Hay fever

An underappreciated and chronic disease

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Allergic rhinitis continues to be a significant chronic disease that affects younger, usually healthier people, with considerable impacts on school performance and work productivity. Symptom-directed treatment is usually sufficient but specific immunotherapy should be considered in severely affected patients.

KEY POINTS

- The prevalence of allergic rhinitis has increased more than 10-fold in the past century.
- Allergic rhinitis is a significant chronic disease that affects the younger, usually more healthy population.
- Allergic rhinitis significantly affects quality of life and impairs work performance.
- Inhaled airborne grass pollens are the major cause of hay fever.
- Effective therapies are available, including antihistamines and intranasal corticosteroids.
- Immunotherapy is also effective treatment for more severely affected patients.

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Hay fever, or seasonal allergic rhinitis (AR), is mainly caused by grass pollens. The main hay fever season in southern regions of the country is considered to be when perennial ryegrass, the common temperate grass fodder crop, is flowering. Subtropical Australian grasses have summer flowering times, such that some regions can also have later peaks in grass pollen and, therefore, longer hay fever seasons. Many patients with allergy to grass pollen are also allergic to other allergens that are not seasonal, such as house dust mite, and will have perennial symptoms of AR with a seasonal increase coinciding with the pollen season.

The main symptoms of AR, which is more common in younger people, are nasal obstruction, sneezing, anterior rhinorrhoea and itching. These and the often accompanying allergic conjunctivitis cause tiredness, lack of concentration and irritability, which impair quality of life, with effects on school performance and work productivity.

History and prevalence of hay fever

From 3000 to 250 BC the Chinese used ephedra (ma huang), whose active ingredient is ephedrine, to 'relieve bronchospasm, produce vasoconstriction, reverse congestion and inhibit mucous secretion'. Asthma was described and treated during this period but the first description of hay fever was attributed to Rhazes (circa 865 to 923 AD), who described 'rose fever' in 'A Dissertation on the Cause of the Coryza which occurs in Spring when the Roses give forth their scent'.[1] The recognition and prevalence of rhinitis has increased since the industrial revolution but even in the early 20th century prevalence rates were low, for example 0.82% in Switzerland in 1926.[2,3]

Globally the largest study of allergic rhinoconjunctivitis (ARC) is the International Study of Asthma and Allergies in Childhood (ISAAC), which surveyed 1.2 million children in 98 countries and reported a prevalence for rhinoconjunctivitis of 14.6% and for asthma and eczema of 14.1% and 7.3%, respectively.[4] In Australia, the latest Australian Institute of Health and Welfare statistics from 2011 indicate a current prevalence for AR of 14.9%.[5] As for asthma, the prevalence of rhinitis has plateaued, but the prevalences of food allergy and anaphylaxis continue to increase.

Rhinitis is most common in the second, third and fourth decades of life. The European Multicentre Allergy Group (MAS) cohort followed 1314 newborns and demonstrated a prevalence of rhinitis over twice that of asthma and eczema at the age of 13 years.[6]

A timeline showing the history of allergy is provided in Figure 1.

Factors affecting prevalence of rhinitis

Several factors affect the prevalence of rhinitis, including regional factors, effects of viral infections and hygiene hypothesis in early life.

- The ISAAC demonstrates the variability of prevalence between and within countries, suggesting the influence of local allergic factors is important. The Australian Bureau of Statistics National Health Survey 2007-08 showed Canberra to have the highest regional prevalence of self-reported hay fever (21% in the ACT compared with 13% in NSW).[5] Genetic risk factors for allergic diseases exist, and a child of two atopic parents has a 60 to 80% chance of developing an allergic disease.
- Females have a greater lifelong incidence of rhinitis, approximately 14% higher than males.
- There is a general correlation between prevalence and socio-economic status but the current data challenges the statement that allergic disease is a disease of industrialised and developed countries.[4]
- Being born in the spring or winter months has been linked to a higher risk of AR but the data are mixed.
- Firstborn children have a higher prevalence of rhinitis in more affluent countries only.[7] However, children with more siblings and children attending day care centres have lower prevalences of rhinitis.[8]
- Several large primary prevention studies (house dust mite and/or dietary measures) to date have not shown that at-risk children can be prevented from developing atopic disease.[9]
- Migration has been shown in several countries to present a risk for the development of allergic diseases.[10,11] An older Australian study has shown that after 10 years of residence in Australia up to 60% of South-East Asian immigrants developed hay fever.[12]
- Smoking during pregnancy, passive cigarette smoking and home mould exposure are associated with an increased risk of AR.[13]
- Urban rural differences have been consistently demonstrated, with lower rates of allergic disease in farm settings.[14]

Clinical features of allergic rhinitis

The main symptoms of AR are nasal obstruction, sneezing, anterior rhinorrhoea and itching. Allergic conjunctivitis occurs in 60% of patients with AR and is characterised by itchy, red and watery eyes; skin involvement and keratitis occurs less frequently. Additional symptoms of AR are itchy throat and ears and postnasal

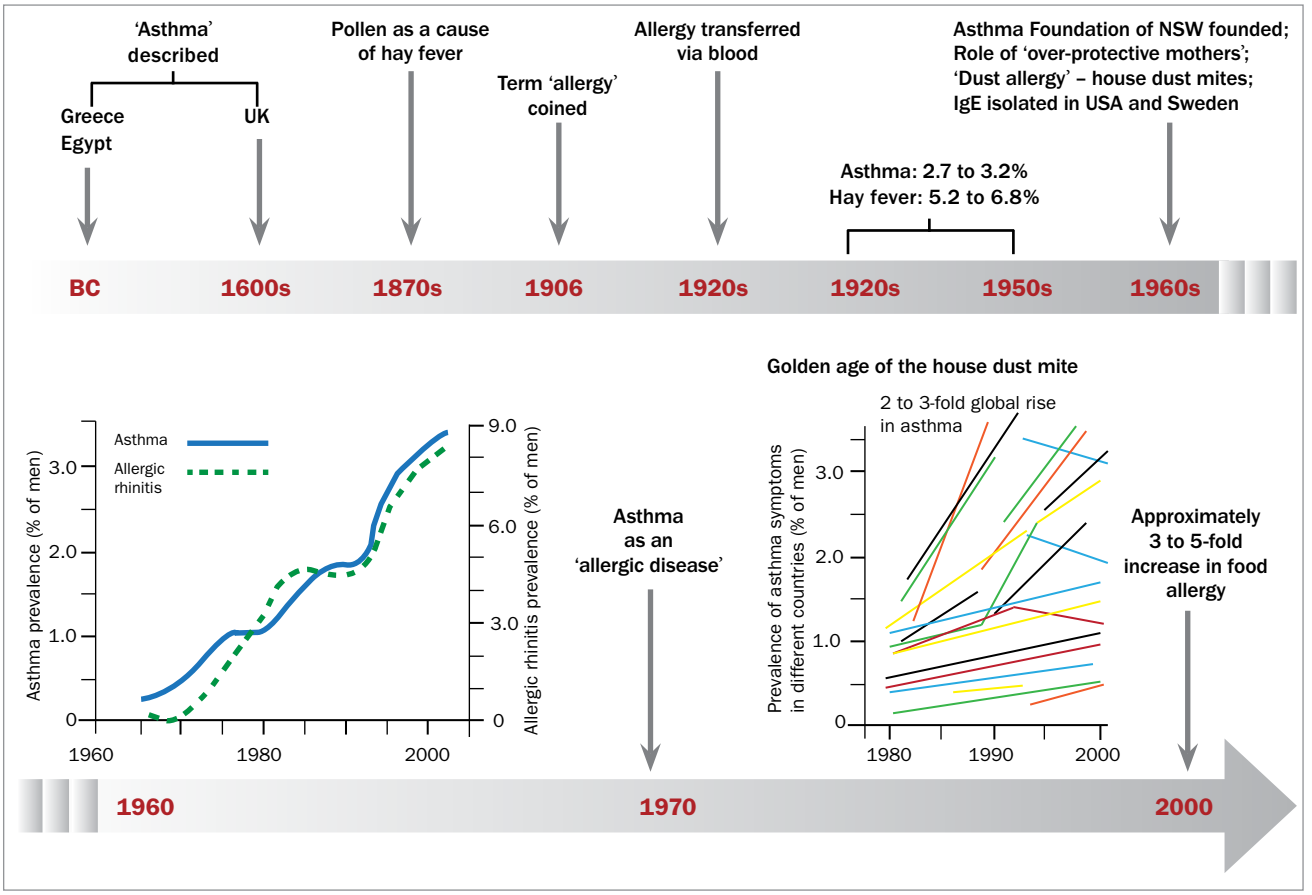


Figure 1. A timeline of allergy.

Courtesy of Associate Professor Euan Tovey, Woolcock Institute, University of Sydney, NSW. Graphs adapted from (left) Latvala J, et al. Trends in prevalence of asthma and allergy in Finnish young men: nationwide study, 1966–2003. BMJ 2005; 330: 1186-1187; and (right) Eder W, et al. The asthma epidemic. N Engl J Med 2006; 355: 2226-2235.

drip. These symptoms can all result in tiredness, lack of concentration and irritability.

It is important to distinguish AR from an intercurrent viral upper respiratory tract infection (URTI) and sinus disease. URTIs usually include a sore throat and are self-limiting, and in sinus disease there is usually congestion, a reduced sense of smell, a mucoid or purulent discharge and facial pressure/pain.

A recent survey of 3383 adult patients with AR estimated that, according to the Allergic Rhinitis and its Impact on Asthma (ARIA) classification, the majority had more severe forms of the disease, with 12% having mild intermittent, 9% mild persistent, 24% moderate-severe intermittent and 56% moderate-severe persistent forms.[15] The study also reported the existence of comorbidities such as conjunctivitis (54%), asthma (38%), sinusitis (14%), sleep disturbances (9%) and nasal polyps (5%). Other reported associations are otitis media with effusion and possibly dental malocclusion.

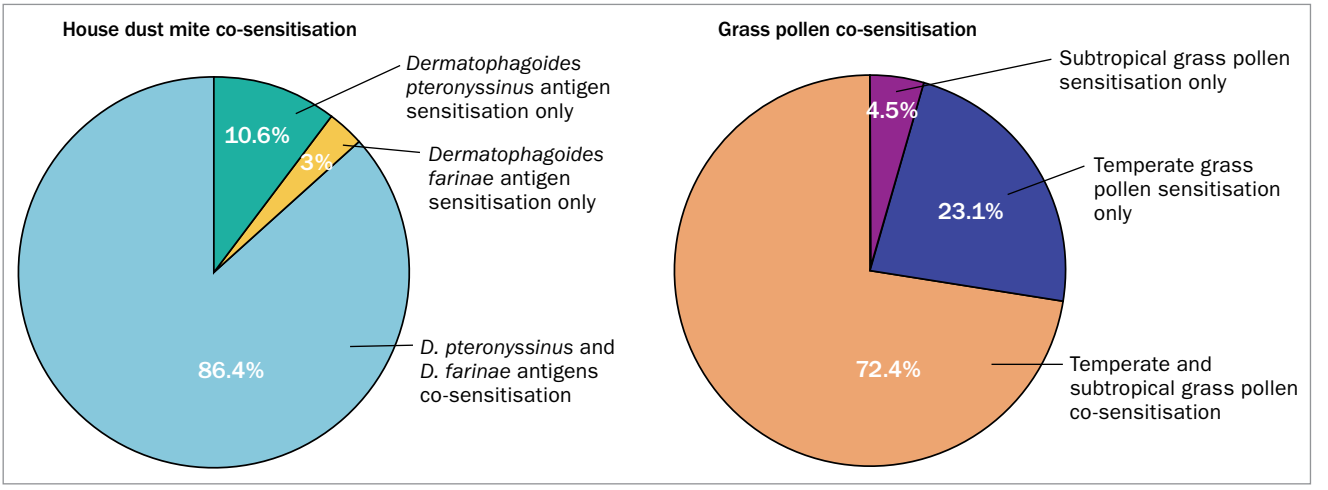
Quality of life and economic/societal burden

Many studies now show that chronic rhinitis impairs the quality of life of patients, the most significant impairments being the repeated need to blow the nose, disrupted sleep and inability to concentrate. However, others reported are decreased physical functioning, energy, general health perception, social and emotional functioning and mental health, and also pain. Rhinitis reduces work productivity by 23 to 40% and also examination performance.[16,17]

How to diagnose AR

The diagnosis of AR depends on the patient's clinical history and also evidence of IgE-mediated sensitivity to allergen. The latter can be determined by skin prick testing using individual allergens (and performed in the surgery) or by serum allergen-specific IgE testing, which uses individual allergens or a mix of allergens.

Conditions that can be confused with AR include nonallergic rhinitis, recurrent



Figures 2a and b. House dust mite (a, left) and grass pollen (b, right) sensitisation in a Sydney-based population, as determined by skin prick testing.[18]

Data and charts courtesy of Andrew Kam, St Vincent's Centre for Applied Medical Research, Sydney, NSW.

viral infections, nasal polyposis and chronic rhinosinusitis.

For seasonal AR (hay fever), positive results to sensitivity testing for pollen from grasses (temperate and/or subtropical), weeds and/or trees would be expected, and possibly also to outdoor moulds. If immunotherapy is likely to be considered later, it is important to determine all the sensitising agents for the individual to guide the choice of allergen extracts to use for the immunotherapy.

A significant proportion of patients with AR in Australia have sensitisation patterns that result in their having perennial symptoms with an additional seasonal increase in symptoms. A recent survey of 1421 Sydney-based patients attending an allergy practice for allergy assessment showed that 77% were atopic on skin prick testing.[18] Of these patients, co-sensitisation to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* occurred in 86%, monosensitisation to *D. pteronyssinus* occurred in 11% and to *D. farinae* in 3.0%, and co-sensitisation to house dust mite (i.e. *D. pteronyssinus* and/or *D. farinae)* and cockroach occurred in 27% (Figure 2a). Regarding sensitisation to grasses in these patients, co-sensitisation to both temperate and subtropical grasses occurred in about 72%, and monosensitisation to temperate and subtropical grasses in 23% and 5%, respectively (Figure 2b). Co-sensitisation to house dust mite and grasses occurred in 36% of these atopic patients.

Nonspecific irritant triggers also play an important role in many patients with AR, similar to patients with asthma. Some of these triggers are mediated by TRP receptors (transient receptor potential cation channels), which sample the environment. Increased numbers of these receptors have been identified in patients with all forms of rhinitis. The TRPV1 receptor, also known as the capsaicin receptor, detects (i.e. is activated by) heat (temperatures above 43°C), acidity, capsaicin, ethanol and allyl isocyanate (in wasabi, mustard), all of which are irritants. The TRPA1 receptor detects cold (temperatures below 17°C), oxidative products, allyl isocyanate, acrolein, lipopolysaccharide, smoke, dietary isocyanates and pungent compounds, also all irritants.

Pollen allergenicity

What is an allergen?

The term allergen is frequently used to name a substance that triggers an allergic reaction in sensitised patients. Often the term is used more broadly to describe complex biological sources of allergens such as house dust mite faeces or grass pollen. It is more correct, however, to consider the allergen to be the component, often a protein or glycoprotein, within an allergen source to which specific IgE antibodies bind.

The capacity to bind allergen-specific IgE is a measurable property of the allergen. Another key property of an allergen is its capacity to sensitise patients by inducing an adaptive immune response culminating in excess production of specific IgE. The attachment of allergen to its specific IgE bound to high-affinity IgE Fc receptors on the surface of mast cells or circulating basophils (sensitised cells) triggers the immediate release of preformed inflammatory mediators such as histamine, which can be quantified.

Properties that confer pollen allergenicity

In its natural form an allergen is not an isolated molecule. Patients are exposed to the allergen, usually a protein, in the presence of other nonallergenic components contained within the allergen source. Many of these other components, such as lipids or endotoxins, interact with

the mucosal innate immune system to influence allergenicity.

The allergenicity of a pollen depends on the intrinsic allergenicity of the allergenic components as well as the immunomodulatory properties of other substances within the allergen source. Only a tiny fraction of the known protein types are allergens.[19] Certain properties confer allergenicity to allergenic proteins generally, for instance enzymatic functions as exemplified by cysteine protease activity of the house dust mite allergen Der p 1; however, the intrinsic qualities of pollen allergen components that confer high allergenicity are still being discovered.[20]

Several trees (e.g. birch and olive), weeds (e.g. ragweed) and grasses produce highly allergenic pollens. The allergenic properties of these pollens are still being investigated.

Regional and seasonal variability in allergen potency (i.e. the amount of allergen within the pollen) has been observed.[21] Ecological factors within the local environment influence the level of pollen production as well as the allergen content within the pollen. These factors include the nutrient composition of the soil, temperature, sunlight, moisture availability and carbon dioxide concentration.[22]

Pollen allergenicity is also affected by urbanisation and pollution. Pollutants such as heavy metals or diesel exhaust may indirectly affect pollen quality by influencing the plant growth and gene expression.[23] Pollutants can also directly affect pollen allergenicity; for example, airborne diesel exhaust particles can act as carriers for allergen-containing starch granules derived from ryegrass pollen and this could provide an adjuvant effect on the inflammatory response to the allergen.[24]

Allergenic pollen in Australia

Many of the allergenic plants identified in Australia are exotic species of grasses, trees and weeds. Although deciduous exotic trees such as birch are used as street trees in temperate southern cities such as Canberra, Melbourne and Hobart, the pollen season of these trees is short and they appear to be less of a major allergy concern than they are in Europe.

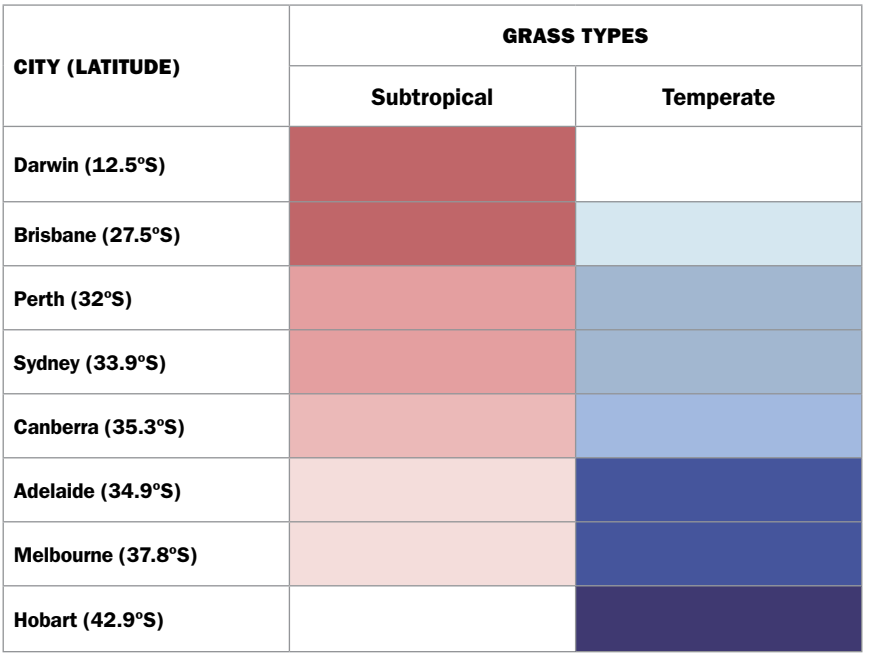


Figure 3. Grass pollen latitudinal exposure gradient for Australian cities. (The darker the colour, the greater the pollen exposure.)[28]

Ragweed is a highly invasive weed with highly allergenic properties. Eradication programs are thought to have restricted the spread of ragweed but the potential remains for the geographical range to increase and for there to be a significant allergy threat from ragweed in the future. Ragweed sensitisation was reportedly as high as 34% in 206 volunteers assessed for sensitivity to ragweed by skin prick test in the Northern Rivers area of New South Wales, and 37.9% in 506 adult allergy/asthma patients from Perth.[25,26] However, co-sensitisation or cross-reactivity with pollen of other weed species that may share homologous allergen components could account for some of the positivity in these two studies.

Grass pollens constitute the major outdoor allergen source in Australia. However, knowledge of grass pollen aerobiology in Australia is incomplete, with existing grass pollen count data drawn from short-term studies of few sites without uniform techniques. Considerable regional variability has been observed in the timing and levels of exposure to airborne grass pollen in Australian cities, due in part to the dominant type of grass (temperate or subtropical) in the region, as indicated in the grass pollen latitudinal exposure gradient shown in Figure 3.[27,28] Biogeographical gradients are apparent in the starts and peaks of the grass pollen seasons in Australia and New Zealand, with shorter seasons in southern cities and longer seasons with multiple peaks in cities closer to the equator.[28] Notably patients with AR show higher allergic sensitivity to pollen of the temperate grass perennial ryegrass in Melbourne and to pollen of the subtropical grasses Bahia and Bermuda in Brisbane (Figures 4a to d).[29]

Importantly, patients show reciprocal patterns of inhibition of specific IgE to subtropical or temperate grass pollens depending on their origin.[30-32] This suggests that exposure to different types of grass pollens drives patterns of sensitisation.

Figures 4a to 4d. Examples of common grasses in Australia that produce allergenic pollen. a (top left). Bermuda (couch) grass (*Cynodon dactylon*); b (top right). Bahia grass (*Paspalum notatum*); c (bottom left). Johnson grass (*Sorghum halepense*); and d (bottom right). Perennial ryegrass (*Lolium perenne*). Bermuda, Bahia and Johnson are subtropical grasses and ryegrass is a temperate grass.

When is the pollen season in Australia?

The main hay fever season in Australia is considered to be the spring peak in airborne grass pollens in southern cities that is largely due to flowering of temperate grass fodder crops such as perennial ryegrass. This peak in grass pollen usually occurs between late October and early December in Hobart, Melbourne, Adelaide, Canberra, Sydney and Perth. However, grasses have long flowering seasons in many parts of Australia and grass pollen can be found throughout most of the year.

In regions where both temperate and subtropical grasses grow (between the tropics and latitudes of about 37°S) a summer peak in grass pollen due to subtropical grasses occurs as well as the spring peak. Cities within these latitudes include Adelaide, Canberra, Sydney and Perth.

Further north in Brisbane, the peak grass pollen season usually occurs over a longer period, between January and April. In Darwin, in the tropics, grass pollen levels remain low throughout most of the year with an increase in May and June.

The need for pollen monitoring in Australia

Given the high burden of hay fever and allergic asthma in Australia, there is a need for a national standardised pollen counting and forecasting network to help in the understanding and management of pollen allergies in our communities.[27] A collaborative national pollen monitoring network is being established, and thus far airborne pollen counts are available for Melbourne, Canberra, Sydney, Brisbane and Adelaide from the following websites:

- www.melbournepollen.com.au
- www.canberrapollen.com.au
- www.sydneypollen.com.au
- www.brisbanepollen.com.au
- http://asthmaaustralia.org.au/SA/Adelaide_Pollen_Count.

Local pollen monitoring networks are likely to become increasingly beneficial in the short- and medium-term future. Episodes of thunderstorm asthma epidemics coinciding with high grass pollen count days have been reported across southeastern Australia.[33-35] Beyond these acute episodes of thunderstorm asthma epidemics, grass pollen levels have been associated with emergency presentations and admissions for asthma in children in Melbourne and grass pollen challenge has been shown to induce allergic airway inflammation.[36,37] However, not all high pollen count days trigger increases in asthma symptoms or hospital admissions. More research is required to understand the complex interactions between pollen exposures, weather and health outcomes, as well as their impacts on the management of healthcare services.

Future risks of increased pollen allergy

The Intergovernmental Panel on Climate Change 5th Assessment Report identifies AR as a condition likely to increase with global warming.[38] The capacity to observe and adapt to changes in pollen aerobiology requires accurate knowledge of current airborne pollen levels.

TABLE. TREATMENT OF ALLERGIC RHINITIS ACCORDING TO SYMPTOM SEVERITY*

Treatment	Intermittent symptoms		Persistent symptoms	
	Mild	Moderate to severe	Mild	Moderate to severe
Allergen avoidance	+	+	+	+
Oral or intranasal antihistamine	+	+	+	+/–
Intranasal corticosteroid	–	+	+	+
Montelukast	+	+	+	+/–
Chromones	+	+	+	+/–
Specific immunotherapy	–	+	+	+

* Allergic rhinitis severity according to the 2008 Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (www.whiar.org/Documents&Resources.php).

Changes in the biogeographical ranges of plants with allergenic pollen are likely with climate change.[39] Increasing levels of carbon dioxide are predicted to increase the allergenicity of ragweed pollen and to increase the biomass of subtropical grasses. Continuing urbanisation and pollution are also likely to intensify the allergenic impact of weed pollens by providing more habitats and stimulating enhanced pollen allergen potency. An accurate and thorough understanding of current trends in the distribution, timing and levels of airborne allergenic pollen is important for current and future management of allergen exposure.[22]

Allergen avoidance

Pollen allergens generally cannot be avoided in the outdoor setting. The length of the season relating to some pollen is short and so it may be possible to avoid that pollen – for example, ragweed and birch pollens, but these pollens are not common in Australia. It has been suggested that patients stay indoors on high pollen count days, which may be possible in some circumstances. However, pollen allergen is detectable indoors, suggesting that this is not likely to be a completely effective avoidance strategy.[40] Nasal filters may reduce symptoms of rhinitis but their use is not widely promoted and they do not protect against coexistent allergic conjunctivitis.[41]

Analysis of the Sydney skin prick testing data has suggested that local environmental factors such as humidity and rainfall affect levels of sensitisation and that selection of accommodation might be important.[18] For example, this data showed that living more than 5 km from the coast was associated with higher sensitisation to cockroach, mould and plant allergens.

Single intervention methods for house dust mite avoidance are not effective but multimodality avoidance may be of some benefit.[42] This partly reflects our lack of knowledge regarding personal house dust mite exposure, which is now felt to occur more during the daytime, hence previous strategies targeting night-time exposure may have been misdirected.[43] Other animal allergens – cats, dogs and laboratory animals – may be able to be avoided.

Treatment of allergic rhinitis

Pharmacological treatment

A graded approach to the drug treatment of AR is shown in the Table and available drugs in Boxes 1 and 2. In the previously mentioned survey of 3383 patients with AR, in which the most frequently used drugs were oral antihistamines (77.1%) and topical corticosteroids (60.8%), response to treatment was rated as excellent in 12%, good in 41%, fair in 31%, poor in 15% and very bad in 1% of patients.[15] The frequency of treatment dissatisfaction was much greater in patients with moderate to severe AR and this group was more likely to receive immunotherapy.

A trial of treatment should be undertaken using appropriate medication for two to four weeks, at which time the patient should be reviewed.[44] If response to treatment is not adequate then treatment should be stepped up or added to and the patient again reviewed after two to four weeks. If treatment remains unsuccessful then the diagnosis should be reviewed and specialist referral considered. Specific therapy directed towards allergic conjunctivitis may need to be considered.

Intranasal therapy

Intranasal therapy is targeted directly to the diseased organ. Saline, corticosteroid, antihistamine, decongestant, anticholinergic and mast cell stabiliser intranasal preparations are available, and also some combination therapies. The relatively new combined antihistamine and corticosteroid nasal spray azelastine/fluticasone propionate combines rapid relief antihistamine therapy with slower onset anti-inflammatory intranasal corticosteroid therapy and is, as expected, more effective than the individual components.[45] It is most important that patients are instructed in the correct use of intranasal devices. Instructional videos are available about using intranasal sprays, such as that produced by the National Asthma Council Australia (www.nationalasthma.org.au/how-to-videos/using-your-nasal-spray).

Although some intranasal therapies can be used for symptomatic relief on an as-needed basis, such as intranasal saline, antihistamines and decongestants, in patients with more severe and persistent disease a trial of intranasal corticosteroids is recommended for at least a month to

1. INTRANASAL ANTIHISTAMINES AND CORTICOSTEROIDS AVAILABLE IN AUSTRALIA*

Intranasal antihistamines

- Azelastine
- Levocabastine

Intranasal corticosteroids

- Beclomethasone
- Budesonide
- Ciclesonide
- Fluticasone furoate
- Fluticasone propionate
- Mometasone
- Triamcinolone

Combination products

- Azelastine/fluticasone propionate

* All but ciclesonide, fluticasone furoate and the combination product azelastine/fluticasone propionate are available over the counter.

determine efficacy. If the trial is successful then regular use of intranasal corticosteroids can be continued long term.

Compliance with therapy in a chronic disease is always an issue. Patients tend to aim for symptom control, which is not the same as disease control. Patients need to be informed of the slow onset of action of intranasal corticosteroids and the need for regular use.

The most common side effect of intranasal corticosteroid therapy is nasal bleeding, which occurs in about 10% of cases. Checking the correct use of the delivery device and then restarting treatment after about a week is appropriate. If bleeding recurs, a lower dose should be tried or an alternative therapy suggested.

Patients who are prescribed intranasal corticosteroids are often concerned about corticosteroid-related side effects. A recent meta-analysis, however, showed no evidence of histological damage as a result of intranasal corticosteroid use and, indeed, evidence of tissue repair.[46]

Seven different intranasal corticosteroid preparations are available in Australia and most of these are available as over-the-counter medications (Box 1). None are PBS subsidised but their costs have reduced and the cheapest ones are now 12 to 28 cents per spray, or about $10 to $20 per month. A nonsedating antihistamine tablet may cost upwards of 30 cents, or about $10 per month, making the costs of intranasal corticosteroids and oral antihistamines very similar.

Treating children

Most antihistamines can be used in children aged 12 months and older. Intranasal corticosteroids can be used from the age of 2 years; examples include fluticasone furoate and triamcinolone.

Treating pregnant women

Nonmedicinal therapy for AR should be used if possible during pregnancy, such as nasal strips to relieve congestion at night and intranasal saline sprays. The antihistamines pheniramine and dexchlorpheniramine and the intranasal corticosteroid budesonide are category A medicines; promethazine, a category C medicine, should be avoided.

Treating the elderly

Rhinitis is more likely to have a nonallergic or vasomotor component in elderly patients than in younger patients. Usually a symptom-targeted approach is most effective in the elderly, such as ipratropium for rhinorrhoea and saline for dryness and crusting.

It should be ensured that concomitant medications are not contributing to symptoms in elderly patients with AR. Commonly used medications that may contribute are antihypertensives (ACE inhibitors, beta blockers, amiloride, prazosin, hydralazine), psychotropics (risperidone, chlorpromazine, amitriptyline), phosphodiesterase type 5 inhibitors (sildenafil, tadalafil), NSAIDs (ibuprofen) and gabapentin.

Other therapies

Leukotriene receptor antagonists (such as montelukast) are considered as effective as antihistamines in the treatment of patients with AR.

2. ORAL ANTIHISTAMINES AVAILABLE IN AUSTRALIA*

- Cetirizine
- Desloratadine
- Fexofenadine
- Loratadine

* All are available over the counter.

Omalizumab and newer monoclonal antibodies such as mepolizumab are expected to have efficacy in patients with AR but current costs are prohibitive.

Rhinolite therapy is a form of intranasal UV light therapy that has been established in some centres in Australia but its overall efficacy is unclear.

Surgery

Surgery has a limited but important role to play in the treatment of patients with AR, especially in relieving obstruction that does not always respond to medical therapies. Correction of septal deformities and inferior turbinate reduction surgery can be very effective in selected patients. Vidian neurectomy helps severe rhinorrhoea, particularly in nonallergic rhinitis.

Specific allergen immunotherapy

Immunotherapy is only suitable for patients with AR, and is not used in patients with nonallergic rhinitis. It is the only therapy that can modify the course of the disease and potentially provide a cure. Studies in children have shown that immunotherapy can reduce future sensitisation and the development of other allergic disease such as asthma. One study has shown that new sensitisation developed in 35% of controls compared with 3% of patients who had undergone sublingual immunotherapy (SLIT; odds ratio [OR], 16.85; confidence interval [CI], 5.73–49.13) and that mild persistent asthma was less frequent in SLIT patients

(OR, 0.04; CI, 0.01–0.17).[47] Indeed, the World Allergy Organization have described SLIT as disease-modifying therapy.[48] This form of therapy is used extensively in Europe, with an estimated 5.5 million patients treated between 2007 and 2011.

The mechanism of action of immunotherapy is complex. Some studies support the induction of regulatory T cells that suppress both Th1 and Th2 cytokine responses, whereas others show an immune deviation from a Th1 to a Th2 responsiveness.

Immunotherapy has been well demonstrated to be an effective form of therapy for both perennial and seasonal AR, with improvements in symptom scores, medication scores and quality of life.[49]

The selection of allergens to place in an extract will depend on the patient's allergen sensitivity determined by skin testing and their current exposure. In general, cockroach and fungal extracts should not be mixed with pollen, mite or dander extracts. It is important that a sufficiently high dose of cumulative allergen extract is administered, usually over a three-year period.

Subcutaneous immunotherapy (SCIT) requires a build-up phase, usually over 10 weeks, and then monthly maintenance injections for three years. The injection must be administered under medical supervision because of the small risk of a systemic allergic reaction (2 to 3%), although most of these reactions are mild. However if a patient also has asthma, the asthma must be well controlled and lung function reasonable (forced expiratory flow in 1 second greater than 70%) before undertaking immunotherapy. Premedication with antihistamines can reduce systemic side effects. It is recommended that patients be observed for 30 minutes after an injection. Immunotherapy can be continued during pregnancy but should not be commenced during pregnancy.

Until recently immunotherapy has only been available as SCIT, using extracts of allergens for injection. Sublingual drops of allergen extracts are now available (SLIT) and a tablet form of grass pollen is also available. The oral preparations are safer and more suitable for the paediatric population (over 5 years of age) although they are considerably more expensive. SLIT has a very rapid build-up phase, over days rather than weeks. Although safer that SCIT, it has a high incidence of local side effects (irritation and swelling of the oral mucosa) but systemic reactions are uncommon, which is why patients can self-administer.

Contraindications to immunotherapy include current pregnancy, uncontrolled asthma, autoimmune diseases, malignancies and significant cardiac disease (especially if beta blockers are being used).

SCIT is cheaper than SLIT. The costs depend on how many allergens are administered; for a single extract, the cost of SCIT is generally less than $400 per year (excluding injection-related costs) and for SLIT in the vicinity of $1000 per year. Cost-effectiveness measured in QALYs (quality adjusted life years) is estimated at USD$17,000 to $25,000 per QALY gained, which is considered to be an acceptable cost.[50]

There are few data comparing SCIT and SLIT but a series of small studies suggest that efficacy is similar.[51,52]

Conclusion

AR continues to be a significant chronic disease that affects the younger, usually healthier population. It coexists with other chronic allergic diseases such as asthma and eczema and these can singly or in combination significantly affect a patient's quality of life. Treatment is frequently symptom-directed but in most patients who are more severely affected specific immunotherapy needs to be considered. MT

References

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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