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Alleviating allergic rhinoconjunctivitis
A task for all seasons

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Key points

- Allergic rhinoconjunctivitis is common and needs to be distinguished from nonallergic rhinitis.
- The allergen profile in Australia is different from that overseas.
- Regular intranasal corticosteroids are safe and effective if used correctly.
- Immunotherapy is highly efficacious but not a cure.
- Control of allergic rhinoconjunctivitis improves asthma control.
- Sublingual immunotherapy is as effective as subcutaneous immunotherapy.

Allergic rhinoconjunctivitis is common, impacts significantly on the quality of life of the sufferer and is responsible for an enormous economic burden. Symptoms may occur all year round or seasonally, or have seasonal flares depending on the allergen causing the symptoms.

Although allergic rhinoconjunctivitis is often regarded as trivial, it has a significant impact on quality of life and can impair cognitive function and development. It affects up to one in six Australians and is responsible for an enormous economic burden through loss of productivity. The characteristic nasal symptoms of sneezing, nasal congestion, itch, discharge and pressure are often associated with eye symptoms – redness, itch and tearing. It is important to distinguish allergic rhinitis from nonallergic rhinitis, which causes less itch and sneezing and may have different triggers.

CAUSES

Allergic rhinoconjunctivitis is caused by an immune response to airborne allergens to which an individual has been sensitised. Symptoms may be seasonal or perennial depending on the specific allergens involved. The profile of allergens most likely to be responsible for allergic rhinoconjunctivitis differs in Australia from that overseas, with a greater burden of house dust mite (*Dermatophagoides pteronyssinus*) and subtropical grasses. In fact, house dust mite, specifically the proteins released from dust mite faeces, is the most important contributor to perennial allergic rhinoconjunctivitis in Australia.

Sensitisation to airborne grass pollen contributes to the classic seasonal 'hayfever' symptoms over spring. Grasses responsible in Australia include perennial ryegrass and, in northern regions, subtropical grasses such as couch (also known as Bermuda grass) and paspalum (also known as Bahia grass).[1] These grasses produce pollen between October and December, with the period varying slightly year to year and geographically around Australia.

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Other potential contributors to allergic rhinoconjunctivitis include the pollen of certain weeds, such as plantain, which flowers from August to May, and trees such as casuarina (Australian bush oak/pine), which may cause symptoms for longer periods of the year. In contrast, wattle generally does not cause allergic rhinoconjunctivitis as its pollen grains are comparatively large and do not usually become airborne.

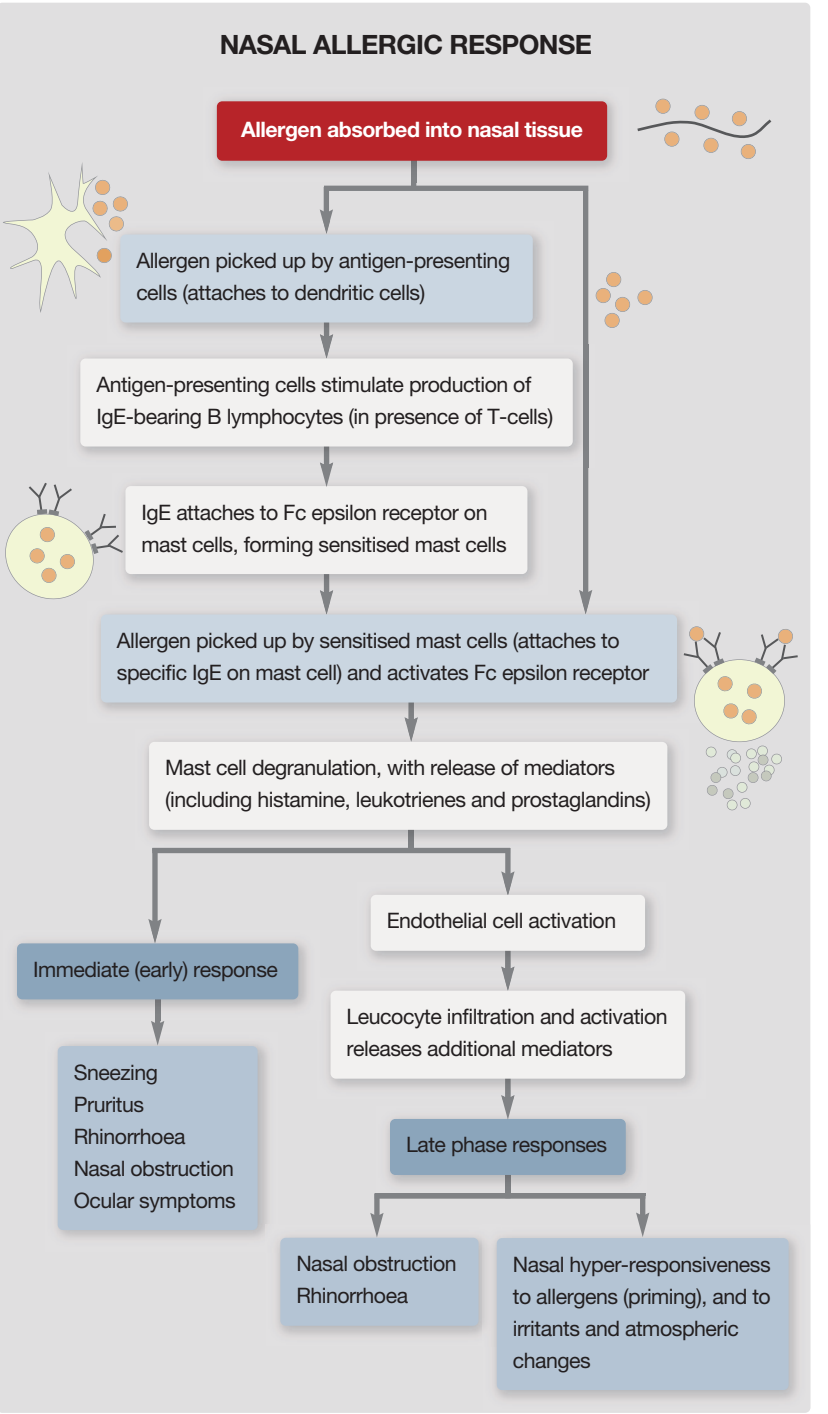
Moulds such as *Alternaria, Penicillium* and *Cladosporium* are another potential contributor to allergic rhinoconjunctivitis. The symptoms may be associated with a change in rainfall, but usually there is no clearly identifiable pattern. Pet dander can also contribute, with cats a more common cause than dogs. The cat allergen responsible is secreted by their sebaceous glands and attached to their hairs. Cat allergen can persist in housing for up to six months after the cat has been removed.[2]

PATHOGENESIS

In a genetically predisposed individual, exposure to an allergen results in production of allergen-specific IgE. Individuals with atopy are more likely to become sensitised. Further exposure to the allergen then elicits an inflammatory response. This involves IgE binding to the allergen and activating receptors (Fc epsilon receptor 1) on mast cells and basophils. This in turn leads to the release of mediators, including histamine, leukotrienes, prostaglandins, tryptase and other chemokines and cytokines, which cause the symptoms of allergic rhinoconjunctivitis (see the flowchart on this page).

The early phase response presents with sneezing, itching, rhinorrhoea, nasal congestion and ocular symptoms. A late phase response, with similar symptoms, occurs four to six hours after the initial exposure as a result of recruitment of basophils, eosinophils and polymorphonuclear leucocytes. If there is persistent allergen exposure then the late phase inflammatory response may result in chronic symptoms.

This IgE-mediated response is the hallmark of allergic rhinoconjunctivitis and results in inflammation of the nasal mucosa and nasal airway hyper-reactivity.



SYMPTOMS AND DIAGNOSIS

The diagnosis of allergic rhinoconjunctivitis can be made clinically, and sensitisation confirmed by either skin prick testing or allergen-specific IgE testing. The classic nasal

ALLERGEN MIXES USED FOR IN VITRO SPECIFIC IGE TESTS*

Dust mite
Dermatophagoides pteronyssinus, Dermatophagoides farinae, cockroach

Animal dander
Cat, dog, horse, cow

Mould
Alternaria, Aspergillus, Cladosporium, Penicillium

Pollen
Perennial ryegrass, Bahia (paspalum), plantain, ragweed, goosefoot

Grass
Bermuda (couch), Timothy, perennial ryegrass, meadow, Johnson, Bahia (paspalum)

Weed
Ragweed, mugwort, plantain, goosefoot, saltwort

Tree
Olive, willow, white pine, acacia, eucalyptus, melaleuca

* Precise mixes may vary between laboratories.

symptoms of sneezing and congestion, itch, discharge and pressure are commonly associated with conjunctivitis, which manifests with redness, tearing and itchy eyes. 'Atopic shiners' are a darkening of the skin under the eyes caused by congestion.

Patients with allergic rhinoconjunctivitis may also present with poor sleep, difficulty concentrating, malaise and even anxiety disorders if the underlying allergic rhinoconjunctivitis is not diagnosed and managed.[3,4] Patients may have concomitant symptoms of asthma; it is estimated that 40% of people with allergic rhinoconjunctivitis also have asthma, while some 30 to 80% of people with asthma have allergic rhinoconjunctivitis.[5]

It is important to distinguish allergic rhinoconjunctivitis from nonallergic rhinoconjunctivitis as management is different. The absence of nasal itch and sneezing suggests nonallergic rhinitis. Symptoms aggravated by irritant triggers, such as perfumes, flowers, smoke, windy days and alcohol, particularly red wine, also suggest nonallergic nasal airway reactivity. However, patients may have components of both allergic and nonallergic rhinitis contributing to their symptoms.

Determining whether symptoms are perennial or seasonal may help identify the main allergen contributing to allergic rhinoconjunctivitis, but seasonal flares of perennial rhinoconjunctivitis can make it difficult to distinguish from the seasonal form. Recent allergy guidelines recommend classifying allergic rhinoconjunctivitis as episodic or persistent (more than four days per week for four weeks or more), and further as mild, moderate or severe (impairing activities of daily living).[6]

In vitro specific IgE tests

A test that is generally available to GPs is in vitro testing for specific IgE against allergens such as dust mite and animal dander. Radioallergosorbent testing (RAST) is no longer routinely performed, superseded by ELISA (enzyme linked immunoassay).

Under current funding arrangements in Australia, only four specific IgE tests are reimbursable on one blood collection, and thus laboratories provide testing against mixes of similar allergens (see the box on this page, top left). If a specific allergen is required then it must be specified (e.g. cat in an animal dander mix). In vitro specific IgE testing is not influenced by medications or skin disease and, unlike skin prick testing, does not require specific expertise, but can be more expensive.

Skin prick testing

Skin prick testing is the preferred method of testing but is not readily available or accessible. Performance of these tests by untrained personnel without appropriate selection of allergens may lead to misleading results. All skin prick tests should be performed with positive and negative controls. Some GPs have been trained to perform skin prick tests and, if performed and interpreted correctly, skin prick testing has high sensitivity and provides immediate results. Recent use of antihistamine (up to 72 hours before the test) may cause false negative results in skin prick testing.

Correct identification of the allergen(s) responsible for symptoms is a prerequisite for prescribing immunotherapy (desensitisation). The use of in vitro specific IgE and skin prick testing assists in the diagnosis, but should not be used without appropriate clinical correlation.

MANAGEMENT OF ALLERGIC RHINOCONJUNCTIVITIS

Allergen avoidance

Pharmocotherapy
- First line monotherapy
  - Intranasal corticosteroids (see Table 2)
- Oral antihistamines (add on, or first line for mild symptoms)
  - Fexofenadine
  - Cetirizine or levocetirizine
  - Loratadine or desloratadine
- Intranasal antihistamine
  - Azelastine
  - Levocabastine
- Leukotriene receptor antagonists (add on therapy only)
  - Montelukast
- Topical decongestants (add on therapy for less than five days only)
- Normal saline irrigation

Immunotherapy
- Sublingual
- Subcutaneous

TABLE 1. PHARMACOLOGICAL ACTIONS OF DRUGS USED IN ALLERGIC RHINOCONJUNCTIVITIS[7]

	Antihistamines		Leukotriene antagonists	Corticosteroids (nasal)	Decongestants		Ipratropium (nasal)	Cromones (nasal)*
	Oral	Nasal			Oral	Nasal		
Action on symptoms								
Rhinorrhoea	++	++	++	+++	0	0	+++	+
Congestion	+	+	+	+++	++	++++	0	+
Sneezing	++	++	++	+++	0	0	0	+
Pruritus	++	++	+	+++	0	0	0	+
Ocular symptoms	++	0	++	++	0	0	0	0
Onset of action	1 h	15 min	48 h	12 h	1 h	5 to 15 min	15 to 30 min	–
Duration	12 to 24 h	6 to 12 h	24 h	12 to 48 h	12 to 24 h	3 to 6 h	4 to 12 h	2 to 6 h

* For example, sodium cromoglycate.

MANAGEMENT

Management involves avoidance of allergens where possible (e.g. cat allergy), combined with appropriate pharmacological treatment (see the box on page 46, right, and Tables 1 and 2).[7]

Allergen avoidance

House dust mite avoidance appears logical if affordable and practicable for patients who are sensitised to dust mite allergen. A meta-analysis investigating the use of impermeable bedding covers and removal of carpets found that these measures reduced but did not completely eliminate symptoms.[8]

Anecdotally, symptoms appear to improve in drier, arid environments and during overseas travel if dust mite is the major allergen responsible.

Intranasal corticosteroids

First-line management of allergic rhinoconjunctivitis involves daily use of appropriate intranasal corticosteroids. Their mechanisms of action are outlined in the box on page 49. It is important to emphasise to patients that these medications are management measures and not curative. The choice of intranasal corticosteroid depends on cost, tolerability and the patient's age (Table 2).

Corticosteroid sprays may occasionally cause irritating effects, such as nose bleeds in up to 10% of patients, and the extremely rare septal perforation. However, studies have shown no evidence of mucosal damage after up to five years of use. As a precaution, the intranasal spray should be directed away from the septum (Figure).[9]

There has also been concern about the potential effect of intranasal corticosteroids on growth in children and on the hypothalamic–pituitary axis. Systemic absorption is undetectable for third generation intranasal corticosteroids such as mometasone and less than 1% for fluticasone furoate.[10] Nevertheless, these medications should be used at the lowest dose and preferably given before sleep, as nasal mucosal inflammation is greatest at night.[11]

For patients with concomitant allergic conjunctivitis (up to 70% of those with allergic rhinitis), the use of intranasal corticosteroids alone may reduce eye symptoms.[12] Proposed mechanisms are

TABLE 2. INTRANASAL CORTICOSTEROIDS USED FOR ALLERGIC RHINOCONJUNCTIVITIS

Medication	Comments	Age group
Beclomethasone	Needs twice daily dosing, cheaper	>3 years
Budesonide	Category A	>6 years
Ciclesonide	No benzalkonium chloride preservative – taste and smell free	>6 years
Fluticasone furoate	<1% systemic absorption	>2 years
Fluticasone propionate	Cheaper	>12 years
Mometasone	Undetectable systemic absorption	>3 years
Triamcinolone	Cheaper	>12 years

MECHANISMS OF ACTION OF INTRANASAL CORTICOSTEROIDS

Intranasal corticosteroids reduce symptoms and exacerbations by the following mechanisms:

- Reducing mucosal inflammation, which reduces late phase reactions, priming and nasal hyper-responsiveness
- Reducing mucosal mast cells, which reduces acute allergic reactions
- Suppressing glandular activity and vascular leakage
- Inducing vasoconstriction

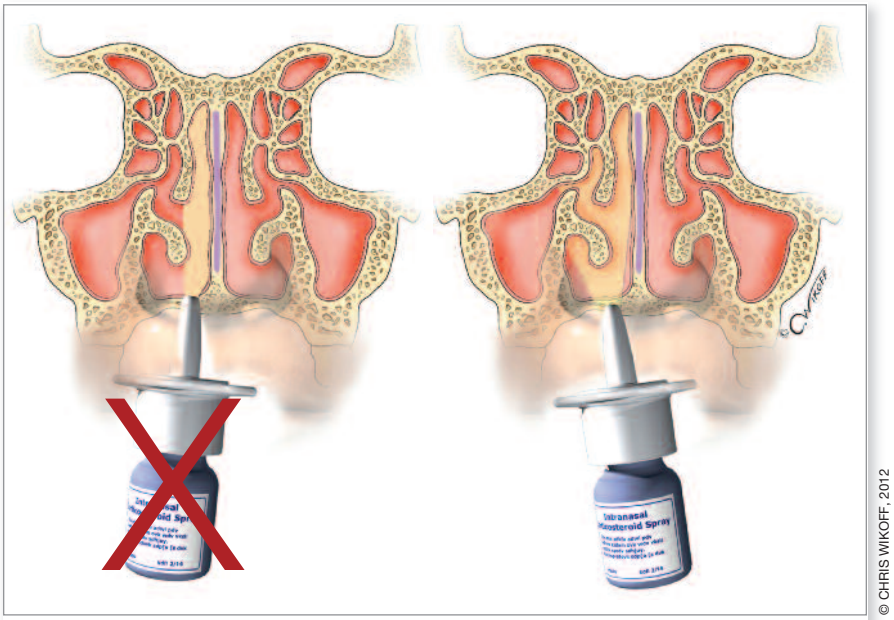


Figure. Correct administration of a nasal spray. a (left). Incorrect technique, with the nozzle pointing towards the nasal septum. b (right). Correct technique, with the nozzle held just inside the nose and directed laterally towards the outside wall. This optimises exposure of the mucosa overlying the inferior turbinate.

via the neural ocular reflex and retrograde movement of corticosteroids along the nasal lacrimal duct.[13] These patients may also benefit from the addition of antihistamine eye drops to the intranasal corticosteroids. Oral antihistamines may cause more ocular drying than topical antihistamines.[14]

Decongestants

The use of decongestants for short periods (up to five days) may relieve congestion and allow intranasal corticosteroids to be used effectively – an obstructed nasal passage is a common reason for corticosteroids to be ineffective. A few days of decongestant immediately before use of the corticosteroid spray will allow it to act on the inflamed nasal mucosa. However, intranasal decongestants should be used infrequently and only for short periods, as regular use may lead to rebound phenomena and rhinitis medicamentosa.[15]

Antihistamines

Oral antihistamines may be used for mild symptoms of allergic rhinoconjunctivitis or in addition to intranasal corticosteroids for more severe symptoms. Second generation (e.g. cetirizine, loratadine) or third generation (levocetirizine, desloratadine, fexofenadine) antihistamines should be used, as the central nervous system side effects of somnolence and drowsiness are minimised. Antihistamines are inferior to intranasal corticosteroids and should be a second option.[16]

Intranasal antihistamines such as azelastine or levocabastine may be used for rapid onset of action, but the preference in both guidelines and clinical experience is for intranasal corticosteroids.[6] Azelastine may leave a bitter taste in the mouth and if inadvertently swallowed may be sedating. A combination antihistamine and corticosteroid spray is in development.

Cromoglycate (a cromone)

Intranasal sodium cromoglycate (a mast cell stabiliser) is safe but less efficacious than other available treatment and must be used up to four times per day.[6]

Leukotriene receptor antagonists

Leukotriene receptor antagonists such as montelukast are an option for patients who cannot tolerate intranasal corticosteroids but may also be used in addition to corticosteroids. They may be trialled in patients with difficult to control rhinitis, particularly those with concomitant asthma. Montelukast is expensive and thus a trial for a month may be reasonable to determine efficacy.

Specific situations

In young children with allergic rhinoconjunctivitis, nonsedating antihistamines such as cetirizine may be used. However, intranasal corticosteroids such as mometasone are indicated in children older than two years with persistent allergic rhinoconjunctivitis symptoms.

Pregnant women may use budesonide nasal corticosteroid sprays as budesonide in these preparations is a category A

drug – a drug used by large numbers of women without any proven harm to a fetus. Other intranasal corticosteroid sprays are category B drugs – drugs that have been used safely in a limited number of women of childbearing age with no harm to the fetus. Sodium cromoglycate nasal spray is category A, and second generation antihistamines such as cetirizine and loratadine are category B drugs.

Optimising the management of allergic rhinitis in those with concomitant asthma may help control asthma flares.

Immunotherapy

Immunotherapy should be considered in patients with allergic rhinoconjunctivitis when allergen avoidance and medications are inadequate in controlling symptoms or when side effects are intolerable. It should also be considered in those who wish to minimise long-term pharmacological therapy.

Immunotherapy is highly efficacious in children and may also reduce their risk of developing asthma (the 'atopic march') by about half.[17-19]

Options are sublingual immunotherapy (in tablet or drop form) and subcutaneous immunotherapy, which is ideally begun and supervised by a trained allergist or immunologist who is experienced with its initiation and management. Sublingual immunotherapy at appropriate doses has a sound scientific basis and should not be confused with naturopathy or homeopathy. Immunotherapy usually takes two to three years and provides benefits for up to three years or more, depending on the individual patient.

Sublingual immunotherapy has the advantage of being able to be administered at home but the disadvantage of greater cost – about double that of subcutaneous immunotherapy. Sublingual immunotherapy also has a better safety profile, but common local effects include tingling and gastrointestinal discomfort.

REFERRAL

Patients should generally undergo a trial of intranasal corticosteroids for a course of usually six to eight weeks before referral to an immunologist or allergist. They should be referred if immunotherapy is considered or there are significant residual symptoms after pharmacotherapy.

Other indications for referral include coexisting asthma or nasal polyposis, and complications such as otitis media or recurrent sinusitis. Patients who require oral corticosteroids to control symptoms, those who have intolerable side effects that affect work or school, and where management might be enhanced by identification of further triggers should also be referred.

RESOURCES

Reliable resources on allergic rhinoconjunctivitis are available at the websites of the Australasian Society of Clinical Immunology and Allergy (ASCIA; http://www.allergy.org.au) and the World Allergy Organization Global Resources in Allergy (http://www.worldallergy.org).

CONCLUSION

Allergic rhinoconjunctivitis is a common condition that impacts significantly on the quality of life of the sufferer and is responsible for an enormous economic burden. Symptoms can occur all year round or seasonally, or have seasonal flares, depending on the allergen/s causing the symptoms. It is important to differentiate allergic from nonallergic rhinoconjunctivitis. Allergic rhinoconjunctivitis can be diagnosed clinically, and sensitisation confirmed by either skin prick testing or allergen-specific IgE testing.

Intranasal corticosteroids and non-sedating oral antihistamines are safe, effective treatments. Review by an immunologist or allergist should be considered if immunotherapy is required or simple pharmacological measures are not effective. MT

REFERENCES

References are included in the pdf version of this article available at www.medicinetoday.com.au.

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