Healthed The General Practice Education Day

House dust mite allergy, rhinitis and asthma.

Dr. David Heyworth-Smith
Clinical Immunologist and Allergist

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

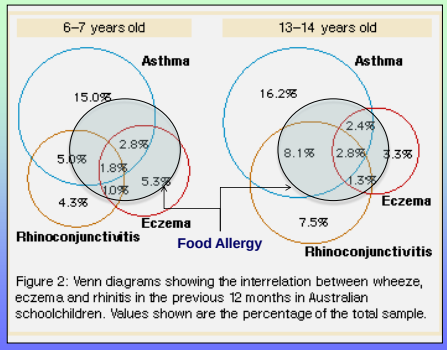
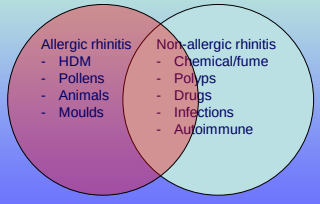


Figure 2: Venn diagrams showing the interrelation between wheeze, eczema and rhinitis in the previous 12 months in Australian schoolchildren. Values shown are the percentage of the total sample.

Colin F Robertson, Marita 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:

Intermittent
. < 4 days per week
. or < 4 weeks

Persistent
. ≥ 4 days per week
. and ≥ 4 weeks

Mild
normal sleep
& no impairment of daily activities, sport, leisure
& normal work and school
& no troublesome symptoms

Moderate-severe
one or more items
. 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 Snuffle 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
    - Cetirizine
    - Fexofenadine
    - etc

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

    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 AA[1–4]

Phase II EEC trial (Nolte)[1]	Phase III AR trial (Demoly)[2]	Phase III AA trial (Virchow)[3]
• **Population** HDM AR ± asthma in an EEC	• **Population** HDM AR ± asthma	• **Population** HDM AR + HDM AA
• **Primary endpoint outcome** Efficacy by 8 weeks and nasal symptoms (TNSS) reduced by 49% at 24 weeks (p<0.001 vs placebo)	• **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	• **Primary endpoint outcome** 34% reduced moderate or severe asthma exacerbation risk (p=0.017, vs placebo during the ICS withdrawal period)

AA - Allergic Asthma; AR - Allergic Rhinitis; EEC - Environmental Exposure Chamber; HDM - House Dust Mite; ICS - inhaled Corticosteroids; TNSS, total nasal symptom score.
References. 1. Nolte H et al. J Allergy Clin Immunol 2015; 135:1494–501 | 2. Demoly P et al. J Allergy Clin Immunol 2016; 137:444–51.
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 that 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.

SCIT	Aqueous Alum Allergoids	Holister Stier Stallergens ALK Inmunotek Western Allergy Sequirus
SLIT	Liquid Tablet	Allpyral, Alustal, Alutek, Clustoid, Staloral, Actair, Oralair, Acarizax Actair, etc.

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 polyposis