to avoid open-ended pharmacological treatment or have undesirable side-effects from pharmacological treatment

Immunotherapy

- Subcutaneous immunotherapy (SCIT)
 - Induction: Weekly injections for between 6-12 weeks
 - Monthly injections for 3 years
 - Medical centre visits for injections because of low risk of systemic reactions
 - Risk of acute bronchospasm in asthmatic patients at time of injection
 - Non-PBS. Variable cost ~ \$50/month
 - I prefer to avoid in children <12 years of age
 - Good efficacy data for HDM, pollens, cat, dog
 - Preferred if mould spore immunotherapy is required



Immunotherapy

- Sublingual immunotherapy (SLIT)
 - Daily oral (sublingual) drops or tablet
 - Taken at home
 - Duration 3 years
 - Good safety data including in asthma
 - More expensive than SCIT
 - Non-PBS. Cost \$50-\$90 per month
 - Well tolerated by children
 - Infrequent mild oral allergic symptoms at first few doses
 - First dose should be administered under medical supervision



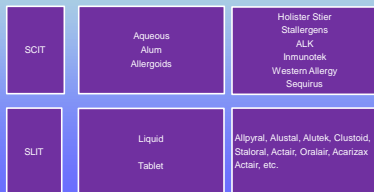
Immunotherapy

- Pros:
 - Long term remission of allergic disease (2-10 years)
 - Symptomatic improvement
 - Reduction in medication
 - Pharmaco-economic benefit
 - May prevent allergic progression in children (i.e. prevent asthma in children with rhinitis)
- Cons:
 - Modestly intensive and modestly expensive (up-front) programmes
 - Acute allergic reactions (SCIT)
 - "Efficacy" 75% to 25% decreasing with increasing age
 - Can make eczema worse in the short term (but may be beneficial in the long run)



Immunotherapy Treatments

- Unfortunately: A confusing multiplicity of treatments that are not easily interchangeable due to lack of standardised components, concentrations and protocols.



Surgery for allergic rhinitis:

A role where maximal medical management has failed and in specific cases including:

- Significant adenoidal hypertrophy
- Turbinate hypertrophy
- Bilateral Concha Bullosa
- Refractory nasal polypsis

