

Allergic rhinitis: Not a trivial disease

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INTRODUCTION

Allergic rhinitis is a significantly underestimated disease in terms of its impairment on quality of life and the consequences of undertreatment are not trivial.

Over the past 30 years there has been an exponential increase in the prevalence of allergic rhinitis, now present in between 17% and 28% of the South African population. In view of the close association between allergic rhinitis and asthma (over 70% of asthmatics have associated allergic rhinitis), an international initiative endorsed by the World Health Organization (WHO) has developed the Allergic Rhinitis and its Impact on Asthma (ARIA) document which provides international guidelines for evidence-based treatment of allergic rhinitis¹.

These guidelines have been endorsed by the South African Rhinitis Working Group of the Allergy Society of South Africa. Adoption of these guidelines will lead to effective and appropriate treatment of rhinitis and prevention of co-morbidity.

WHAT CONTRIBUTES TO THE INCREASING PREVALENCE OF RHINITIS?

Population studies indicate that the more "sophisticated" or Westernised people become, the more likely they are to develop allergies. The modern Westernised indoor environment with carpets and air-conditioning is conducive to close exposure to house dust mites, cockroaches and pet allergens. However, in addition

to exposure other factors play an influencing role on the expression of the diseases and not all individuals who are "sensitised" to the allergen express an allergy. It is possible that pollutants such as diesel exhaust fumes, contribute to the increasing prevalence of pollen induced allergic rhinitis.

Factors such as diet, nutrition, time of allergen exposure and concurrent exposure to other factors such as endotoxins at a young age appear to play modifying roles on the expression of allergic diseases such as rhinitis. It is also clear that the concurrent association of asthma with rhinitis is more common in younger people than in individuals over the age of 40.

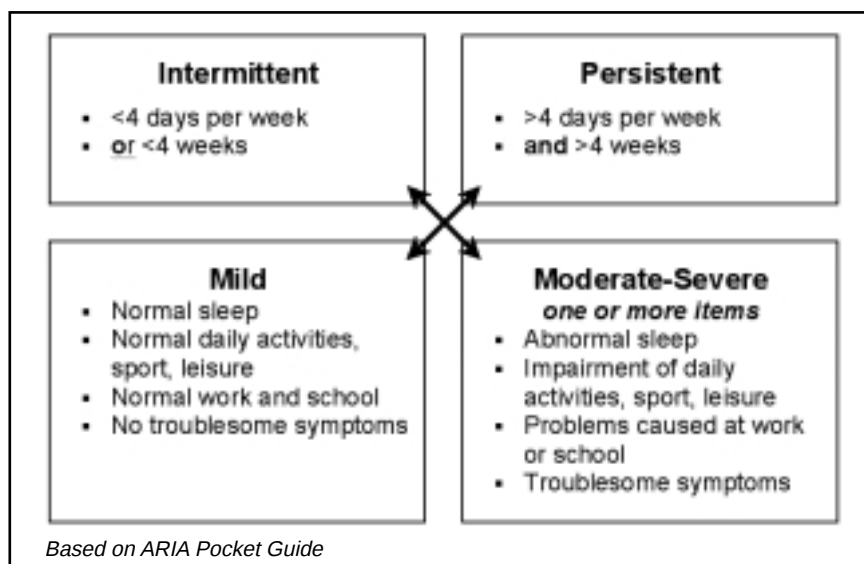
HOW DO WE CLASSIFY ALLERGIC RHINITIS? (Figure 1)

Previously allergic rhinitis was described as "seasonal" or "perennial", but the newly adopted classification of the WHO ARIA guidelines recommends a **new** classification. The term "seasonal" has been replaced by "intermittent" and "perennial" has been replaced by "persistent". This is in line with the internationally accepted GINA classification of asthma.

Thus, in South Africa patients who are house dust mite sensitive usually have "persistent rhinitis" as mites are found all year round, especially along the coast and in more humid areas of South Africa.

However, although "seasonal" or intermittent rhinitis is typically due

FIGURE 1: ARIA CLASSIFICATION OF ALLERGIC RHINITIS



to pollens (e.g. tree pollens and floral pollens) most of the grass pollenosis in South Africa results in **persistent** rhinitis, for 8-10 months of the year in the Gauteng, Northern and Mpumalanga provinces, and thus many such patients will require **chronic** treatment for their rhinitis. Thus the new classification has definite implications for patient management and reimbursement from their medical aids.

IMPORTANT CAUSES OF ALLERGIC RHINITIS

The most important causes of "seasonal" or "**intermittent**" rhinitis are the grass pollens:²

- Bermuda and Rye grass pollens account for more than 90% of pollen allergies.
- African grasses such as Kikuyu, Buffalo and Eragrostis are also important in about 40% of subjects.
- Tree pollens have a short allergy season. African Acacia species are allergenic but unusual causes of rhinitis. More common causes are the Oaks, Planes, Poplar and occasionally, Eucalyptus.
- Port Jackson and Jackaranda trees produce a lot of pollen but are not usually the cause of patient symptoms.
- Weed pollens are less important in South Africa.
- English plantain and Khakibos may cause symptoms.
- Maize (Zea Mays) pollen is important in farming areas.

The most important "perennial" allergens causing **persistent** rhinitis are the indoor allergens. These include:

- House dust mites: Three species cause disease in South Africa (Dermatophyoides pteronyssinus, Dermatophyoides farinae and Blomia Tropicalis).
- Storage mites (important in farm workers).
- Cats.
- Dogs.
- Moulds (Alternaria, Aspergillus, Cladosporium and Epicoccum).
- Latex (especially in health care workers).
- Occupational allergens (e.g. Bakers flour, alpha amylase, rodent urine, isocyanates).



EARLY ACQUISITION OF SENSITIVITY TO GRASS POLLENS

Although allergic rhinitis is typically a disease of adolescents and young adults, the acquisition of sensitivity to house dust mites often occurs in the first year of life, particularly in infants with atopic dermatitis. These infants have a 50% higher risk of developing rhinitis and asthma.

A recent survey by Dr. Marcelle Groenewald of children in the Pretoria area found that of 800 children attending an allergy clinic, up to 20% of the children were sensitised to grass pollen by the age of 3 and that by the age of 13, 90% of the children were sensitised to grass pollens.

ASSESSMENT OF ALLERGIC RHINITIS

A. A detailed history should address all of the following

- Family history.
- Seasonality of symptoms.
- Home environment (pets, cigarette smoking).
- Work environment (occupational allergen exposure, latex).
- Sporting activities.
- Location of residence (coastal, inland).

- Type of symptomatology (rhinorrhoea, sneezing, blocking, itching).
- Co-morbid symptoms (ears, sinuses).
- History of asthma (exercise induced, seasonal, night, cough).
- Response to therapy.
- Use of over-the-counter medicines (especially vasoconstrictor drops).

B. Examine the patient

- Atopic facies, Dennies lines, allergic salute.
- Examine the inferior turbinates by inspection (pallor, swelling mucus).
- Examine the palate and throat. Look for cobble stoning of the posterior pharyngeal wall.
- Chest examination.
- Conjunctival examination.
- Ear examination and hearing.
- Sinus examination and paranasal structures.
- Does the patient have asthma?

INVESTIGATION OF THE PATIENT WITH ALLERGIC RHINITIS

Identification of the specific allergen causing the patient's symptoms is the key to appropriate management

of the patient. Patients with "vasomotor rhinitis" will have negative allergy tests and often have a normal appearance of the lining of the nasal mucosa. For these patients allergen avoidance and antihistamines have no role to play in their management.

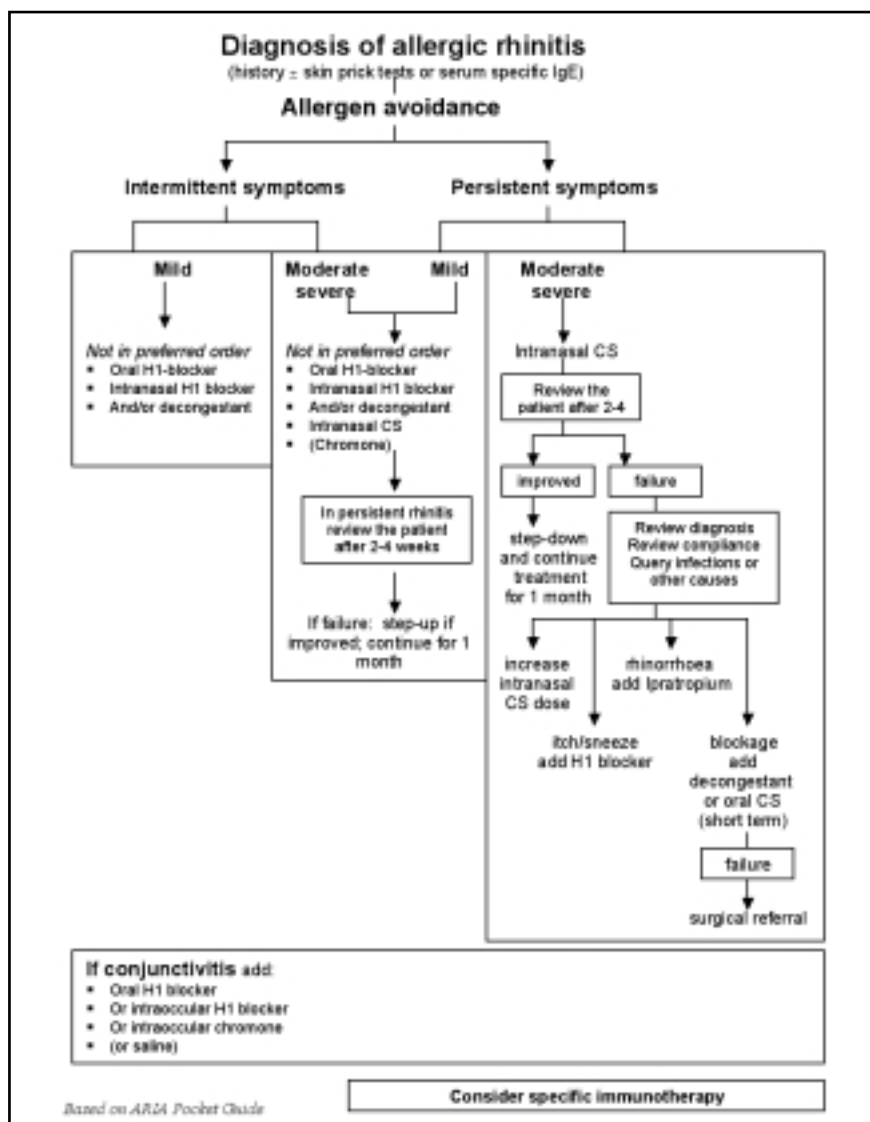
The most cost effective investigation would include a limited panel of skin prick tests (approximately 6-8 allergens) or RASTs based on the locality and the sort of environment the patient lives or works in. These should be "selected" based on the patient's individual history. Routine screens with large allergy test panels are not cost effective and often inappropriate.

A history of pet exposure, seasonality or variation in relation to work greatly assists selecting appropriate tests (e.g. flour, latex, pollens).

Without identification of specific allergen sensitivity, avoidance is not possible and neither is allergen immunotherapy. Without allergen immunotherapy it is not possible to modify the disease, prevent asthma or effect a cure of the rhinitis.

It is also useful to conduct a nasal smear, staining specifically for eosinophils using Hansels stain as part of the clinical work up for rhinitis, particularly when the history suggests an infective or vasomotor element. In infective rhinitis sheets of neutrophils are seen. In vasomotor rhinitis neither eosinophils nor neutrophils are seen. In allergic rhinitis clumps of eosinophils are seen.

FIGURE 2: TREAT IN A STEPWISE APPROACH (Adolescents and Adults)



TREATMENT PRINCIPLES (Figure 2)

A. General advice

- Avoidance of specific allergen exposure.
- Avoid non specific triggers (smoke, perfumes, sulphur dioxide).
- Explain to the patient that "histamine"-like symptoms need treatment with an antihistamine and that obstructive symptoms require intranasal steroids.
- Explain the dangers of the abuse of over-the-counter nasal sprays.

B. Oral antihistamines

- First line treatment for acute seasonal rhinitis symptoms (itching, sneezing, rhinorrhoea).
- Use on a daily or prn basis.
- Use non-sedating, quick acting preparations.

- It may have anti-inflammatory effects.
- Avoid older sedating antihistamines.

C. Topical intranasal steroids

- More important for perennial rhinitis and for severe seasonal exacerbations.
- Essential if nasal blocking/congestion is present.
- Correct technique is important.
- Used on a regular basis (not prn).
- Relatively free of side effects.
- Can be used for children as young as 3 years old.
- Will effectively prevent seasonal exacerbation of bronchial hyper-reactivity.

D. Decongestants

- Only use for short term (a few days).
- Use oral decongestants and

avoid intranasal sprays.

- Use if coryza is present.
- Resistance is an important problem.

E. Anti-cholinergics

- Ipratropium bromide is effective if rhinorrhoea is the major symptom particularly of the vasomotor variety of rhinitis.

F. Injected steroids

- To be avoided - these sometimes effect a quick symptom relief, but symptoms often rebound.
- They should be reserved for cases where all other measures have failed and should not be given more than twice in a year.
- Take care in patients with obesity, hypertension, diabetes and patients with mood disorders.

G. Immunotherapy

- Immunotherapy holds great promise as a curative treatment for allergic rhinitis.
- Immunotherapy provides excellent long-term prevention of symptoms caused by grass pollens and house dust mites.
- Immunotherapy given to young patients with allergic rhinitis reduces their risk for developing asthma in later life by about 50%.
- Patients who are monosensitive to grass pollens or house dust mites are excellent candidates for immunotherapy.
- Immunotherapy is cost effective in the long term and the only current treatment modality for rhinitis offering a cure.

H. Refer to specialist

If patients have atypical symptoms or evidence of co-morbid pathology or failure to respond, they should be referred to a specialist.

ALLERGEN AVOIDANCE

The importance of allergen avoidance is underestimated, although it is such a logical treatment modality. Allergen avoidance is dependent upon accurate diagnosis using skin prick tests and/or RASTs.

Avoidance of an indoor allergen such as a pet (by getting rid of the pet) can cure the patient of his symptoms. Avoidance of latex allergens by introducing a powder free environment in the work situation can dramatically reduce rhinitis symptoms in health care workers. Avoidance of house dust mites is a challenge but effective if one focuses on specific effective measures in the bedroom:

- Remove the carpets.
- Hot washing of bedding >60°C.
- Use mite impermeable pillow, mattress and duvet covers.
- Reduction of indoor humidity (close kitchen and bathroom doors, but open the windows so that humidity generated in these areas does not come into the bedrooms).
- Keep bedrooms well ventilated.
- Keep pets out of the house.

Avoidance of outdoor allergens is also possible in certain situations. Trees pollenate for short periods and it may be worthwhile taking a 2-3 week holiday away from home

when the tree in question pollinates. Keeping windows shut (in cars or homes) in the early morning and early evening when the pollen settles is also helpful. Staying in an air-conditioned environment may also avoid pollen exposure. It is also important to avoid mouldy places (e.g. compost heaps, forests, seaweed exposure) if the patient is mould sensitive.

RHINITIS AND ASTHMA

The recognition of the strong relationship between and the frequent co-existence of rhinitis with asthma is emphasised in the ARIA guidelines. The "link" between the two diseases is probably "allergen responsiveness", rather than the continuity of the nose with the chest airways.

In a very important recent study, Peters *et al.*³ used a market scan of 500 million claims to identify prescription drug data used for the treatment of allergic rhinitis and asthma in a detailed study of 4 944 subjects who had both rhinitis and asthma.

By comparing the months when an allergic rhinitis prescription was filled with the months when allergic

rhinitis was untreated, they determined asthma-related events (hospitalisation or emergency room visits within 31 days of allergic rhinitis medication) using incidence density ratio, IDR (using Poisson regression). The IDDR for the treated group was 0.49 ($p=0.001$) indicating that the risk for the development of severe asthma was **half** that of the untreated group.

This paper provided the strongest published evidence supporting the importance of treating rhinitis in asthmatics, both for the patient and for the funder.

THE ROLE OF IMMUNOTHERAPY

Immunotherapy is invariably a form of "combination therapy" combined with allergen avoidance and drug therapy.

Diagnosis of specific allergen sensitivity is essential prior to commencing immunotherapy. The ARIA guidelines reviewed 47 double blind placebo-controlled trials of subcutaneous immunotherapy (SIT) for patients with allergic rhinitis and 9 double blind placebo-controlled studies using sublingual immunotherapy (SLIT).¹ Based on level A



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evidence in the literature and considering the aero-allergens prevalent in South Africa, SIT is recommended for rhinitis patients with house dust mite allergy, grass pollen allergy and cat sensitivity.

SLIT has been shown to be extremely safe and has the added advantage that it can be taken at home away from the major centres. It would seem to be particularly useful in South Africa where there are very few allergy "specialists", for the treatment of house dust mite and grass pollen sensitive rhinitis patients.

MECHANISMS OF ACTION OF IMMUNOTHERAPY

SIT works by switching the cytokine profile of the T cells from TH2 type (interleukin 4, interleukin 5) to a TH1 type (gamma interferon) in the target organ. It is believed that interleukin 10 and interleukin 12 are also important in maintaining the state of tolerance.

The precise mechanisms of SLIT have not yet been elucidated. The total doses of allergen given by SLIT are 50-100 times greater than SIT.

It is believed that oral tolerance is important. Reduction of eosinophils in target organs and elevations in IgG₄ have also been observed during SIT. Other immunological observations during SLIT include a fall in ICAM-1 expression, decreases in IL13 and ECP and reductions in tryptase release in the nose.

IMMUNOTHERAPY ALTERS THE NATURAL COURSE OF ALLERGIC DISEASE

Immunotherapy is the only form of treatment that can alter the natural course of the disease. Long-term efficacy for grass pollen immunotherapy persists for at least three years after discontinuation of the injections. Immunotherapy given to young children prevents the development of new sensitivities and may also significantly reduce the probability of the subsequent development of asthma. Long-term studies have also shown that sublingual immunotherapy has a long-lasting effect, 4-5 years after discontinuation of treatment.⁶

CONSIDERATIONS PRIOR TO IMMUNOTHERAPY FOR RHINITIS:

1. Patients with allergic rhinitis due

to house dust mites, grass pollens or cats⁴ proven by IgE sensitivity to the allergen will benefit if chosen carefully.

2. Immunotherapy of monosensitive patients is more successful than polysensitised patients. "Monosensitive" means that they react to a group of similar allergens (e.g. the grasses or the house dust mite) and are not the patients who show up positive to a wide range of allergens tested.
3. Asthmatics who have seasonal asthma due to grass pollens, or mild to moderate asthma due to house dust mites or cats may also benefit if immunotherapy is given.
4. Specific allergen immunotherapy should be based on **allergen sensitisation** rather than a particular disease manifestation: i.e. it is indicated for monosensitive patients who have either or both asthma and rhinitis.
5. Subcutaneous immunotherapy (SIT) is well established in South Africa, but requires three years of injections. More recently sublingual immunotherapy (SLIT) has become available and is in many ways more applicable to

the South African situation. It is both effective and safe and can be given at home.

6. Patients with rhinitis, conjunctivitis and/or asthma due to grass pollen or mite allergy may receive SLIT⁵ in less specialised areas.
7. Rarely SIT immunotherapy may be given for monosensitivity to horse, dog or tree pollen allergies.
8. Patients with strong sensitivity to fungal allergens (moulds) do not currently do well on immunotherapy for rhinitis or asthma.

CONTRAINDICATIONS TO IMMUNOTHERAPY

1. Serious immunological or immunodeficiency diseases.
2. Malignancy.
3. Severe psychological disorders.
4. Treatment with beta blockers.
5. Poor compliance or unwillingness to continue for at least three years.
6. Severe asthma uncontrolled by pharmacotherapy, or a peak flow less than 80% of predicted values.
7. Cardiovascular disease.
8. Children under 3 years of age.



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RECOMMENDATIONS FOR SUBLINGUAL IMMUNOTHERAPY FOR RHINITIS

1. SLIT should be considered for certain patients who are sensitive to house dust mites or grass pollens in South Africa. In view of its excellent safety profile it may be administered at home and therefore many patients who live away from the major centres where subcutaneous therapy is given will be able to benefit from this form of therapy. It is cheaper than SIT as it involves far fewer doctor visits.
2. It is essential that prior to commencing SLIT, proper and intelligent allergy tests (RASTs or skin prick tests) should be conducted to confirm specific sensitivity. The clinician needs to evaluate (on the basis of the history) whether the symptoms are "year round" (due to mites), or mainly "seasonal" (occurring during the pollen season).
3. Contraindications include patients who have any other immune disease (e.g. immunodeficiency or auto-immunity), other serious medical conditions, or severe asthma. Children under the age of 3 should not receive SLIT until this group has been studied in more detail. Pregnancy is not a contraindication to continuing immunotherapy once it has been initiated.
4. For patients who are highly sensitive to grass pollens a dosage reduction in the maintenance dose may be required at the peak of the pollen season.
5. It is not advisable to commence grass pollen immunotherapy at the height of the grass pollen season (i.e. in spring in the Cape and summer in Gauteng).
6. At present SLIT is only available on a named patient basis in South Africa and a formal application to the MCC is required to use this therapy for each patient.
7. It is important that patients who are put on to SLIT programmes are followed up monthly for the first three months and then at three-monthly intervals. A diary card is useful to document any side effects.
8. Side effects which have been reported in patients receiving

SLIT from the numerous published studies,⁵ fall into the following groups:

- Lip, mouth and tongue irritation (these are by far the commonest).
 - Eye itching and other ocular symptoms.
 - Gastrointestinal symptoms.
 - Rhinitis.
 - Asthma.
 - Urticaria.
 - Angioedema.
9. SLIT should be given for at least three years and it is therefore important that patients should make a commitment to be compliant with medication for this extended period and that they check whether their medical aid schemes will cover the cost of the vaccines or the patients accept responsibility for these expenses themselves.
 10. Further studies are required to determine whether even longer term therapy is necessary.

MONITORING AND FOLLOW UP

1. It is essential that a detailed clinical profile of the patient is documented prior to commencement of immunotherapy. The patient's frequency and severity of symptoms, medication requirements, seasonality of symptoms and potential further exposure to the allergen in the immunisation vaccine must be assessed. Allergen avoidance should be implemented during immunotherapy.
2. It is useful if patients keep a diary of their allergy symptoms, which is returned at each follow up visit.
3. Laboratory monitoring of IgE and specific IgG levels is not informative or predictive of the outcome of immunotherapy for most allergies.
4. Reduction in the patient's usual anti-allergy or asthma medications can be expected since immunotherapy is cost effective. A knowledge of this encourages compliance and the success of this form of therapy.
5. Immunotherapy should be continued for at least three years for mites and grass pollens.

THE WAY FORWARD

Allergic rhinitis is an important

chronic disease resulting in high morbidity and impairment of quality of life. The direct costs to the health funders and the high indirect costs to society resulting from inappropriate treatment call for an evidence-based cost effective approach to the diagnosis and management of this condition. The ARIA guidelines, supported by WHO provide an evidence-based guide for cost effective management. A proper diagnosis is essential and facilitates allergen avoidance.

Recognition of the consequences of undertreatment of rhinitis is particularly important in those patients who have both rhinitis and asthma. Allergen immunotherapy is the only form of treatment for allergic rhinitis which can not only alter the natural history of the disease but prevent the development of asthma and new allergen sensitivities when given to young children with allergic rhinitis. Doctors should embrace this new form of therapy since it is evidence based.

Appropriate chronic medication will not only prevent asthma, sinus and ear infections, but impact significantly on quality of life and reduce the patient's medical expenses in the long run. ✎

See CPD Questionnaire, Page 47

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