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PEER REVIEWED FEATURE
2 CPD POINTS

A clinical approach to allergic rhinitis

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History is a critical aspect of the assessment process in allergic rhinitis, and provides a framework for interpreting investigations including serum specific IgE and skin test results. Management comprises allergen avoidance, symptomatic drug therapy and allergen-specific immunotherapy, the latter being an effective long-term treatment.

Key points

- **Allergic rhinitis is the most common allergic disease in Australia, has a significant morbidity and economic burden and is predicted to increase in prevalence by 70% in the next 35 years.**
- **It is often associated with other allergic diseases, including asthma.**
- **The results of serology or skin prick testing for allergen-specific IgE must be interpreted in the context of the history of allergic triggers.**
- **Symptomatic drug therapy is effective for many patients, especially those with mild to moderate symptoms, but does not alter the long-term course of the condition.**
- **Allergen-specific immunotherapy is an increasingly available, well-tolerated and extremely effective intervention for allergic rhinitis.**

For about one in five people in Australia, the external world can be an unpleasant and potentially dangerous place because of allergic disease. Already one of the most common chronic noncommunicable conditions in the world, allergic disease is predicted to increase in prevalence by approximately 70% in the next 35 years.[1]

Inadequately treated allergic disease creates a significant economic burden throughout the western world through absenteeism and reduced productivity as more than 75% of those with allergic disease are aged between 15 and 64 years. In Australia in 2007, the estimated financial cost to each patient with an allergy was nearly $2000 (direct and indirect costs).[1] Of the broad spectrum of allergic diseases, allergic rhinitis is the most common in this country, being about 50% more prevalent than asthma, the next most common allergic disorder.[1] Worldwide, between 10 and 30% of adults are affected by allergic rhinitis, and prevalence in Australia and New Zealand is among the highest reported.[2]

A significant contributor to morbidity and loss of productivity in patients with allergic rhinitis is sleep disturbance and fatigue, caused by both the condition itself and the side effects of pharmacotherapy, particularly with the older first-generation antihistamines.

The clinical features of allergic rhinitis have been described for many centuries, and in 1929 were summarised by Hansel as: 'The three cardinal symptoms in nasal reactions occurring in allergy are sneezing, nasal obstruction and mucous discharge'.[3] Additional clinical features of allergic rhinitis include itchy nose, itchy throat, itchy and watery eyes (allergic conjunctivitis), and postnasal drip.

By definition, allergic rhinitis is the symptomatic response to localised IgE-mediated inflammation triggered by exposure to an aeroallergen to which the individual is sensitised. Therefore, exposure to an aeroallergen is required. These aeroallergens may be present all year round (perennial; e.g. house dust mite, pets, moulds) or at certain times of the year (seasonal; e.g. pollens), or only in certain occupations (occupational; e.g. mice for laboratory workers, or chemicals).

It is important to be mindful that not all individuals with congestion and nasal discharge have allergic rhinitis. Nonallergic rhinitis is a significant subset of rhinitis, with about 50% of

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those with rhinitis symptoms having nonallergic rhinitis alone or both nonallergic rhinitis and allergic rhinitis.[4,5] Allergic disease, however, needs to be excluded prior to the diagnosis of nonallergic rhinitis. Irritants that trigger nonallergic rhinitis, such as cigarette smoke and perfume, may also exacerbate symptoms in allergic rhinitis, but this is not through allergic mechanisms. The different features of seasonal, perennial and nonallergic rhinitis are summarised in Table 1.

Typical first-line treatments for allergic rhinitis include intranasal corticosteroids and oral antihistamines. These generally provide symptom relief only, with no influence on the natural history of the condition. Allergen-specific immunotherapy has been used since early last century and is an increasingly available, effective and generally well-tolerated therapeutic intervention. It is the only option for long-term relief of symptoms and the reduction in progression of allergic disease in at-risk individuals.

Given the current trend of increasing allergic disease in the western world, and the increasing burden this represents for society, this article provides a simple clinical approach for primary care physicians for the investigation and contemporary management of patients with allergic rhinitis.

DIAGNOSIS

History is by far the most crucial element in the assessment of individuals with allergic rhinitis and diagnosis may be largely provided through a short set of questions. Although the identity of the culprit aeroallergen is often predicted before immunological testing is performed, it must always be confirmed through aeroallergen-specific testing (serum specific IgE or skin testing).

Points to consider when assessing patients are discussed below.

What are the patient's symptoms?

Rhinorrhoea, sneezing, itchy nose and watery and itchy eyes are suggestive of an allergic cause. If nasal blockage and postnasal drainage are more prominent, then nonallergic rhinitis should be considered in the differential diagnosis.

When do symptoms occur?

The timing of symptoms during the year is a crucial aspect of the history, as it provides information on possible seasonal allergens, especially grass, weed and tree pollens.

What triggers does the patient describe?

Specific questioning about symptoms on exposure to certain triggers can provide valuable information. For example, individuals with house dust mite allergy may notice that symptoms are exacerbated by vacuuming or dusting. If there are no readily identifiable aeroallergen triggers, nonallergic triggers should be considered, such as strong fragrances and changes in the weather. Food is not considered a typical trigger for allergic rhinitis, but it can be a trigger for nonallergic rhinitis.

What other medical problems does the patient have?

Allergic rhinitis commonly coexists with asthma, with about 80% of people with asthma having allergic rhinitis and about 25% of those with allergic rhinitis having asthma.[1] It is crucial that patients with both asthma and allergic rhinitis have their asthma well controlled before starting allergen-specific immunotherapy,

especially by the subcutaneous route of administration, as poorly controlled asthma increases the risk of severe systemic reactions during this therapy.

Nasal polyposis is particularly associated with nasal blockage and anosmia. Polyps are generally refractory to topical treatments and immunotherapy, and may require other interventions (including leukotriene receptor antagonists, oral corticosteroids and surgical intervention).

SEASONAL ALLERGIC RHINITIS

In Australia, the most clinically relevant seasonal allergens are grass pollens, particularly temperate grasses such as perennial ryegrass and timothy and subtropical grasses including Bermuda (couch) and bahia.[6] Pollens of some weeds (including plantain and Paterson's curse) and trees (including cypress, olive, silver birch and plane [usually London plane]) may also trigger allergic rhinitis in some individuals. Common native suspects such as wattle are less likely to be the cause of springtime hay fever.

Although all pollens are potentially allergenic, small wind-distributed pollens (such as those from grasses and some weeds and trees) are much more likely to cause allergic rhinitis, conjunctivitis and asthma. Pollens of brightly coloured flowers are typically larger in size and insect-borne, and are less likely to be clinically relevant. The fragrance from these brightly coloured flowers may, however, be a cause of irritation in nonallergic rhinitis.

Most clinically relevant allergenic grasses, weeds and trees within Australia and New Zealand are introduced species from the Northern Hemisphere. Due to significant geographical variability in climate, subtropical grasses have different pollination seasons across Australia. For example, Bermuda grass produces pollen in summer and early autumn in Victoria, but almost all year round in New South Wales and Queensland. Bahia grass shows similar variability between Victoria and Queensland. In addition, Victoria has higher grass pollen counts, with resultant higher allergic rhinitis prevalence, than many other regions of Australia because springtime northerly winds carry pollen from large tracts of grasslands north of its border. As global temperatures increase, it is anticipated that allergen seasons may become longer and subtropical grasses and weeds will become more important allergens in regions with temperate climates.[6,7]

The contribution made to allergic rhinitis by seasonal moulds (including *Cladosporium* and *Alternaria*) is not entirely clear, but they are recognised to trigger asthma in sensitised individuals.[3]

PERENNIAL ALLERGIC RHINITIS

The most common allergen for perennial allergic rhinitis is house dust mite; *Dermatophagoides pteronyssinus* is the most clinically relevant species in Australia and New Zealand.[8] Most house dust mite species require a relative humidity of over 50% to survive, and therefore there are significantly lower levels of dust mite in dry or high altitude environments.[3] The allergen is carried in mite faecal material and may become airborne with disturbance of contaminated soft furnishings such as mattresses, bedding, carpets and soft toys.

Domestic pets and moulds are other significant allergens. Cats and dogs are the most common causes of animal allergy in domestic households. The major sources of cat allergen are sebaceous, salivary and perianal glands, with the fur being an important reservoir. The major allergen of dogs is found in dog fur, but saliva, skin and urine are also clinically relevant allergen sources. Airborne transport of the allergen is common for both animals. Spores from indoor moulds may also be associated with allergic disease, and exposure is increased in humid, poorly ventilated and warm environments, especially bathrooms and kitchens.

CONFIRMING THE CLINICAL DIAGNOSIS

To confirm the presence of allergic rhinitis, sensitisation to relevant aeroallergens must be demonstrated. This may be shown by measuring IgE specific to suspected aeroallergens using serology or skin prick testing methods.

Serology

Serum allergen-specific IgE testing is easily requested by the general practitioner, and should always be considered as a first-line investigation prior to specialist referral. Most laboratories use the ImmunoCAP® or Immulite® systems, which measure the level of IgE in the serum forming a complex with specific individual allergens or mixes of allergens. Specific IgE testing was previously known as RAST (radioallergosorbant test) but RAST is an outdated method and the term is largely obsolete now.

The selection of specific IgE testing should be based on clinical history and trigger patterns. Testing for IgE to single allergens rather than mixes is of more clinical use when considering a patient for allergen-specific immunotherapy because greater information is then available when selecting appropriate allergens for the immunotherapy. A standard battery of serum specific IgE tests should be used with caution because there is a risk of misinterpretation as detectable specific IgE is simply an indication of sensitisation and not necessarily of clinical allergy. In addition, a negative specific IgE does not always rule out allergy as the test is less sensitive than skin prick testing and also a small proportion of patients may have local nasal reactivity to an allergen but not have detectable systemic sensitisation.[9] The interpretation of this test, therefore, should always be performed by an individual with experience in allergies and the clinical context taken into account.

The ordering of a total IgE should also be considered to help interpretation of results, as an extremely high level may increase the likelihood of false-positive specific IgE results. However, it remains unclear what level of total IgE is likely to be clinically significant.[10]

The current Medicare Benefit Schedule rebate for serum specific IgE testing covers the cost of three or four allergens (they differ in price) per test and testing up to four times a year. Patients may be out-of-pocket if more allergens or more frequent testing are ordered.

TABLE 1. PATTERNS OF RHINITIS

Feature	Seasonal allergic rhinitis	Perennial allergic rhinitis	Nonallergic rhinitis
Symptoms	Rhinorrhoea, sneezing, itchy nose, watery eyes, itchy eyes	Rhinorrhoea, sneezing, itchy nose, watery eyes, itchy eyes	Nasal blockage and postnasal drainage more prominent; conjunctival irritation uncommon
Other atopic disease	Common	Common	Less common
Age of onset	Most before 20 years	Most before 20 years	Over 20 years
Timing	Symptoms and medication requirement during affected seasons only Variable across Australia due to geographical variability of grass and tree pollens. Some subtropical grasses cause symptoms only in summer in southern states but during other times of the year as well in more northern states (e.g. Bermuda grass)	Typically have symptoms and medication requirement throughout the year Patients allergic to house dust mite may complain of worsening symptoms during winter because of longer periods indoors	Perennial Can coexist with allergic rhinitis
Triggers	Grass cutting, windy weather, walking out of the house, walking through parks, gardening	Vacuuming, dry dusting, pet exposure, opening old cupboards	No readily identifiable aeroallergens Respiratory irritants: cigarette smoking, strong scent, fragrances Weather changes: temperature, humidity Other triggers include spicy foods, medications, infections
Likely allergens	Grass, weed and tree pollens	House dust mite, cats, dogs, other animals, moulds	None

Skin prick testing

Sensitisation to aeroallergens can also be demonstrated by skin prick testing. Skin prick testing is a very sensitive, rapid and robust assessment for allergic disease. It is, however, highly operator-dependent and requires experience in the interpretation and performance and as a result is not typically available outside specialist clinics. Additionally, skin prick testing can be rendered uninterpretable by common medications used to treat allergic rhinitis, including oral antihistamines.

MANAGEMENT

The management of allergic rhinitis can be divided into three stages:

- allergen avoidance
- pharmacotherapy (symptomatic drug therapy)
- allergen-specific immunotherapy.

Allergen avoidance

Options for allergen avoidance are relatively limited, and may be of limited benefit for certain allergens. General measures to consider around the house include:

- vacuum carpets weekly but be mindful that this can temporarily increase the allergen load in the air
- clean soft furnishings (e.g. curtains) regularly
- consider replacing carpets and curtains with hard floor surfaces and blinds.

HEPA (high-efficiency particulate air) filters in vacuum cleaners may help reduce the allergen load but there is no evidence to support their use in air filtration systems.

House dust mites are particularly difficult to eradicate but some options to consider, together with the above suggestions, include:

- wash bedding in hot water, above 55°C if possible; if unable to wash in hot water, then tumble dry for 20 minutes
- consider using house dust mite impermeable covers, with a pore size of less than 6 µm, on mattresses, bed covers and pillows
- reduce humidity by improving ventilation.

For people with clearly defined animal allergy, avoidance of that animal needs to be considered. If symptoms are mild, removal of the pet from the bedroom may suffice; in severe cases, complete avoidance may be required. Response can be delayed as the major cat allergen may be carried on clothing and remain in the environment for weeks to months after removal of the animal.[3] Unfortunately, there is little evidence that truly 'hypoallergenic' cat or dog breeds exist, and selection of particular breeds is therefore unlikely to meaningfully contribute to allergy control.[11]

Pharmacotherapy

The many safe and easily obtainable systemic and topical agents for the

TABLE 2. SYMPTOMATIC DRUG THERAPY FOR MILD TO MODERATE ALLERGIC RHINITIS

Drug class	Comments
Recommended therapies	
Intranasal corticosteroids	Strongly recommended for both seasonal and perennial allergic rhinitis in adults and children:[3] • more effective than oral antihistamines • safe to use in children • low systemic absorption Improves ocular symptoms as well as nasal symptoms Up to 20% minor epistaxis, but technique may contribute Maximum effect may take up to two weeks[12]
Oral antihistamines (OAHs)	Second-generation OAHs, including cetirizine, loratadine, levocetirizine, desloratadine and fexofenadine, are recommended as they do not cross the blood–brain barrier and therefore have minimal CNS effects such as sedation[12] Can be taken daily and with other medications, including intranasal corticosteroids
Oral leukotriene receptor antagonists	Montelukast is the only agent available in Australia May provide some benefit in seasonal allergic rhinitis, but not better than OAHs[12] Benefit similar to second-generation OAHs Beneficial if coexistent asthma Limited efficacy in perennial allergic rhinitis, especially in adults
Intranasal antihistamines	Azelastine effective in seasonal allergic rhinitis Taste may be bitter Fluticasone/azelastine combination nasal spray may be of benefit and improve compliance with therapy
May be of some benefit	
Intranasal anticholinergics	Ipratropium bromide provides symptomatic relief of rhinorrhoea in perennial allergic rhinitis Little influence on congestion, itching, sneezing or ocular symptoms
Intranasal cromones	Sodium cromoglycate can be beneficial Very well tolerated Not as effective for symptom relief as intranasal antihistamines
Nasal saline	Nasal rinse or spray may be beneficial[13,14] Well tolerated
Intraocular antihistamines	Generally well tolerated, and effective for ocular symptoms, but uncertain if provide additional benefit to intranasal corticosteroids[12]
Intraocular cromones	Generally well tolerated, and effective for ocular symptoms, but uncertain if provide additional benefits to intranasal corticosteroids[12]
Use with caution	
Oral corticosteroids	Can be considered if other measures fail, but only as a short course[12]
Oral decongestants	Includes phenylephrine and pseudoephedrine Relieve symptoms of nasal obstruction Little effect on pruritus, sneezing, rhinorrhoea or ocular symptoms Extensive side effect profile and should be used in caution in patients with heart disease or hypertension Not to be used in children under 2 years of age and only with caution in those aged 2 to 12 years
Intranasal decongestants	Includes oxymetazoline, xylometazoline Courses of less than five days duration recommended, due to risk of side effects
Not recommended	
Intramuscular corticosteroids	Should not be used due to prolonged effect and significant risk of side effects[12]

symptomatic treatment of mild to moderate allergic rhinitis are listed in Table 2.[3,12-14]

Allergen-specific immunotherapy

Allergen-specific immunotherapy is an effective and well-established treatment for patients with moderate to severe allergic rhinitis, coexisting allergic disease (including asthma) or no response to symptomatic drug therapy. It works by shifting an individual's immunological response from an allergic to a nonallergic phenotype via the induction of regulatory T-cells. This is achieved by an increasing and then constant exposure to an allergen source, which continues for three to five years. The therapy can significantly attenuate symptoms for an extended period in some individuals, and reduce requirements for pharmacological therapy. Despite a clinical response to immunotherapy, this does not translate to a drop in total or specific IgE levels or a change in skin test results; there is, therefore, no role for repeat testing to assess response to the therapy.

Subcutaneous immunotherapy (SCIT) has been the backbone of therapy for allergic rhinitis since it was first administered to treat grass pollen allergy over a century ago. In recent years however, and over the past 20 years in Europe, the sublingual route (SLIT), with either drops or tablets, has been increasingly used. Available allergens for SCIT include house dust mite, grass, tree and weed pollens, cat and dog danders, moulds and others, and the number available for SLIT is increasing (house dust mite, animal dander and grass pollens are now available within Australia). Both routes of administration demonstrate significant benefits on nasal, eye and respiratory symptoms, a reduction in medication use and also an improvement in quality of life when compared with placebo. Although there is emerging data that SCIT may be slightly more effective than SLIT, this difference appears to be modest.[15-17] In addition to significant symptom improvement, allergen-specific immunotherapy is the only known therapy to reduce both progression from allergic rhinitis to asthma and the development of further allergies.[18] Both SCIT and SLIT should only be initiated after full specialist assessment.

The risk of systemic reactions with SCIT is low, at less than 1% of patients.[16] However, individuals with uncontrolled asthma are at greatest risk of systemic adverse events, and therefore need to be carefully assessed. The small risk of anaphylaxis in these patients requires that they be observed in the clinic for at least 30 minutes after every injection, and the injections must only be provided in a facility with the capacity to treat anaphylaxis.

SCIT can also be logistically troublesome, as patients are required to visit their general practitioner or allergy specialist on a monthly basis for injections for at least three years in order to complete the course of therapy. As a result of this inconvenience, and the frequency of adverse reactions to SCIT, SLIT is increasing in popularity. Although it is recommended that administration by the patient of the first dose of SLIT be observed by the prescribing clinician, further doses are managed by

the patient at home, thus providing greater flexibility and freedom.

Adverse reactions do occur in SLIT but the majority of these are mild, with up to 75% of patients experiencing local reactions of the oral mucosa or gastrointestinal symptoms, most often during the up-dosing phase of therapy (the first few days).[15] Systemic reactions are extremely uncommon, occurring in less than one in 1000 doses administered (less than 0.1%), and most of these are relatively minor cutaneous or upper respiratory symptoms.[15,18] There is also evidence of greater frequency of adverse reactions with higher doses of SCIT and SLIT.

Even though SLIT is well tolerated and accepted by patients, compliance with allergen-specific immunotherapy remains relatively poor. Persistence with this immunotherapy is variable, with reported compliance rates over a three-year course of therapy ranging from 10 to 80% for SLIT and 13 to 89% for SCIT.[15,19,20] Noncompliance with SCIT is reported to be largely due to inconvenience and side effects, whereas for SLIT cessation of therapy is more likely to result from laxity of self-administration and the therapy's significantly greater short-term comparative cost. Neither of these interventions are subsidised through the Pharmaceutical Benefits Scheme, and SLIT can cost in the order of several thousands of dollars for a full three-year treatment course. There is, however, evidence that allergen-specific immunotherapy provides significant cost savings in the long term compared with symptomatic drug therapy.[21]

It is anticipated that the options for allergen-specific immunotherapy will increase in coming years, with a greater range of allergens, better safety and tolerance profiles and more options for the route of delivery. Nasal, epicutaneous and intralymphatic routes of administration are under investigation.[22]

MANAGEMENT OF ALLERGIC RHINITIS IN PREGNANCY

As the prevalence of allergic rhinitis is at its peak during adult years, it is likely that general practitioners will need to deal with its management during pregnancy. In addition to allergic rhinitis, nonallergic rhinitis driven by hormonal changes may exacerbate nasal congestion in about one in five women at any stage of gestation.[2]

As with any therapy, the clinician must be mindful of the potential risks of allergen-specific immunotherapy during pregnancy. There is a small risk of systemic allergic reaction, as previously mentioned, and because this places the foetus at risk it is not recommended that allergen-specific immunotherapy for allergic rhinitis be started during pregnancy. If, however, pregnancy occurs while the patient is stable on the maintenance phase of allergen-specific immunotherapy then continuation of therapy can be considered.[18]

CONCLUSIONS

Allergic rhinitis is one of the most common upper respiratory allergy conditions encountered by primary care physicians, and is increasing in prevalence. History is a critical aspect of the assessment process and provides the framework in which to interpret specific investigations, including specific IgE or skin test results. Intranasal corticosteroids and oral antihistamines are effective and safe treatments for mild to moderate allergic rhinitis. Referral to an appropriate specialist for assessment for allergen-specific immunotherapy should be considered in all patients with moderate to severe allergic rhinitis, coexisting allergic disease (including asthma) or no response to symptomatic drug therapy.

Allergen-specific immunotherapy is an excellent and increasingly available option for the longer-term management of allergic rhinitis, and provides the only means of preventing the development of further allergies in susceptible individuals. This therapy should be monitored closely, given the small but reported risk of systemic reactions, especially in those with poorly controlled asthma. SLIT is an increasingly available and effective option for allergen-specific immunotherapy, and is better tolerated than SCIT and provides greater freedom for the patient.

It is recommended that allergen-specific immunotherapy only be prescribed after careful assessment by a medical practitioner experienced in the investigation and management of allergy, to ensure that the correct therapy is selected based on the patient's history, allergen sensitisation profile and also coexisting allergic and other diseases. In addition, the practitioner must be well versed in the management of adverse events associated with pharmacological therapy and allergen-specific immunotherapy, to ensure the optimal outcome is achieved. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

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