MedicineToday 2013; 14(10): 18-28

PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

Allergic rhinoconjunctivitis returns

The new spring season 2013

JANET RIMMER MD, MB BS, FRACP

The prevalence of allergic rhinoconjunctivitis peaks in the spring and early summer months, the time of year when most plants flower and produce pollen. Allergy assessment continues to be a cornerstone for the diagnosis of allergic rhinoconjunctivitis.

Key points

- **Seasonal allergic rhinoconjunctivitis is caused by exposure to pollen and also moulds.**
- **Northern Hemisphere plants introduced into Australia generally produce larger quantities and more allergenic pollen than plants native to Australia.**
- **Patients with the condition should be asked about both seasonal and perennial allergic triggers as often both are important.**
- **The nasal and ocular symptoms of allergic rhinoconjunctivitis may be accompanied by systemic symptoms such as poor sleep quality, fatigue and irritability.**
- **Allergy assessment is the basis of diagnosis and is essential for the facilitation of immunotherapy.**
- **Most patients with asthma also have rhinitis, and 15 to 30% of patients with allergic rhinoconjunctivitis have concomitant asthma.**

An editorial in the journal *Allergy* in 2012 entitled 'Davos Declaration: allergy as a global problem' stated that allergic disease has undergone an epidemic increase in the past few decades and now affects 10 to 30% of the world's population.[1] In some allergic diseases, such as anaphylaxis, the condition can be life-threatening and in others, such as allergic rhinoconjunctivitis, it is a chronic condition, but they all can cause a significant socioeconomic burden. It should be noted that the term allergic rhinoconjunctivitis is generally preferred now, rather than allergic rhinitis, as it emphasises the fact that ocular symptoms occur in up to 80% of patients with allergic rhinitis, although their presence may need to be specifically asked about.

Hayfever is also known as seasonal allergic rhinoconjunctivitis and is caused by exposure to pollen and also moulds. It affects up to 21% of the Australian population, with the prevalence highest in the Australian Capital Territory and lowest in Queensland and the most affected age group being 25 to 44 years of age.[2] The pollen season in Australia is prolonged and commences in September each year. It is maximal in November but persists through until March in certain areas. As some species of grass produce pollen in the winter months, patients affected by this pollen will appear to have perennial symptoms.

This review concentrates on seasonal allergens but patients should be asked about both seasonal and perennial allergic triggers as commonly both are important. Nonallergic triggers of rhinitis, such as temperature changes and strong smells, may also be relevant and should be considered.

CLASSIFICATION OF ALLERGIC RHINOCONJUNCTIVITIS

Allergic rhinoconjunctivitis has traditionally been defined as seasonal or perennial,

Dr Rimmer is Clinical Associate Professor at Sydney Medical School – Central, The University of Sydney, and a Respiratory Physician and Allergist at St Vincent's Clinic, Sydney, NSW.

ARIA DEFINITION OF ALLERGIC RHINITIS[6]

Pattern of symptoms*

Intermittent

Symptoms are present:

- less than four days per week, or
- for less than four consecutive weeks

Persistent

Symptoms are present:

- four or more days per week, and
- for four or more consecutive weeks

Severity of symptoms

Mild

Absence of moderate to severe features

Moderate to severe

Any of the following are present:

- sleep disturbance
- impaired daily activities
- impaired school, work performance
- troublesome symptoms

ABBREVIATION: ARIA = Allergic Rhinitis and its Impact on Asthma.

* The terms intermittent and persistent are not synonymous with seasonal and perennial and cannot be used interchangeably.

implying that symptoms are either occurring only in the spring season or all year round, respectively. This usually means that different allergenic triggers are involved: seasonal allergens such as grass, tree and weed pollens in seasonal allergic rhinoconjunctivitis and perennial allergens such as dust mite and cat and dog danders in perennial allergic rhinoconjunctivitis.

However, most individuals with allergic rhinoconjunctivitis have a combination of the seasonal and perennial forms. A study of 2347 Italian young men with allergic rhinitis showed that 17% had seasonal allergic rhinitis (pollen sensitisation), 11% had perennial allergic rhinitis (perennial allergen sensitisation) and 72% were sensitised to both seasonal and perennial allergens.[3] As a result of this overlap and also a desire to capture the effect of the disease on quality of life parameters, the definition of allergic rhinitis that has been in use since 1999 uses the terms persistent/intermittent and mild/moderate-severe, as outlined in the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (see the box on this page).[4-6] The terms intermittent and persistent are not synonymous with seasonal and perennial and cannot be used interchangeably.

In the ARIA definition, there is an emphasis on the persistence and severity of symptoms. This definition more closely parallels that used in asthma and has also served to highlight the links between allergic rhinoconjunctivitis and asthma. Most patients with asthma (both allergic and nonallergic) also have rhinitis, whereas 15 to 30% of patients with allergic rhinoconjunctivitis have concomitant asthma.[2]

EPIDEMIOLOGY

As noted above, allergic rhinoconjunctivitis is a global disorder but there are significant variations worldwide that may relate to climate (tropical regions have a higher prevalence of allergic rhinoconjunctivitis), socioeconomic

Figure 1. Wind-pollinated plants such as pasture grasses (e.g. cocksfoot pictured here) and many weeds produce large amounts of airborne allergenic pollen that can cause allergy in susceptible people over a wide area.

status (high income countries have higher prevalence of allergic rhinoconjunctivitis) or availability of reliable information. Using a standard questionnaire approach, the International Study of Asthma and Allergies in Childhood (ISAAC) study has provided worldwide prevalence data for asthma and allergic rhinoconjunctivitis, and confirms the presence of wide differences.[7] In addition, large interregional differences have been documented, such as prevalences ranging from 2.9% for allergic rhinitis and 3.8% for allergic rhinoconjunctivitis in Şanliurfa, Turkey, to 54.1% for allergic rhinitis and 39.2% for allergic rhinoconjunctivitis in Ibadan, Nigeria, both of which are urban communities.[8] Studies in children suggest that the prevalence of allergic rhinitis has doubled in the last 20 years.[7]

It is of interest that migrants to Australia may present with symptoms of allergic rhinoconjunctivitis after about seven years of living in Australia.[9]

SEASONAL TRIGGERS

Pollens

Pollen is produced by flowering plants, including trees, grasses and flowers (usually weeds – i.e. plants growing where they are not wanted and in competition with cultivated plants). Some plants (such as wattle) produce small amounts of pollen that is distributed by birds and bees from one flower to another to effect pollination. Other plants (such as pasture grasses and many weeds) rely on the wind to disperse their pollen, and produce vast quantities of very fine and lightweight pollen that can spread over long distances, hence causing allergies even in people living a long way from the source (Figure 1). In general, Northern Hemisphere plants produce larger quantities and more allergenic pollen than Australian native plants.

Pollen production is seasonal and can be influenced by the prevailing winds, the presence of drought (which can affect levels over a whole season) and thunderstorms (which can result in a spike of pollen levels and give rise to 'thunderstorm asthma' epidemics that are accompanied by allergic rhinoconjunctivitis). In Darwin, in the tropical far north of Australia, the peak pollen load is in the dry season, April to May. In subtropical Brisbane, the highest pollen counts are in the period December to March. Further from the equator in the temperate southern part of Australia (Sydney and Melbourne), the main flowering period is from October to December. Pollen levels also tend to be higher inland. Trees tend to flower in late winter and early spring, grasses flower next, and the weed plantain flowers from August until May.

Global warming is likely to cause an increase in the abundance of tropical and subtropical grasses as they will also be able to grow further south. Additional effects of global warming may include earlier seasons, higher pollen load and possibly more allergenic pollen.

Grass pollens

Both temperate and subtropical or tropical grasses are grown in Australia. There are hundreds of Australian native grasses but most of the grasses used for agricultural purposes have been introduced, and have pollen that is more allergenic than the pollen of native grasses. The clinical importance of the different climatic zone types of grasses is that there is minimal skin test cross-reactivity between temperate and tropical grasses so grasses from each group need to be used for skin prick testing.

There are regional differences in the proportion of grass pollen in the total pollen load in the air – for example, in Sydney and Melbourne about 20% of airborne pollen is grass whereas in Brisbane the proportion is as high as 71%. Extreme pollen counts are defined as more than 100 pollen grains per cubic metre; by contrast, hospital admissions for asthma are associated with more than 30 pollen grains per cubic metre. Although daily pollen counts are available in many Australian capital cities, the methods of counting are not standardised.

Temperate grasses include canary grass, cocksfoot (also known as orchard grass), perennial ryegrass, tall fescue, veldt grass, annual bluegrass (also known as winter grass), Kentucky bluegrass and timothy grass. Subtropical and tropical grasses include bahia grass, Bermuda grass (also known as couch grass), Johnson grass, bambasti grass, buffalo grass, love grass, kikuyu grass, Rhodes grass and setaria.

Weeds

Several introduced plants with highly allergenic pollen have become weeds in Australia. They include plantain, pellitory-of-the-wall, Paterson's curse, ragweed and Parthenium weed (Figures 2a to c).

Plantain is a very common weed that is present in all areas of Australia except the Northern Territory and generally flowers between August and May. It is sometimes used as a crop and has purported medicinal properties.

Pellitory-of-the-wall (*Parietaria judaica* or *P. officinalis;* commonly known as



Figures 2a to c. Weeds in Australia with highly allergenic pollen include (a, left) common plantain, (b, centre) pellitory-of-the-wall (*Parietaria judaica* or *P. officinalis*; also known as asthma weed) and (c, right) ragweed.

asthma weed in Australia, and also as spreading pellitory) was accidentally introduced in a shipload of marble from Italy in the early 1900s. It is mainly found in Sydney but has spread to Victoria and Western Australia. In New South Wales it flowers from August to April, but it has much shorter flowering seasons in the other states and territories.

Paterson's curse (also known as Salvation Jane) is an attractive flowering plant that was deliberately brought from England in the late 1800s by Dr Paterson. This plant has taken over large tracts of pasture in rural Australia and produces highly allergenic pollen in the spring and early summer. There is no skin test available to test for this allergen.

Ragweed and Parthenium weed were introduced in pasture seed imported from the USA. They have spread throughout Queensland and northern New South Wales. Ragweed has a short autumnal flowering season, from March to May, and Parthenium weed flowers from September to March.

Trees

White Cypress pine (also known as Murray pine) is a native Australian tree that produces highly allergenic pollen. Its growth extends from the western slopes and plains of Eastern Australia across to Western Australia, south of the Tropic of Capricorn and it flowers from late July through to the end of September.

The many species of Australian pine (also known as she-oaks or casuarinas) produce allergenic pollen throughout the year and may cause hayfever symptoms at any time of the year.

Wattle and other Australian natives may be very colourful and are frequently blamed for early spring symptoms but allergy tests seldom confirm that they are allergenic.

The pollen of introduced trees, which are planted for their autumn colours, is more allergenic than pollen from native Australian trees. Olive trees have been introduced into Australia, mainly South Australia, Victoria and New South Wales, and produce highly allergenic pollen. Silver birch trees grow in the cooler regions and their pollen may be a cause of allergy in all states and territories except Queensland and the Northern Territory.

The London plane tree is used extensively in some areas as an urban landscaping tree (Figure 3). It produces pollen from August to October and also trichomes (leaf hairs) and bristle fibres associated with the fruiting body. A study in Sydney that recruited subjects complaining of plane tree sensitivity showed that only 23% were skin test-positive to plane tree pollen and it was thought that the airborne trichomes, which do not carry allergen, may cause mucosal irritation.[10]

Moulds

Alternaria

Alternaria is a ubiquitous fungus found in urban, rural, indoor and outdoor environments. Its spores are small enough to easily enter the lungs, having a diameter of 2 to 8 μm (less than that of airborne pollen grains). It is most commonly found outdoors growing on plants, and causes plant diseases such as blights, spots and sooty mould (Figure 4). Spore counts are highest in summer.

Levels of exposure vary widely between individuals, and are greatest with increased outdoor physical activity. Rates of sensitisation can also vary widely – for example, almost 50% of children in Arizona, USA, are sensitised but only about 20% in Wagga Wagga, NSW.[11] Associations between *Alternaria* spore counts, allergic rhinoconjunctivitis symptoms and asthma symptoms have been demonstrated in Australian populations.[12]

Other moulds

Although there are numerous airborne moulds, such as *Aspergillus, Cladosporium* and *Penicillium*, their relation to allergic disease such as allergic rhinoconjunctivitis is often not well established. *Aspergillus* has been associated with allergic bronchopulmonary aspergillosis (ABPA), allergic fungal sinusitis, pulmonary aspergillosis and invasive pulmonary fungal disease.

PERENNIAL TRIGGERS

Triggers of perennial allergic rhinoconjunctivitis include dust mites, cats (allergen is from the sebaceous glands), dogs (allergen is in the saliva), cockroaches and some moulds. Although these allergens

Figure 3. London plane tree. Trees introduced into Australia often have pollen that is more allergenic than the pollen of native trees.

can be present all year round, there are seasonal variations – for example, house dust mite (HDM) allergen is highest in Sydney in March.[13]

The European house dust mite (*Dermatophagoides pteronyssinus*) and the American house dust mite (*D. farinae*) are the main sources of dust mite allergens in Australia. The dust mite allergen is located in faecal particles. Although traditionally most dust mite exposure was considered to occur at night and avoidance measures have been largely directed at minimising exposure in bed at night, recent data have demonstrated that most exposure occurs during the daytime.[14]

NONALLERGIC TRIGGERS

Rhinitis may be triggered by strong odours (such as perfumes), household sprays, dust, foods (especially wine), medications, pollution, weather change, temperature change, cigarette smoke and occupational exposure to, for example, chemicals. Nonallergic rhinitis can be difficult to distinguish from allergic rhinitis but has different triggers and does not respond to treatment with antihistamines.

SYMPTOMS

Allergic rhinitis can be simply defined as symptomatic inflammation of the nasal mucosa with at least two nasal symptoms present for more than one hour a day plus the presence of atopy. Nasal symptoms include sneezing, rhinorrhoea, nasal congestion or obstruction and nasal pruritus. Patients present mainly with congestion or sneezing, rhinorrhoea and pruritus, although there is an overlap. Itchy ears and palate can also be troublesome symptoms.

Patients will often complain of a sensation of postnasal drip; this is often very troublesome, leading to repetitive throat clearing, and can be difficult to treat. The concept of postnasal drip is complex and it is unclear whether it represents a true increase in nasal and throat secretions or an altered throat sensation. In a study that examined the effect of the pollen season in singers who were allergic to grass pollen, an increase in laryngeal irritation, secretions and globus sensation was recorded in addition to expected nasal symptoms.[15]

There are associated ocular symptoms, including ocular itchiness, erythema and/or lacrimation, in 60 to 70% of patients (allergic rhinoconjunctivitis). There can be additional symptoms such as effects on quality of life, sleep, daytime concentration and work capacity.[16,17] Patients will sometimes present with predominant fatigue. If these other symptoms are not assessed, there is a danger of underestimating disease severity. The questionnaire in the box on page 24 can help identify disease type.[6]

Specific quality of life questionnaires are frequently used in research studies to identify disease severity and response to therapy – for example, the Rhinoconjunctivitis Quality of Life Questionnaire.[18] Many of these questions can be easily used in general practice and will often clearly identify how severe the condition is for the individual patient. Example questions are listed below.

- How many tissues do you use on a bad day?
- How many times do you sneeze a day?
- What activities have been limited by your nose and/or eye symptoms in the last week?
- Do your nose/eye symptoms affect your sleep?
- As a result of your rhinitis do you suffer from fatigue, thirst, reduced productivity, tiredness, poor concentration, headaches and/or exhaustion?
- How affected are you by practical issues like having to carry tissues, needing to blow your nose and/or rub your nose and/or eyes repeatedly?
- Do your symptoms make you frustrated, irritable and/or embarrassed?

It is now recognised, analogous to severe asthma, that about 20% of patients

Figure 4. Lesions caused by *Alternaria* on a leaf of an apple tree. *Alternaria* spores are smaller than airborne pollen grains and are a cause of seasonal allergic rhinoconjunctivitis.

ALLERGIC RHINITIS QUESTIONNAIRE[6] *

Symptoms 1 to 6 suggest an alternative diagnosis, symptoms 7 to 11 suggest allergic rhinitis.

Do you have any of the following symptoms?

1. Symptoms on one side of the nose only
2. Thick green or yellow discharge from your nose
3. Postnasal drip with thick mucus and/or runny nose
4. Facial pain
5. Loss of sense of smell
6. Repeated nose bleeds

Do you have any of the following for more than one hour most days or on most days during the season if your symptoms are seasonal?

7. Watery, runny nose
8. Violent sneezing, repeated attacks of sneezing
9. Nasal obstruction or congestion
10. Nasal itching
11. Red, itchy eyes

* Adapted from Bousquet J, Reid J, van Weel C, et al Allergic rhinitis management pocket reference 2008. Allergy 2008; 63: 990-997.[6]

with allergic rhinitis and rhinosinusitis have symptoms that are poorly controlled despite the use of adequate treatment. Adequate treatment is defined as avoidance of triggers and first-line therapy (intranasal corticosteroids and antihistamines) for four weeks. This group has been labelled as having SCUAD, or severe chronic upper airway disease.[19]

Contributing factors to poor symptom control may include continued environmental triggers (e.g. cigarette smoke), hormonal factors, corticosteroid resistance, neuroinflammatory influences and, possibly, genetic factors. Compliance and adherence to therapy remain important issues, with immunotherapy compliance found to be as low as 50% after one year.[20] The correct technique for nasal spray use is also important, with suboptimal techniques shown in 57% of subjects.[21]

HOW TO ASSESS PATIENTS

The history, severity of symptoms and triggers should provide an initial diagnosis of allergic rhinitis or allergic rhinoconjunctivitis. This should be followed by identification of complications and associated conditions. Physical examination may only be abnormal when patients are symptomatic. Patients can have red swollen eyelids, injected conjunctivae or periocular dermatitis from frequent rubbing. The term 'allergic shiners' refers to the dark circles and puffy skin under the eyes that is attributed to poor lymphatic drainage. The nose can be runny and erythematous, and there may be a nasal crease from frequent rubbing of the nose. An estimate of nasal obstruction can be determined from asking the patient to sniff in through each nostril.

Inspection of the nasal mucosa can show oedematous inferior turbinates and a cobblestone appearance to the mucosa. The mucosa is often described as bluish, but this is not a very consistent sign. Complicating conditions such as nasal polyposis and asthma should be sought.

Objective assessments include estimation of nasal airflow, which can be done with a simple sniff test or a peak nasal inspiratory flow meter. More sophisticated measurements such as acoustic rhinometry and rhinomanometry can be performed, usually by ENT surgeons. Spirometry should be undertaken if the patient has, or is suspected of having, asthma.

The patient's atopic status should be assessed using either skin testing or specific IgE tests. Skin prick testing is frequently used in Australia because of its speed in establishing a diagnosis, the ability to demonstrate the results directly to the patient and its cost-efficiency. Blood testing or specific IgE testing (RAST tests) should be performed where skin prick test solutions are not available or the patient has widespread eczema or dermatographism, which can make the skin test results difficult to read. However, if immunotherapy is to be considered, testing with single allergen discs rather than mixed discs will need to be done before choosing an extract. Repeated testing may be needed as the rate of aeroallergen sensitisation increases with age: sensitisation rates of 10 to 20% at ages 2 up to 6 years, 30 to 60% at 6 up to 12 years, and 50 to 70% at ages 12 to 18 years have been demonstrated.[22]

Differential diagnoses should be considered, including nonallergic rhinitis and rhinitis associated with systemic disease or the use of drugs. Complications should be identified, such as infectious rhinosinusitis, nasal polyposis and lower respiratory tract disease (asthma).[23]

TREATMENT

Generally, antihistamines are used for the treatment of mild intermittent allergic rhinoconjunctivitis. These and intranasal corticosteroids are used for more persistent, severe disease and may need to be combined with other therapies. The ARIA guidelines provide an algorithm for the treatment of allergic rhinoconjunctivitis and when to step up therapy.[6] The Australasian Society of Clinical Immunology and Allergy (ASCIA) website has a treatment plan for allergic rhinoconjunctivitis that can be downloaded (www.allergy.org.au/patients/allergic-rhinitis-hay-fever-and-sinusitis/allergic-rhinitis-treatment-plan).

Table 1 provides an overview of currently available therapies. Of these, antihistamines, intranasal corticosteroids and immunotherapy will be discussed further here. Allergen avoidance for pollens is difficult as the pollen is airborne from a wide area so management of a local environment may have little or no effect. Dust mite avoidance remains controversial in terms of efficacy, partly because factors affecting exposure are poorly understood.[14]

Antihistamines

Antihistamines work best on the symptoms of sneezing, itch and rhinorrhoea and less well on nasal obstruction. Four

TABLE 1. THERAPIES FOR ALLERGIC RHINOCONJUNCTIVITIS

Treatment	Route of administration	Comments
Allergen avoidance	–	Not practical for pollens Multiple modalities needed for house dust mite
Antihistamines	Systemic, intranasal, ocular	Useful for mild rhinitis Ineffective for nasal obstruction Can treat both nasal and ocular symptoms
Corticosteroids	Systemic	For short-term use only
	Intranasal	Effective long-term option
	Ocular	For short-term use only
Decongestants	Systemic	For short-term use only
	Topical (intranasal)	For short-term use only
Sodium cromoglycate	Topical (intranasal, intraocular)	Frequent dosing needed
Immunotherapy	Subcutaneous immunotherapy, sublingual immunotherapy, sublingual grass pollen extract (tablet)	Specific antiallergy therapy
Cellulose, microionised powder	Intranasal	Acts as a barrier to allergen deposition
Phototherapy, ultraviolet A and B	Intranasal	Needs further evaluation Available through selected practitioners
Saline	Intranasal spray, irrigation	Some benefit demonstrated
Surgery	Nasal	Useful in selected cases only, does not remove the allergic diathesis Procedures include inferior turbinate reduction, functional endoscopic sinus surgery, correction of nasal septal deformity and vidian neurectomy
Antileukotriene receptor antagonist (montelukast)	Systemic	Effective, expensive
IgE-selective humanised monoclonal antibody (omalizumab)	Subcutaneous injection	Effective but currently only available on PBS for severe asthma
Complementary medicine	Herbal, acupuncture	Doubtful efficacy

histamine receptors (H_1, H_2, H_3 and H_4) have been identified but so far only blockers of the H_1-receptor are used clinically for allergic rhinoconjunctivitis. These are available in Australia as the first generation (older) antihistamines and the second generation or new antihistamines. The second generation antihistamines are poorly absorbed via the blood–brain barrier and have minimal effects on sedation or impairment of psychomotor performance, and for this reason this class of H_1-antihistamines is preferred.

The first generation medications available in Australia are pheniramine, promethazine, dexchlorpheniramine, trimeprazine and doxepin. Pheniramine and dexchlorpheniramine both have a Category A rating for use in pregnancy whereas the others are Category C. Promethazine is the only systemic preparation of antihistamine. Several of the first generation antihistamines can be used in children aged 2 years and older. Onset of action is generally one to two hours (based on wheal and flare suppression) and dosing is greater than once daily.

The second generation antihistamines available in Australia include loratadine, desloratadine, fexofenadine, cetirizine and

TABLE 2. INTRANASAL CORTICOSTEROIDS FOR ALLERGIC RHINOCONJUNCTIVITIS

Corticosteroid	Spray/drops	Schedule*	Pregnancy category†	Use in children
Beclomethasone dipropionate	Spray	S2	B3	12 years and over
Budesonide	Spray	S2, S4	A	6 years and over or 12 years and over, depending on preparation
Ciclesonide	Spray	S4	B3	12 years and over
Fluticasone propionate	Spray, drops	S2 (sprays); S4 (drops)	B3	12 years and over
Mometasone furoate	Spray	S4	B3	3 years and over
Fluticasone furoate	Spray	S4	B3	2 years and over
Triamcinolone	Spray	S2	B3	12 years and over

* S2 = Pharmacy Medicine; S4 = Prescription Only Medicine.

† Pregnancy Category A = Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed; Category B3 = Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

levocetirizine. Cetirizine and levocetirizine have a faster onset of action (one hour) than the other agents; all are given once daily.[24] Loratadine syrup can be used in children aged 1 year and older but other preparations are for those aged 6 years and older or 12 years and older. All are Category B1 or B2-rated for use in pregnancy. Topical intranasal or ocular preparations are available and generally have a faster onset of action; these include olopatadine, azelastine, ketotifen and levocabastine.

In trials, antihistamines will produce a 70% improvement in clinical symptom score compared with placebo, which produces a 30 to 50% symptom improvement. Before the introduction of generic brands, antihistamines tablets cost about $1.00 each but now tablets of the second generation antihistamines are upwards of 40 cents and those of first generation antihistamines are about half that price (first generation antihistamines, however, require more frequent dosing).

Intranasal corticosteroids

In Australia there are seven different intranasal corticosteroid preparations currently available on prescription and over-the-counter (Table 2). The price of intranasal corticosteroids varies but ranges from 5 cents a spray to 50 cents a spray. In the future, combined antihistamines plus intranasal corticosteroids and intranasal corticosteroids plus decongestants are likely to be available. Intranasal corticosteroids are generally more cost-effective than antihistamines for allergic rhinoconjunctivitis.

Although all the intranasal corticosteroids have similar general efficacy, the older ones (triamcinolone, beclomethasone and budesonide) have greater bioavailability (31 to 46%) compared with the newer ones (mometasone, fluticasone, ciclesonide; less than 1% bioavailability). The newer intranasal corticosteroids hence have a better side effect profile, especially when the total corticosteroid dose delivered to both upper and lower airway is considered.[25] It has been suggested that fluticasone furoate has a faster onset of action and controls ocular symptoms better.

Fluticasone furoate and mometasone furoate are the only intranasal corticosteroids that can be used in children as young as 2 to 3 years of age.

Ciclesonide is available in a nasal spray formulation for upper airway use (as well as in a formulation for inhalation in asthma prevention). Ciclesonide is a prodrug and is activated by airway intracellular esterases. The hypotonic nasal spray formulation has been shown to promote nasal retention and absorption of the prodrug. As ciclesonide has not been compared head to head with other intranasal corticosteroids, it is not known whether these properties translate into clinical superiority.[26]

Immunotherapy

The efficacy of immunotherapy depends on selection of the right patients, the correct dose and the appropriate dose of allergen. Effective immunotherapy can provide over 40% improvement in symptoms of both asthma and allergic rhinoconjunctivitis, with similar effects in adults and children.[27]

The range of allergen formulations available for immunotherapy includes rapid-acting preparations and slow-release

TABLE 3. SCIT AND SLIT COMPARED

Feature	SCIT	SLIT
Time to complete therapy	Three to five years	Three to five years
Uptitration	10 weeks	Nil to one week, depending on preparation
Route of administration	Injection	Sublingual
Administration	Under medical supervision	Self
Refrigeration	Yes	Yes/no, depending on preparation
Approximate cost per year	$560.00	$760 to $1160, depending on preparation
Local side effects	50% of patients	20-30% of patients
Systemic side effects	0.13% of patients	Rare
Use of multiple allergens	Yes	Limited

ABBREVIATIONS: SCIT = subcutaneous immunotherapy; SLIT = sublingual immunotherapy.

preparations for subcutaneous immunotherapy (SCIT), oral solutions for sublingual immunotherapy (SLIT) and, more recently, a sublingual tablet containing grass pollen extract. A tablet containing house dust mite allergen is likely to be available in the next one to two years.

In the past 10 years there has been increased use of SLIT in Australia, and currently there is about equal usage of subcutaneous and sublingual therapies. The similarities and differences between the two therapies are summarised in Table 3. Most sublingual immunotherapy is for house dust mite allergy; when it is for grass allergy, about three-quarters of the grass mixes used contain a tropical grass. The sublingual route offers a more convenient mode of delivery and greater safety but is more expensive.

Most patients are polysensitised to allergens, with monosensitisation to house dust mite allergen occurring in 6% and to grass pollen in 2.4%. About 7% of those allergic to grass pollen are sensitised to temperate grass pollens alone (local Sydney data courtesy of Professor Katelaris, University of Western Sydney, Sydney). This is of relevance when selecting subjects for treatment with the grass pollen extract tablet, which was developed in Europe and contains a mix of five temperate grasses (ryegrass, timothy grass, sweet vernal grass, meadow grass/Kentucky bluegrass and cocksfoot). In other words, this product is not effective if allergic rhinoconjunctivitis is due to tropical grasses, as is often the case in Australia. Additionally, patients who are polysensitised may need to use a mixed extract or two or more separate extracts; the latter is thought to be more efficacious.

SLIT shows evidence of onset of action after 30 days of treatment.[28] The length of benefit of immunotherapy is not extensively studied but improvements up to 12 years have been documented.[29,30] There is a suggestion that SCIT is slightly more efficacious than SLIT, at least for allergic rhinoconjunctivitis due to grass pollen, and that allergen monotherapy may be more effective.[31]

Immunotherapy is contraindicated in patients who are taking beta blockers (oral and ocular preparations) or have unstable asthma and in the presence of an autoimmune disease. It should not be commenced during pregnancy but can be continued through a pregnancy and during breastfeeding.

CONCLUSION

Allergic rhinoconjunctivitis continues to be a significant health problem in Australia. It is acknowledged that, especially in those individuals with moderate to severe disease, nasal and ocular symptoms are accompanied by systemic symptoms such as poor sleep quality, fatigue and irritability. Allergy assessment continues to be a cornerstone for the diagnosis and is essential for the facilitation of immunotherapy. MT

REFERENCES

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

COMPETING INTERESTS: Dr Rimmer has participated in the Avamys Advisory Board.

Allergic rhinoconjunctivitis returns

The new spring season 2013

JANET RIMMER MD, MB BS, FRACP

REFERENCES

1. Ring J, Akdis H, Lauener R-P, et al. Davos declaration: allergy as a global problem. Allergy 2012; 67: 141-143. Erratum: Allergy 2012; 67: 712.
2. Australian Institute Health and Welfare (AIHW). Allergic rhinitis ('hay fever') in Australia. Cat. no. ACM 23. Canberra: AIHW; 2011. Available online at: www.gov.au/asthma/2007-2008 (accessed September 2013).
3. Ciprandi G, Cirillo I, Vizzaccaro T, et al. Seasonal and perennial allergic rhinitis: is this classification adherent to real life? Allergy 2005: 60: 882-887.
4. Bachert C, van Cauwenberge P, Khaltaev N; WHO. Allergic rhinitis and its impact on asthma. Executive summary of the workshop report. 7-10 December 1999, Geneva, Switzerland. Allergy 2002; 57: 841-855. Erratum in Allergy 2002; 57: 1208. (Bousquet, J [corrected to Bachert, C].)
5. Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol 2010; 126: 466-476.
6. Bousquet J, Reid J, van Weel C, et al Allergic rhinitis management pocket reference 2008. Allergy 2008; 63: 990-997.
7. Bjorksten B, Clayton T, Ellwood P, Stewart A, Strachan D; ISAAC Phase 111 Study Group. Worldwide time trends for symptoms of rhinitis and conjunctivitis: phase 111 of the International Study of Asthma and Allergies in Childhood. Pediatr Allerg Immunol 2008; 19: 110-124.
8. Katelaris CH, Lee BW, Potter PC, et al. Prevalence and diversity of allergic rhinitis in regions of the world beyond Europe and North America. Clin Exp Allergy 2012; 42: 186-207.
9. Leung RC, Carlin JB, Burdon JG, Czarny D. Asthma, allergy and atopy in Asian migrants in Melbourne. Med J Aust 1994; 161: 418-425.
10. Sercombe JK, Green BJ, Rimmer J, Burton PK, Katelaris CH, Tovey ER. London plane tree bioaerosol and allergenic sensitization in Sydney, Australia. Ann Allergy Asthma Immunol 2011; 107: 493-500.
11. Andersson M, Downs S, Mitakakis T, Leuppi J, Marks G. Natural exposure to Alternaria spores induces allergic rhinitis symptoms in sensitized children. Pediatr Allergy Immunol 2003; 14: 100-105.
12. Downs SH, Mitakakis TZ, Marks GB, et al. Clinical Importance of Alternaria exposure in children Am J Respir Crit Care Med 2001; 164: 455-459.
13. Crisafulli D, Almqvist C, Marks GB, Tovey ER. Seasonal trends in house dust mite allergen in children's beds over a 7-year period. Allergy 2007; 62: 1394-1400.
14. Tovey ER, Willenborg CM, Crisafulli DA, Rimmer J, Marks GB. Most personal exposure to house dust mite aeroallergen occurs during the day. PLoS One 2013; 8: e69900.
15. Verguts MM, Eggermont A, Decoster W, de Jong FI, Hellings PW. Laryngeal effects of nasal allergen provocation in singers with allergic rhinitis. Eur Arch Otorhinolaryngol 2011; 268: 419-427.
16. Rimmer J, Downie S, Bartlett, Gralton J, Salome C. Sleep disturbance in perennial allergic rhinitis: measured by actigraphy. Ann Allergy Asthma Immunol 2009; 103: 190-194.
17. De la Hoz Caballer B, Rodriguwz M, Fraj J, Cerecedo I, Antolin-AMerigo D, Colas C. Allergic rhinitis and its impact on work productivity in primary care practice and a comparison with other diseases: the CAPRI study. Am J Rhinol Allergy 2012; 26: 390-394.
18. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. Clin Exp Allergy 1991; 21: 77-83.
19. Hellings PW, Fokkens WJ, Akdis C, et al. Uncontrolled allergic rhinitis and chronic rhinosinusitis: where do we stand today? Allergy 2012: 68: 1-7.
20. Bukstein D, Luskon AT, Farrar JR. The reality of adherence to rhinitis treatment: identifying and overcoming barriers. Allergy Asthma Proc 2011; 32: 265-271.
21. Nabi S, Rotenberg BW, Vukin I, Payton K, Bureau Y. Nasal spray adherence after sinus surgery: problems and predictors. J Otolaryngol Head Neck Surg 2012; 41 Suppl 1: S49-S55.
22. Sahiner UM, Civelek E, Yavuz ST, Buyuktiryaki AB, Tuncer A, Sekerek BE. Skin prick testing to aeroallergen extracts: what is the optimal panel in children and adolescents in Turkey? Int Arch Allergy Immunol 2012; 157: 391-398.
23. Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology 2012; 50: 1-12.
24. Holgate ST, Adkinson NF, Busse WW, et al. Middleton's allergy: principles and practice, 7th ed. Philadelphia: Mosby; 2008.
25. Rimmer J, Katelaris C. Allergic rhinitis: focus on the intranasal route of fluticasone furoate. Clin Med Rev Therapeut 2010: 2 July 14 (doi: 10.4137/CMRT.S1606).
26. Sato H, Nave R, Nonaka T, et al. Uptake and metabolism of ciclesonide and retention of desisobutyryl-ciclesonide for up to 24 hours in rabbit mucosa. BMC Pharmacol 2007; 7: 2210-2217.
27. Lin SY, Erekosima N, Kim JM, et al. Sublingual immunotherapy for the treatment of allergic rhinoconjunctivitis and asthma. a systematic review. JAMA 2013; 309: 1278-1288.
28. Horak F, Zieglmayer P, Zieglmayer R, et al. Early onset of action of a 5-grass pollen 300-IR sublingual immunotherapy tablet evaluated in an allergen challenge chamber. J Allergy Clin Immunol 2009; 124: 471-477.
29. Niggemann B, Jaconsen L, Dreborg S, et al. Five-year follow-up on the PAT study: specific immunotherapy and long term prevention of asthma in children. Allergy 2006; 61: 855-859.
30. Eng PA, Borer-Reinhold M, Heijnen IA, Gnehm IP. Twelve-year follow-up after discontinuation of preseasonal grass pollen immunotherapy in childhood. Allergy 2006; 61: 198-201.
31. Di Bona D, Plaia A, Leto-Barone MS, La Piana S, Di Lorenzo G. Efficacy of subcutaneous and sublingual immunotherapy with grass allergens for seasonal allergic rhinitis: a meta-analysis-based comparison. J Allergy Clin Immunol 2012: 130: 1097-1107.