



VERSION 2.0 CLINICAL ISSUES

Allergies

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ABBREVIATIONS

CFC	chlorofluorocarbon
COPD	chronic obstructive pulmonary disease
СОХ	cyclo-oxygenase
DXA	dual-energy X-ray absorptiometry
ED	emergencydepartment
EIB	exercise-induced bronchoconstriction
FEV ₁	forced expiratory volume overone second
FEV ₆	forced expiratory volume over six seconds
FSANZ	Food Standards Australia and New Zealand
FVC	forcedvitalcapacity
GORD	gastro-oesophageal reflux disease
HFA	formulated with hydrofluroalkane propellant
ICS	inhaled corticosteroid
ICU	intensive care unit
lgE	ImmunoglobulinE
IL	interleukin
IU	international units
IV	intravenous
LABA	${\sf long-acting beta_2-adrenergic receptor agonist}$
LAMA	long-acting muscarinic antagonist

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NATIONAL ASTHMA COUNCIL AUSTRALIA

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Suite 104, Level 1 153-161 Park Street South Melbourne VIC 3205 Australia **LTRA** leukotriene receptor antagonist MBS Medical Benefits Scheme National Health and Medical Research Council NHMRC **NIPPV** non-invasive positive pressure ventilation **NSAIDs** nonsteroidal anti-inflammatory drugs OCS oral corticosteroids OSA obstructive sleep appoea PaCO carbon dioxide partial pressure on blood gas analysis PaO oxygen partial pressure on blood gas analysis PBS **Pharmaceutical Benefits Scheme** PEF peak expiratory flow pressurised metered-dose inhaler or 'puffer' pMDI PPE personal protective equipment **SABA** short-acting beta2-adrenergic receptor agonist SAMA short-acting muscarinic antagonist SaO₂ oxygen saturation peripheral capillary oxygen saturation measured SpO₂ by pulse oximetry TGA Therapeutic Goods Administration

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Allergies and asthma

Overview

Asthma and allergies are closely linked. Most people with asthma have allergic asthma.

Allergy testing is not mandatory as part of the diagnostic process for patients with suspected asthma, but may be indicated when identifying allergens will guide management or when other clinically significant allergies are suspected (e.g. food allergies). It may also be useful when considering the prognosis for wheezing infants.

The appropriate investigation of allergies depends on the individual's risk. For patients with severe or unstable asthma, or a history of anaphylaxis, referral to a specialist for investigation is recommended to minimise risk.

In addition to the principles of asthma management that generally apply to all patients with asthma, effective management of allergic asthma involves:

- management of allergies, including investigating and treating allergic rhinitis if present
- avoidance of relevant allergic triggers, where practical and shown to be effective
- specific allergen immunotherapy, where indicated and shown to be effective.
- See: <u>Diagnosing asthma in children</u>
 - See: <u>Diagnosing asthma in adults</u>
 - See: Managing asthma in children
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Assessing allergies to guide asthma management

Recommendations

When taking a history in a patient with suspected asthma, ask about allergies, and the circumstances and timing of symptoms.

How this recommendation was developed Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Assess and manage the risk of thunderstorm asthma.

O. How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• NACA, 2017¹

When performing a physical examination in a patient with suspected asthma, inspect the upper airway for signs of allergic rhinitis (e.g. swollen turbinates, transverse nasal crease, reduced nasal airflow, mouth breathing, darkness and swelling under eyes caused by sinus congestion).

O How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider allergy testing as part of diagnostic investigations if you suspect allergic triggers, or to guide management.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider allergy tests (skin prick test or specific IgE assay) for common aeroallergens for children with recurrent wheezing when the results might guide you in (either of):

- assessing the prognosis (the presence of allergies in preschool children increases the probability that the child will have asthma at primary school age)
- managing symptoms (e.g. advising parents/carers about management if avoidable allergic triggers are identified).

Notes: Allergy tests are not essential in the diagnostic investigation of asthma in children. The finding of allergic sensitisation on skin-prick testing or specific IgE does not necessarily mean that it is clinically important.

Blood test (immunoassay for allergen-specific immunoglobulin E) can be used if skin prick testing is unavailable, impractical or inappropriate.

O How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If allergy testing is needed, refer to an appropriate provider for skin prick testing for common aeroallergens.

Notes

If staff are trained in the skin prick test procedure and its interpretation, skin prick testing can be performed in primary care. If not, refer to an appropriate provider.

When performing skin prick testing, follow Australasian Society of Clinical Immunology and Allergy (ASCIA) guidance: <u>Skin prick testing for the</u> <u>diagnosis of allergic disease. A manual for practitioners</u>



How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• Australasian Society of Clinical Immunology and Allergy, 2013²

Blood test (immunoassay for allergen-specific immunoglobulin E) can be used if skin prick testing is (any of):

- unavailable
- impractical (e.g. a patient who is unable to cooperate with test procedure, a patient taking antihistamines when these cannot be withdrawn, or a patient taking tricyclic antidepressants or pizotifen)
- contraindicated (e.g. patients with severe dermatographism, extensive skin rash, or those at risk of anaphylaxis including patients with occupational asthma due to latex sensitivity).



How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• Australasian Society of Clinical Immunology and Allergy, 2013²

To investigate allergies in a person with severe or unstable asthma, or a history of anaphylaxis, refer to a specialist allergist for investigation to minimise risk.

O How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• Australasian Society of Clinical Immunology and Allergy, 2013²

Consider offering referral to an appropriate specialist (e.g. respiratory physician, occupational physician or allergist) for patients with:

- suspected or confirmed work-related asthma
- other significant allergic disease (e.g. suspected food allergies or severe eczema).



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If patients are likely to visit practitioners who offer alternative diagnostic tests, explain that none of the following alternative diagnostic practices should be used in the diagnosis of asthma or allergies:

- cytotoxic testing (Bryans' or Alcat testing)
- hair analysis
- iridology

- kinesiology
- oral provocation and neutralisation
- pulse testing
- radionics (psionic medicine, dowsing)
- tests for 'dysbiosis'
- vega testing (electrodermal testing)
- VoiceBio.

O How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• Australasian Society of Clinical Immunology and Allergy, 2007³

More information

Allergies and asthma: links

There is a strong link between asthma and allergies:^{4, 5}

- The majority of people with asthma have allergies.
- Immunoglobulin E-mediated sensitisation to inhalant allergens is an important risk factor for developing asthma, particularly in childhood.
- In individuals with asthma, exposure to relevant allergens can worsen asthma symptoms and trigger flare-ups, including severe acute asthma.
- Allergens are a common cause of occupational asthma.

Although atopic sensitisation increases the risk of developing asthma, most people who are allergic to inhalant allergens or food allergens do not have asthma.⁵ Among people with food allergies, asthma may be a risk factor for fatal anaphylaxis due to food allergens.^{6, 7} However, foods are rarely a trigger for asthma symtpoms.

Neither asthma nor allergy is a single disease – each has multiple phenotypes and is a complex of several different diseases with different aetiologies, genetic risk factors and environmental risk factors.⁴

See: Work-related asthma

Go to: National Asthma Council Australia's Asthma and allergy information paper

Links between allergic rhinitis and asthma

Prevalence, aetiology and symptoms

Asthma and allergic rhinitis frequently coexist. At least 75% of patients with asthma also have rhinitis, although estimates vary widely.⁸ Patients with asthma may have both allergic and non-allergic rhinitis.

Allergic rhinitis that starts early in life is usually due to a classical IgE hypersensitivity. Adult-onset asthma or inflammatory airway conditions typically have more complex causes. Chronic rhinosinusitis with nasal polyps is not a simple allergic condition and generally needs specialist care.⁹

Symptoms and signs of allergic rhinitis can be local (e.g. nasal discharge, congestion or itch), regional (e.g. effects on ears, eyes, throat or voice), and systemic (e.g. sleep disturbance and lethargy). Most people with allergic rhinitis experience nasal congestion or obstruction as the predominant symptom. Ocular symptoms (e.g. tearing and itch) in people with allergic rhinitis are usually due to coexisting allergic conjunctivitis.¹⁰

Patients may mistake symptoms of allergic rhinitis for asthma and vice versa. Allergic rhinitis is sometimes more easily recognised only after asthma has been stabilised.

► Go to: National Asthma Council Australia's Managing allergic rhinitis in people with asthma information paper

Effects on asthma

Allergic rhinitis is an independent risk factor for developing asthma in children and adults.^{11, 12, 13, 14, 15} However, the use of antihistamines in children has not been shown to prevent them developing asthma.⁸

The presence of allergic rhinitis is associated with worse asthma control in children and adults.^{16, 17, 18, 19} The use of intranasal corticosteroids in patients with concommitant allergic rhinitis and asthma may improve asthma control in patients who are not already taking regular inhaled corticosteroids.²⁰

Both rhinitis and asthma can be triggered by the same factors, whether allergic (e.g. house dust mite, pet allergens, pollen, cockroach) or non-specific (e.g. cold air, strong odours, environmental tobacco smoke).

Food allergies do not cause allergic rhinitis. Most people with allergic rhinitis are sensitised to multiple allergens (e.g. both pollens and house dust mite), so symptoms may be present throughout the year.

Pollens (e.g. grasses, weeds, trees) and moulds are typically seasonal allergens in southern regions, but can be perennial in tropical northern regions.²¹ However, ryegrass is not found in tropical regions (see <u>Thunderstorm asthma</u>).

Pollen calendars provide information on when airborne pollen levels are likely to be highest for particular plants.

Thunderstorm asthma

Seasonal allergic rhinitis, which in Australia is typically associated with sensitisation to perennial ryegrass (*Lolium perenne*), is an important risk factor for thunderstorm asthma.²²

Go to: ASCIA's Pollen calendar

Go to: National Asthma Council Australia's Epidemic thunderstorm asthma information paper

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Treatment of allergic rhinitis in adults and adolescents

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/102

Intranasal corticosteroids

If continuous treatment is required, an intranasal corticosteroid is the first-choice treatment unless contraindicated. Intranasal corticosteroids are more effective in the treatment of allergic rhinitis than other drug classes including oral H₁-antihistamines, intranasal H₁-antihistamines and montelukast.^{20, 8, 23} Intranasal corticosteroid are most effective when taken continuously.²⁰

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in adults and adolescents with allergic rhinitis.^{20, 8} They are also effective for ocular symptoms.²⁴

All available intranasal corticosteroids appear to be equally effective.²⁰

The onset of action is between 3 and 36 hours after first dose and, in practice, the full therapeutic effect takes a few days.²⁵

The addition of an oral H_1 -antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more effective than intranasal corticosteroid monotherapy.²³

Intranasal corticosteroids are well tolerated. Common (>1%) adverse effects include nasal stinging, itching, nosebleed, sneezing, sore throat, dry mouth, cough.²⁶ Nose bleeds are usually due to poor spray technique or crusting. Evidence from studies mainly in adults suggests that intranasal corticosteroids do not cause atrophy of nasal epithelium.²⁷

Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects when given in recommended doses.^{20, 28} Studies in adults evaluating effects on the hypothalamic-pituitary axis using morning cortisol concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion show no adverse effects with beclomethasone dipropionate, budesonide, ciclesonide, fluticasone propionate, fluticasone furoate, or triamcinolone acetonide.²⁰

In patients with asthma already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be taken into account when calculating the total daily corticosteroid dose. Drug-drug interactions (e.g. with CYP3A4 inhibitors such as such as erythromycin, clarithromycin, ritonavir and itraconazole) may change the metabolism or increase absorption of corticosteroids administered by any route, increasing the risk of adrenal suppression.²⁶

Combination intranasal corticosteroid plus intranasal antihistamines

Combined intranasal fluticasone propionate and azelastine hydrochloride in a single device is more effective than fluticasone propionate alone for a range of nasal and ocular symptoms.^{20, 23, 22}

The onset of therapeutic action is approximately 30 minutes after dosing.²²

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference

to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.²⁹

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms.^{23, 30} They can provide adequate relief for some individuals when taken continuously or intermittently.²⁰ Available agents appear to be equally effective.²⁸

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{20, 31} In adults with allergic rhinitis, oral antihistamines usually produce no further improvement when added to intranasal corticosteroid treatment.²⁰

Common (>1%) adverse effects include drowsiness, fatigue, headache, nausea and dry mouth.²⁶ Oral antihistamines can also cause ocular dryness.³²

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H_1 -antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.⁸

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.²⁰ They have a rapid onset of action (15–30 minutes).²⁰

The most common (>1%) adverse effect is local irritation.²⁶ Bitter taste is more common intranasal antihistamines than with intranasal corticosteroids.²⁰

Montelukast

Leukotriene receptor antagonists are no more effective than oral H_1 -antihistamines.^{8, 23} Montelukast is less effective than intranasal corticosteroid in the treatment of allergic rhinitis.^{20, 8} In most studies, adding montelukast to an intranasal corticosteroid was not more effective than intranasal corticosteroid alone.²³

Montelukast is approved by TGA for treatment of in adults with asthma or seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{33, 34, 35, 36, 37} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares, depression, and aggression.³⁷ Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.³⁷

Other nasal sprays

Ipratropium bromide spray is effective in managing persistent rhinorrhoea in patients with allergic rhinitis, but not blockage or itch.⁸ It is indicated for use in adults and adolescents over 12 years old.

Intranasal sodium cromoglycate is less effective than intranasal corticosteroids, but is effective in some patients for prevention and treatment of allergic rhinitis and is associated with minimal adverse effects.²⁸

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

► Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Treatment of allergic rhinitis in children

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/102

Intranasal corticosteroids

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in school-aged children with allergic rhinitis.^{20, 8} However, there is weaker evidence to support their efficacy in children than in adults.⁸ There is limited evidence to guide the treatment of allergic rhinitis in preschool children.²³

The addition of an oral H₁-antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more

effective than intranasal corticosteroid monotherapy.²³

TGA-approved indications vary between age groups. Intranasal corticosteroids indicated for children aged under 12 years include fluticasone furoate (age 2 years and over), mometasone furoate (age 3 years and over), and budesonide (age 6 years and over).

Intranasal corticosteroids are well tolerated. Evidence from studies mainly in adults suggests that they do not cause atrophy of nasal epithelium.³⁸ Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects in children when given in recommended doses.²⁰²⁸ Studies in children evaluating effects on the hypothalamic-pituitary axis using morning cortisol concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion showed no adverse effects with ciclesonide, fluticasone propionate, fluticasone furoate, mometasone furoate, or triamcinolone acetonide.²⁰ One knemometry study showed reduced lower leg growth rate in children using intranasal budesonide.²⁰ In studies using stadiometry over 12 months, higher-than-recommended doses of intranasal beclomethasone dipropionate were associated with growth suppression, but fluticasone propionate and mometasone furoate showed no effects on growth compared with placebo.²⁰

In children already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be taken into account when calculating the total daily corticosteroid dose.

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.²⁹

These antihistamines can be taken long term by children. Eighteen months of treatment with cetirizine was well tolerated in a large, prospective, multi-country, randomised controlled trial in infants with atopic dermatitis aged 12–24 months.²⁰

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms,^{23, 30} including in preschool children. ²³ They can provide adequate relief for some individuals when taken continuously or intermittently.²⁰ Available agents appear to be equally effective.²⁸

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{20, 31} The addition of oral antihistamines to intranasal corticosteroids has not been demonstrated to be an effective strategy in children.³⁹

TGA-approved indications vary between age groups. Less sedating oral antihistamines indicated for children under 12 years include cetirizine (1 year and over), loratatidine (1 year and over), desloratadine (6 months and over), and fexofenadine (6 months and over).

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H_1 -antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.⁸

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.²⁰ They have a rapid onset of action (15–30 minutes).²⁰

Montelukast

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Montelukast is approved by TGA for the treatment of asthma in children over 2 years, and for the treatment of seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{33, 34, 35, 36} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares (especially in children), depression, and aggression (especially in children).³⁷ Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.³⁷

The potential association of montelukast with behaviour-related adverse events should be mentioned to parents when commencing treatment, and treatment should be stopped if such adverse events are suspected.

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

► Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Non-recommended medications for allergic rhinitis

Intranasal decongestants have a limited role in the management of allergic rhinitis because they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa (rhinitis medicamentosa), which can lead to dose escalation by patients, with a risk of atrophic rhinitis. Intranasal decongestants can be considered for a patient with severe nasal congestion to gain rapid relief of symptoms until the full effect of intranasal corticosteroids is achieved.

Oral decongestants (e.g. pseudoephedrine or phenylephrine) should not generally be used in the management of allergic rhinitis. They are indicated for short-term use only (e.g. acute infectious rhinitis, or during air travel by a patient with symptomatic rhinitis, as a single tablet taken one hour before landing). They are associated with adverse effects including palpitations, tachycardia and insomnia.

Oral corticosteroids should be avoided as a treatment for allergic rhinitis. In exceptional circumstances, their use might be considered in consultation with an allergy specialist.

Topical ocular alpha agonist vasoconstrictors (including in combination with antihistamines) should not be used for allergic conjunctivitis because they can cause conjunctivitis medicamentosa.

Nasal saline irrigation for allergic rhinitis

Nasal irrigation (via a syringe, rinse bottle, spray or other device) can improve nasal symptoms, mucociliary clearance, and quality of life.⁴⁰ Saline administered by spray or other devices was used at least twice daily in most studies that showed a benefit.⁴⁰

Isotonic solution is preferable to hypertonic solution because it supports optimal mucociliary clearance.⁴⁰ Isotonic saline is solution is inexpensive and has no known adverse effects.⁴⁰ Patients can use either commercially manufactured saline solutions or home-made normal saline: 1 teaspoon (5 g) rock or sea salt in 500 mL of water (preferably bottled or boiled).

There is not enough evidence to determine:

- whether solutions should be buffered or non-buffered, sterile or non-sterile
- whether various additives provide any advantage
- whether inhaling steam or an irritant decongestant (e.g. eucalyptus, menthol) before saline irrigation provides any extra benefit. However, patients are more likely to adhere to simple and convenient regimens, regardless of theoretical advantages. Caution is required with steam inhalation to avoid burns.

If patients are using both saline irrigation and an intranasal corticosteroid or intranasal H₁-antihistamine, they should perform saline irrigation first. Saline can be used again after waiting at least an hour after using an intranasal corticosteroid.

Young children are unlikely to tolerate nasal irrigation.

Surgical turbinate reduction

Turbinate reduction surgery can be considered when nasal obstruction is due to turbinate hypertrophy and symptoms do not respond to medical treatment. It should not be performed in young children except after thorough investigation and review.

Inferior turbinate hypertrophy secondary to inflammation is a common cause of nasal obstruction in patients with allergic rhinitis.⁴¹ Several surgical procedures are available to correct this problem.⁴² The ideal surgical reduction should preserve the mucosa and physiological function.⁴¹

Short-term adverse outcomes of inferior turbinate reduction include nasal bleeding, scarring and crusting. Rarely, it may worsen symptoms when patients have non-specific rhinitic conditions or sino-nasal somatisation disorders ('empty nose syndrome').⁴² There is no evidence that turbinate surgery creates these conditions, but sino-nasal surgery may exacerbate the symptoms.

Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.^{3,5,6,8,9}

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.^{3, 5} Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.³

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.^{1, 9, 10}

Data from thunderstorm asthma epidemics suggest that the risk of asthma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known asthma).³

The worst outcomes are seen in people with poorly controlled asthma.¹ Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.⁵

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.¹¹

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.⁴

Go to: National Asthma Council Australia's <u>Epidemic thunderstorm asthma</u> information paper Go to: ASCIA's <u>Pollen calendar</u>

Go to: <u>Vic Emergency's Thunderstorm asthma forecast (Victoria only)</u>

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Allergy tests in adults with asthma

Allergy tests have a very limited role in the clinical investigation of asthma. They may be useful to guide management if the patient is sensitised to aeroallergens that are avoidable and avoidance has been shown to be effective, or in the investigation of suspected occupational asthma.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) recommends skin prick testing as the first-choice method for investigating allergies in a person with asthma.²

Patients who need allergy tests are usually referred to a specialist for investigation. GPs with appropriate training and experience can also perform skin prick tests for inhalent allergens, if facilities to treat potential systemic allergic reactions are available, or arrange for allergy tests (skin prick testing or blood tests) to be performed by an appropriate provider. Skin prick testing for food allergens should only be performed in specialist practices.

Asthma, particularly uncontrolled or unstable asthma, may be a risk factor for anaphylaxis during skin prick testing;² however, anaphylaxis due to skin prick testing is extremely rare. As a precaution, ASCIA advises that skin prick testing in people with severe or unstable asthma should be performed only in specialist practices.² ASCIA's manual on skin prick testing lists other risk factors.²

Go to: Australasian Society of Clinical Immunology and Allergy Skin Prick Testing Working Party's <u>Skin prick testing for the diagnosis of allergic disease. A manual for practitioners</u>

Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

Allergy tests in children

Skin-prick testing

Allergy tests have a very limited role in the clinical investigation of asthma. They may be useful to guide management if the child is sensitised to aeroallergens that are avoidable (e.g. advise parents against getting a cat if skin-prick testing has shown that the child is sensitised to cat allergens, or advise parents that there is no need to remove a family pet if the child is not sensitised).

Skin-prick testing is the recommended test for allergies in children.

Risk factors for anaphylaxis during skin prick testing are thought to include asthma (particularly uncontrolled or unstable asthma), age less than 6 months, and widespread atopic dermatitis in children.² As a precaution, the Australasian Society of Clinical Immunology and Allergy (ASCIA) advises that skin prick testing should be performed only in specialist practices for children under 2 years and children with severe or unstable asthma.² ASCIA's manual on skin prick testing lists other risk factors.²

► Go to: Australasian Society of Clinical Immunology and Allergy Skin Prick Testing Working Party's Skin prick testing for the diagnosis of allergic disease. A manual for practitioners

Total serum IgE testing

In children aged 0–5 years, total serum immunoglobulin E measurement is a poor predictor of allergies or asthma.⁴³

Specific serum IgE testing

Among children aged 1-4 years attending primary care, those with raised specific IgE for inhaled allergens (e.g. house dust mite, cat dander) are two-to-three times more likely to have asthma at age 6 than non-sensitised children.⁴³ Sensitisation to hen's egg at the age of 1 year (specific IgE) is a strong predictor of allergic sensitisation to inhaled allergens at age 3 years.⁴³

See: <u>Allergies and asthma</u>

Pet allergens

Contact with pets (e.g. cats, dogs and horses) can trigger asthma, mainly due to sensitisation to allergens in sebum or saliva. Exposure can trigger flare-ups or worsen symptoms.⁴

The amount of allergen excreted differs between breeds.⁴ Although some breeders claim that certain breeds of dogs are less likely to trigger asthma ('hypoallergenic' breeds), allergen levels have not been shown to be lower in the animal's hair or coat,⁴⁴ or in owner's homes⁴⁵ with these breeds than other breeds.

Cat allergens easily spread on clothing and are found in places where cats have never been.⁴

The most effective method of allergen avoidance for people with asthma who are allergic to cats or dogs is to not have these pets in the home. However, the allergen can persist for many months, or even years, after the pet has been removed.⁴

There is not enough clinical trial evidence to determine whether or not air filtration units are effective to reduce allergen levels in the management of pet-allergic asthma.⁴⁶

Other strategies for reducing exposure to pet allergens include:

- washing hands and clothes after handling pets
- washing clothes and pet bedding in hot water (> 55°C)
- frequent vacuuming of the home using a vacuum with a HEPA filter
- cleaning hard floors with a damp/antistatic cloth or a steam mop, and cleaning air-conditioning or heating ducts
- grooming pets regularly (where possible, the patient should be absent while this occurs), and washing pets regularly, but no more than the vet recommends.
- ► Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

House dust mite

Exposure to house dust mite (mainly *Dermatophagoides pteronyssinus*) is a major asthma trigger in Australia.⁴ These microscopic mites live indoors, feed on skin scales, and thrive in temperate and humid climates such as coastal Australia.

Strategies that have been proposed for reducing exposure to house dust mites include:⁴

- encasing bedding (pillows, mattresses and doonas) in mite-impermeable covers
- weekly washing bed linen (pillow cases, sheets, doona covers) in a hot wash (> 55°C)
- using pillows manufactured with anti-microbial treatments that suppress fungal growth and dust mites
- removing unnecessary bedding such as extra pillows and cushions where dust mites might live and breed
- removing soft toys, or washing them in a hot wash (> 55°C) every week

- vacuuming rugs and carpets weekly using a vacuum with a high-efficiency particulate air (HEPA) filter, while allergic person is absent
- cleaning hard floors weekly with a damp or antistatic cloth, mop or a steam mop and dusting weekly using a damp or antistatic cloth
- regularly washing curtains or replacing curtains with cleanable blinds
- spraying the area with chemicals that kill mites (acaricides), such as benzyl benzoate spray or liquid nitrogen. Acaricide sprays are not commonly used in Australia.

Some clinical trials assessing the dust mite avoidance strategies (e.g. the use of allergen-impermeable mattress and pillow covers, acaricide sprays, air filters, or combinations of these) have reported a reduction in levels of house dust mite.^{47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58} However, reduced exposure may not improve symptoms.

Overall, clinical trials assessing dust mite avoidance for patients with asthma do not show that these strategies are effective in improving asthma symptoms, improving lung function or reducing asthma medication requirements in adults or children, compared with sham interventions or no interventions.⁵⁹ The use of allergen-impermeable mattress covers, as a single mite-reduction intervention in adults, is unlikely to be effective in improving asthma.⁶⁰

Use of mite allergen-impermeable covers for bedding (e.g. mattress covers, pillow covers, doona covers) was a component of some of the multi-component strategies for reducing house dust mite exposure that have been shown to be effective for improving asthma symptoms or control.

► Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

Pollens

Allergy to airborne pollen grains from certain grasses, weeds and trees is common in people with asthma in Australia.⁴ The highest pollen counts occur on calm, hot, sunny days in spring or early summer, or during the dry season in tropical regions.

Exposure to pollen:^{4, 61}

- may worsen asthma symptoms during the pollen season
- can cause outbreaks of asthma flare-ups after thunderstorms
- is usually caused by imported grasses, weeds and trees (which are wind pollinated) the pollen can travel many kilometres from its source
- is not usually caused by Australian native plants (although there are exceptions, such as Cypress Pine)
- is not usually caused by highly flowered plants as they produce less pollen (which is transported by bees) than wind pollinated plants.

Completely avoiding pollen can be difficult during the pollen season. Strategies that have been proposed for avoiding exposure to pollens include:⁴

- avoiding going outdoors on days with high pollen counts (particularly 7-9 am and 4-6 pm), on windy days or after thunderstorms
- keeping car windows closed, ensuring the vehicle has a pollen cabin air filter and setting the cabin air to recirculate
- showering (or washing face and hands thoroughly) after being outside with exposure to pollen
- drying bed linen indoors during the pollen season
- holidaying out of the pollen season or at the seaside
- not mowing the grass, and staying inside when it is being mown
- wearing a facemask and/or glasses in special situations where pollen can't be avoided, e.g. if mowing is unavoidable
- removing any plants the patient is sensitive to from their garden.

Daily pollen indices and forecasts are available from news media websites (e.g. www.weatherzone.com.au).

Moulds

Building repairs to reduce dampness in homes (e.g. leak repair, improvement of ventilation, removal of water-damaged materials) may reduce asthma symptoms and the use of asthma medicines.⁶² A systematic review and meta-analysis found that damp remediation of houses reduced asthma-related symptoms including wheezing in adults, and reduced acute care visits in children.⁶² In children living in mouldy houses, remediation of the home may reduce symptoms and flare-ups, compared with cleaning advice about moulds.⁶³

Other strategies that have been proposed for avoiding exposure to moulds include:⁴

- removing visible mould by cleaning with bleach or other mould reduction cleaners (patients should avoid breathing vapours)
- using high-efficiency air filters
- removing indoor pot plants
- drying or removing wet carpets
- treating rising damp as soon as it is detected
- avoiding the use of organic mulches and compost.
- See: Asthma triggers

Triggers in the workplace

A wide range of occupational allergens has been associated with work-related asthma. Investigation of work-related asthma is complex and typically requires specialist referral.

Table. Examples of common sensitising agents and occupations associated with exposure

Agent	Occupations			
Low molecular weight agents				
Wood dust (e.g. western red cedar, redwood, oak)	 Carpenters Builders Model builders Sawmill workers Sanders 			
Isocyanates	 Automotive industry workers Adhesive workers Chemical industry Mechanics Painters Polyurethane foam production workers 			
Formaldehyde	 Cosmetics industry Embalmers Foundry workers Hairdressers Healthcare workers Laboratory workers Tanners Paper, plastics and rubber industry workers 			

Agent	Occupations			
Low molecular weight agents				
Platinum salts	Chemists			
	Dentists			
	Electronics industry workers			
	Metallurgists			
	Photographers			
High molecular weight agents				
Latex	Food handlers			
	Healthcare workers			
	Textile industry workers			
	Toy manufacturers			
Flour and grain dust	• Bakers			
	Combine harvester drivers			
	• Cooks			
	• Farmers			
	• Grocers			
	Pizza makers			
Animal allergens (e.g. urine, dander)	Animal breeders			
	Animal care workers			
	• Jockeys			
	Laboratory workers			
	Pet shop workers			
	Veterinary surgery workers			

Source: Adapted from Hoy R, Abramson MJ, Sim MR. Work related asthma. *Aust Fam Physician* 2010; 39: 39-42. Available from: http://www.racgp.org.au/afp/201001/35841

Asset ID: 45

See: Work-related asthma

Alternative diagnostic tests for asthma and allergy

The Australasian Society of Clinical Immunology and Allergy (ASCIA) recommends against the following techniques for the diagnosis and treatment of allergy, asthma and immune disorders because they have not been shown to be reliable or accurate:³

- cytotoxic testing (Bryans' or Alcat testing)
- hair analysis
- iridology
- kinesiology
- oral provocation and neutralisation

- pulse testing
- radionics (psionic medicine, dowsing)
- tests for 'dysbiosis'
- vega testing (electrodermal testing)
- VoiceBio.

ASCIA also recommends against the use of conventional tests in the investigation of allergies in inappropriate clinical situations, or where the results are presented in a manner amenable to misinterpretation, e.g.³

- food-specific IgE (RAST, ImmunoCap testing)
- food-specific lgG, lgG4
- lymphocyte subset analysis.

► Go to: Unorthodox Techniques for the Diagnosis and Treatment of Allergy, Asthma and Immune Disorders, ASCIA Position Statement

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Managing allergies as part of asthma management

Recommendations

Manage allergic asthma according to the principles of asthma management in children or adults, with these considerations:

- Assess and manage risk for thunderstorm-triggered asthma in affected regions.
- Identify other clinically relevant allergic triggers and manage, or advise avoidance as appropriate, taking into account the cost, burden, and potential effectiveness of avoidance.
- Manage co-occurring allergic rhinitis.
- Consider specific immunotherapy for patients who meet all the criteria.

O How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specific allergen immunotherapy (sublingual immunotherapy or subcutaneous immunotherapy) in patients with allergic rhinitis or allergic asthma who have a history of proven, clinically important sensitisation to a particular allergen that cannot feasibly be avoided and for which for specific allergen immunotherapy is available.

Make sure the patient or parents understand that long-term treatment (at least 3 years) is necessary, and understand the cost and risks of the treatment.

Notes

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Both forms of specific allergen immunotherapy require at least 3 years of treatment and should initially be prescribed by an allergy specialist (allergist or clinical immunologist) where possible. Sublingual therapy for house dust mite allergic asthma is only approved for patients who also have allergic rhinitis, and whose asthma is not well controlled with inhaled corticosteroids.

For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered, and they will need specialist supervision during treatment.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Australasian Society of Clinical Immunology and Allergy, 2013¹
- Australasian Society of Clinical Immunology and Allergy, 1997²

Omalizumab treatment can be considered for adults and adolescents aged 12 years and over, with moderate-to-severe allergic asthma despite inhaled corticosteroid treatment, and raised IgE levels.

Note: For adults and adolescents with severe allergic asthma who may be eligible for PBS subsidy, whose asthma is not well-controlled despite optimal inhaled therapy, refer immediately for specialist assessment, because patients only become eligible for PBS subsidisation for omalizumab after at least 6 months' care by a specialist experienced in the management of severe asthma. After treatment is established, ongoing treatment with omalizumab may be administered by a GP, with 6-monthly review of ongoing eligibility at the specialist clinic.

O How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Katelaris et al. 2009³
- Chung et al. 2014⁴

Omalizumab treatment can be considered for children aged 6 to 11 years with severe allergic asthma (documented exacerbations despite daily high-dose inhaled corticosteroids with or without another maintenance treatment) and raised IgE levels.

Note: For children with severe allergic asthma who may be eligible for PBS subsidy, whose asthma is not well-controlled despite optimal inhaled therapy, refer immediately for specialist assessment, because patients only become eligible for PBS subsidisation for omalizumab after at least 6 months' care by the same specialist.



O How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Chung et al. 2014⁴
- Katelaris et al. 2009³

Benralizumab or mepolizumab can be considered as an add-on treatment for patients aged 12 years and over with severe refractory eosinophilic asthma. Benralizumab is given by subcutaneous injection every 4 weeks for the first three injections then every 8 weeks. Mepolizumab is given by subcutaneous injection every 4 weeks.

Note: For adults and adolescents with severe allergic asthma who may be eligible for PBS subsidy, whose asthma is not well-controlled despite optimal inhaled therapy, refer for specialist assessment, because patients only become eligible for PBS subsidisation for mepolizumab after at least 6 months of treatment by a specialist experienced in the management of severe asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Menzella et al. 2016⁵
- Powell et al. 2015⁶
- Farne et al. 2017⁷

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Consider offering referral to an allergy specialist for:

- patients with poorly controlled asthma or allergic rhinitis, despite appropriate treatment, good adherence and good inhaler technique
- patients considering specific immunotherapy.



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specific allergen immunotherapy in children with allergic rhinitis who have a history of proven, clinically important sensitisation to a particular allergen that cannot feasibly be avoided and for which for specific allergen immunotherapy is available.

Note: Specific allergen immunotherapy is indicated for the management of allergy, not prevention of asthma. However, early treatment before the onset of asthma may reduce the risk of asthma symptoms and asthma medication requirements.

Note: Make sure parents understand that treatment must be long term (3-5 years), and understand the cost and risks of the treatment.

Note: TGA-approved indications for commercially available preparations vary according to age group.

How this recommendation was developed Q

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Kristiansen et al. 2017⁸
- Valovirta et al. 2018⁹
- Jacobsen et al. 2007¹⁰
- Novembre et al. 2004¹¹

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More information

Allergies and asthma: links

There is a strong link between asthma and allergies:^{12, 13}

- The majority of people with asthma have allergies.
- Immunoglobulin E-mediated sensitisation to inhalant allergens is an important risk factor for developing asthma, particularly in childhood.
- In individuals with asthma, exposure to relevant allergens can worsen asthma symptoms and trigger flare-ups, including severe acute asthma.
- Allergens are a common cause of occupational asthma.

Although atopic sensitisation increases the risk of developing asthma, most people who are allergic to inhalant allergens or food allergens do not have asthma.¹³ Among people with food allergies, asthma may be a risk factor for fatal anaphylaxis due to food allergens.^{14, 15} However, foods are rarely a trigger for asthma symtpoms.

Neither asthma nor allergy is a single disease – each has multiple phenotypes and is a complex of several different diseases with different aetiologies, genetic risk factors and environmental risk factors.¹²

See: <u>Work-related asthma</u> Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

Links between allergic rhinitis and asthma

Prevalence, aetiology and symptoms

Asthma and allergic rhinitis frequently coexist. At least 75% of patients with asthma also have rhinitis, although estimates vary widely.¹⁶ Patients with asthma may have both allergic and non-allergic rhinitis.

Allergic rhinitis that starts early in life is usually due to a classical IgE hypersensitivity. Adult-onset asthma or inflammatory airway conditions typically have more complex causes. Chronic rhinosinusitis with nasal polyps is not a simple allergic condition and generally needs specialist care.¹⁷

Symptoms and signs of allergic rhinitis can be local (e.g. nasal discharge, congestion or itch), regional (e.g. effects on ears, eyes, throat or voice), and systemic (e.g. sleep disturbance and lethargy). Most people with allergic rhinitis experience nasal congestion or obstruction as the predominant symptom. Ocular symptoms (e.g. tearing and itch) in people with allergic rhinitis are usually due to coexisting allergic conjunctivitis.¹⁸

Patients may mistake symptoms of allergic rhinitis for asthma and vice versa. Allergic rhinitis is sometimes more easily recognised only after asthma has been stabilised.

► Go to: National Asthma Council Australia's Managing allergic rhinitis in people with asthma information paper

Effects on asthma

Allergic rhinitis is an independent risk factor for developing asthma in children and adults.^{19, 20, 21, 22, 23} However, the use of antihistamines in children has not been shown to prevent them developing asthma.¹⁶

The presence of allergic rhinitis is associated with worse asthma control in children and adults.^{24, 25, 26, 27} The use of intranasal corticosteroids in patients with concommitant allergic rhinitis and asthma may improve asthma control in patients who are not already taking regular inhaled corticosteroids.²⁸

Both rhinitis and asthma can be triggered by the same factors, whether allergic (e.g. house dust mite, pet allergens, pollen, cockroach) or non-specific (e.g. cold air, strong odours, environmental tobacco smoke).

Food allergies do not cause allergic rhinitis. Most people with allergic rhinitis are sensitised to multiple allergens (e.g. both pollens and

house dust mite), so symptoms may be present throughout the year.

Pollens (e.g. grasses, weeds, trees) and moulds are typically seasonal allergens in southern regions, but can be perennial in tropical northern regions.²⁹ However, ryegrass is not found in tropical regions (see <u>Thunderstorm asthma</u>).

Pollen calendars provide information on when airborne pollen levels are likely to be highest for particular plants.

Thunderstorm asthma

Seasonal allergic rhinitis, which in Australia is typically associated with sensitisation to perennial ryegrass (*Lolium perenne*), is an important risk factor for thunderstorm asthma.³⁰

► Go to: ASCIA's <u>Pollen calendar</u> Go to: National Asthma Council Australia's <u>Epidemic thunderstorm asthma</u> information paper

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Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.^{3,5,6,8,9}

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.^{3, 5} Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.³

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.^{1, 9, 10}

Data from thunderstorm as thma epidemics suggest that the risk of as thma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known as thma).³

The worst outcomes are seen in people with poorly controlled asthma.¹ Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.⁵

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.¹¹

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.⁴

Go to: National Asthma Council Australia's <u>Epidemic thunderstorm asthma</u> information paper Go to: ASCIA's <u>Pollen calendar</u> Go to: Vic Emergency's Thunderstorm asthma forecast (Victoria only)

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Specific allergen immunotherapy (desensitisation)

• Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV₁) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.^{31, 32} For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered. These patients will need specialist supervision during treatment.

Options available in Australia

Two forms of specific allergen immunotherapy are available:

- sublingual immunotherapy
- subcutaneous immunotherapy.

Both forms of specific allergen immunotherapy require 3-5 years of treatment. Specific allergy immunotherapy can be repeated.

Although some specific allergen therapies can be prescribed by primary care health professionals, it is recommended that they are

initiated under the care of an allergy specialist (allergist or clinical immunologist), where possible.

Commercial allergen preparations for immunotherapy are available in Australia for aeroallergens including house dust mite, pollens (e.g. grass, tree and weed pollens), animal dander and moulds.

► Go to: ASCIA's <u>Allergen Immunotherapy</u> fact sheet for patients Go to: ASCIA's <u>Allergen immunotherapy e-training for health professionals</u>

Overview of efficacy

There is strong evidence that allergen immunotherapy is effective in the treatment of seasonal and perennial allergic rhinitis.^{33, 34, 35} There is less evidence supporting specific allergen immunotherapy in children than in adults.³⁴ Specific allergen immunotherapy in children with seasonal allergic rhinoconjunctivitis might prevent development of asthma.^{17, 10, 36}

Single-allergen specific allergen immunotherapy is effective in patients sensitised to one allergen and those sensitised to multiple allergens.^{37, 38, 39} In selected cases more than one allergen may be administered as separate extracts. There is weak evidence for the efficacy of allergen mixes.⁴⁰

A systematic review of studies directly comparing subcutaneous immunotherapy and sublingual immunotherapy in the treatment of allergic rhinoconjunctivitis and asthma found:⁴¹

- low-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing asthma symptoms and for reducing a combined measure of rhinitis symptoms and medication use
- moderate-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing nasal and/or eye symptoms.

Sublingual immunotherapy is associated with a lower rate of severe adverse effects (anaphylaxis and death) than subcutaneous immunotherapy, based on indirect comparison.^{16, 42, 43}

Sublingual immunotherapy

Sublingual immunotherapy (self-administered at home) is effective for the treatment of allergic rhinitis in adults and children.^{44, 45} The greatest benefits have been demonstrated in those with allergies to temperate grass pollens or house dust mite.⁴⁵ Therapeutic Goods Administration (TGA)-approved indications for commercially available preparations vary according to age group.

The extract must be held under the tongue without swallowing for 2 minutes (liquid extracts) or 1 minute (tablets).

Sublingual immunotherapy is generally well tolerated.⁴⁴ Local adverse effects are common in children receiving sublingual immunotherapy.¹⁶ Systemic adverse reactions, such as anaphylaxis, are very rare.¹⁶ The majority of adverse events occur soon after beginning treatment.⁴⁵

TGA-approved indications

Asthma: Acarizax (house dust mite) is indicated for adults 18-65 years with house dust mite allergic asthma that is not well controlled by inhaled corticosteroids and is associated with mild-to-severe house dust mite allergic rhinitis.⁴⁶ It is contraindicated in patients with FEV₁ < 70% predicted after adequate treatment, and for patients who have experienced a severe flare-up within the previous 3 months.⁴⁶

Allergic rhinitis: Several commercial preparations of aeroallergens for sublingual immunotherapy in patients with allergic rhinitis are used in Australia, including:

- Acarizax (house dust mite) indicated for adults 18–65 years with persistent moderate to severe house dust mite allergic rhinitis despite symptomatic treatment.⁴⁶
- Actair (house dust mite) indicated for the treatment of house dust mite allergic rhinitis with or without conjunctivitis in adults and adolescents over 12 years diagnosed with house dust mite allergy.⁴⁷
- *Grazax* (Timothy grass [*Phleum pratense*] pollen extract) indicated for adults, adolescents and children older than 5 years with allergic rhinitis induced by Timothy grass⁴⁸
- Oralair tablets (mix of grass pollens) indicated for adults and children over 5 years with grass pollen allergic rhinitis.⁴⁹

Various single allergens and/or multiple allergen mixes are available for use as advised by the treating allergist, available as liquid extracts. Age restrictions vary between products.

Note: PBS status as at October 2016: Treatment with sublingual immunotherapy specific allergen preparations is not subsidised by the PBS.

Subcutaneous immunotherapy

Subcutaneous immunotherapy involves injections in which the dose is gradually increased at regular intervals (usually weekly), or until a therapeutic/maintenance dose is reached. This can take approximately 3–6 months.¹ Treatment is then continued for a further 3–5 years.

Subcutaneous immunotherapy is generally not suitable for younger children (e.g. less than 7 years) because they may not be able to tolerate frequent injections.

Several commercial preparations of aeroallergens for subcutaneous immunotherapy are available in Australia, including various single allergens and/or multiple allergen mixes for use as advised by the treating allergist. Age restrictions vary between products.

Subcutaneous immunotherapy is effective for the treatment of allergic rhinitis and asthma, particularly when single-allergen immunotherapy regimens are used.⁴² There is strong evidence that it reduces asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life, in comparison to placebo or usual care.⁴² There is also moderate evidence that subcutaneous immunotherapy reduces rhinitis/rhinoconjunctivitis medication usage.⁴²

Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects.^{16, 45} The most common systemic reactions are respiratory symtoms. There have been few reports of anaphylaxis.¹⁶ **Note:** PBS status as at March 2019: Treatment with subcutaneous specific allergen immunotherapy preparations is not subsidised by the PBS.

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Treatment of allergic rhinitis in adults and adolescents

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/102

Intranasal corticosteroids

If continuous treatment is required, an intranasal corticosteroid is the first-choice treatment unless contraindicated. Intranasal corticosteroids are more effective in the treatment of allergic rhinitis than other drug classes including oral H₁-antihistamines, intranasal H₁-antihistamines and montelukast.^{28, 16, 35} Intranasal corticosteroid are most effective when taken continuously.²⁸

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in adults and adolescents with allergic rhinitis.^{28, 16} They are also effective for ocular symptoms.⁵⁰

All available intranasal corticosteroids appear to be equally effective.²⁸

The onset of action is between 3 and 36 hours after first dose and, in practice, the full therapeutic effect takes a few days.⁵¹

The addition of an oral H_1 -antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more effective than intranasal corticosteroid monotherapy.³⁵

Intranasal corticosteroids are well tolerated. Common (>1%) adverse effects include nasal stinging, itching, nosebleed, sneezing, sore throat, dry mouth, cough.⁹ Nose bleeds are usually due to poor spray technique or crusting. Evidence from studies mainly in adults suggests that intranasal corticosteroids do not cause atrophy of nasal epithelium.⁵²

Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects when given in recommended doses.^{28, 53} Studies in adults evaluating effects on the hypothalamic-pituitary axis using morning cortisol concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion show no adverse effects with beclomethasone dipropionate, budesonide, ciclesonide, fluticasone propionate, fluticasone furoate, or triamcinolone acetonide.²⁸

In patients with asthma already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be taken into account when calculating the total daily corticosteroid dose. Drug-drug interactions (e.g. with CYP3A4 inhibitors such as such as erythromycin, clarithromycin, ritonavir and itraconazole) may change the metabolism or increase absorption of corticosteroids administered by any route, increasing the risk of adrenal suppression.⁹

Combination intranasal corticosteroid plus intranasal antihistamines

Combined intranasal fluticasone propionate and azelastine hydrochloride in a single device is more effective than fluticasone propionate alone for a range of nasal and ocular symptoms.^{28, 35, 30}

The onset of therapeutic action is approximately 30 minutes after dosing.³⁰

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.⁵⁴

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms.^{35, 55} They can provide adequate relief for some individuals when taken continuously or intermittently.²⁸ Available agents appear to be equally effective.⁵³

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{28, 56} In

adults with allergic rhinitis, oral antihistamines usually produce no further improvement when added to intranasal corticosteroid treatment.²⁸

Common (>1%) adverse effects include drowsiness, fatigue, headache, nausea and dry mouth.⁹ Oral antihistamines can also cause ocular dryness.⁵⁷

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H_1 -antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.¹⁶

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.²⁸ They have a rapid onset of action (15–30 minutes).²⁸

The most common (>1%) adverse effect is local irritation.⁹ Bitter taste is more common intranasal antihistamines than with intranasal corticosteroids.²⁸

Montelukast

Leukotriene receptor antagonists are no more effective than oral H_1 -antihistamines.^{16, 35} Montelukast is less effective than intranasal corticosteroid in the treatment of allergic rhinitis.^{28, 16} In most studies, adding montelukast to an intranasal corticosteroid was not more effective than intranasal corticosteroid alone.³⁵

Montelukast is approved by TGA for treatment of in adults with asthma or seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{58, 59, 60, 61, 62} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares, depression, and aggression.⁶² Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.⁶²

Other nasal sprays

Ipratropium bromide spray is effective in managing persistent rhinorrhoea in patients with allergic rhinitis, but not blockage or itch.¹⁶ It is indicated for use in adults and adolescents over 12 years old.

Intranasal sodium cromoglycate is less effective than intranasal corticosteroids, but is effective in some patients for prevention and treatment of allergic rhinitis and is associated with minimal adverse effects.⁵³

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Treatment of allergic rhinitis in children

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/102

Intranasal corticosteroids

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in school-aged children with allergic rhinitis.^{28, 16} However, there is weaker evidence to support their efficacy in children than in adults.¹⁶ There is limited evidence to guide the treatment of allergic rhinitis in preschool children.³⁵

The addition of an oral H_1 -antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more effective than intranasal corticosteroid monotherapy.³⁵

TGA-approved indications vary between age groups. Intranasal corticosteroids indicated for children aged under 12 years include fluticasone furoate (age 2 years and over), mometasone furoate (age 3 years and over), and budesonide (age 6 years and over).

Intranasal corticosteroids are well tolerated. Evidence from studies mainly in adults suggests that they do not cause atrophy of nasal epithelium.⁶³ Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects in children when given in recommended doses.²⁸⁵³ Studies in children evaluating effects on the hypothalamic-pituitary axis using morning cortisol

concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion showed no adverse effects with ciclesonide, fluticasone propionate, fluticasone furoate, mometasone furoate, or triamcinolone acetonide.²⁸ One knemometry study showed reduced lower leg growth rate in children using intranasal budesonide.²⁸ In studies using stadiometry over 12 months, higher-than-recommended doses of intranasal beclomethasone dipropionate were associated with growth suppression, but fluticasone propionate and mometasone furoate showed no effects on growth compared with placebo.²⁸

In children already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be taken into account when calculating the total daily corticosteroid dose.

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.⁵⁴

These antihistamines can be taken long term by children. Eighteen months of treatment with cetirizine was well tolerated in a large, prospective, multi-country, randomised controlled trial in infants with atopic dermatitis aged 12–24 months.²⁸

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms,^{35, 55} including in preschool children. ³⁵ They can provide adequate relief for some individuals when taken continuously or intermittently.²⁸ Available agents appear to be equally effective.⁵³

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{28, 56} The addition of oral antihistamines to intranasal corticosteroids has not been demonstrated to be an effective strategy in children.⁶⁴

TGA-approved indications vary between age groups. Less sedating oral antihistamines indicated for children under 12 years include cetirizine (1 year and over), loratatidine (1 year and over), desloratadine (6 months and over), and fexofenadine (6 months and over).

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H_1 -antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.¹⁶

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.²⁸ They have a rapid onset of action (15–30 minutes).²⁸

Montelukast

Leukotriene receptor antagonists are no more effective than oral H₁-antihistamines.^{16, 35} Montelukast is less effective than intranasal corticosteroid in the treatment of allergic rhinitis.^{28, 16} In most studies, adding montelukast to an intranasal corticosteroid was not more effective than intranasal corticosteroid alone.³⁵

Montelukast is approved by TGA for the treatment of asthma in children over 2 years, and for the treatment of seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{58, 59, 60, 61} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares (especially in children), depression, and aggression (especially in children).⁶² Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.⁶²

The potential association of montelukast with behaviour-related adverse events should be mentioned to parents when commencing treatment, and treatment should be stopped if such adverse events are suspected.

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

► Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Non-recommended medications for allergic rhinitis

Intranasal decongestants have a limited role in the management of allergic rhinitis because they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa (rhinitis medicamentosa), which can lead to dose escalation by patients, with a risk of atrophic rhinitis. Intranasal decongestants can be considered for a patient with severe nasal congestion to gain rapid relief of symptoms until the full effect of intranasal corticosteroids is achieved.

Oral decongestants (e.g. pseudoephedrine or phenylephrine) should not generally be used in the management of allergic rhinitis. They are indicated for short-term use only (e.g. acute infectious rhinitis, or during air travel by a patient with symptomatic rhinitis, as a single

tablet taken one hour before landing). They are associated with adverse effects including palpitations, tachycardia and insomnia.

Oral corticosteroids should be avoided as a treatment for allergic rhinitis. In exceptional circumstances, their use might be considered in consultation with an allergy specialist.

Topical ocular alpha agonist vasoconstrictors (including in combination with antihistamines) should not be used for allergic conjunctivitis because they can cause conjunctivitis medicamentosa.

Nasal saline irrigation for allergic rhinitis

Nasal irrigation (via a syringe, rinse bottle, spray or other device) can improve nasal symptoms, mucociliary clearance, and quality of life.⁶⁵ Saline administered by spray or other devices was used at least twice daily in most studies that showed a benefit.⁶⁵

Isotonic solution is preferable to hypertonic solution because it supports optimal mucociliary clearance.⁶⁵ Isotonic saline is solution is inexpensive and has no known adverse effects.⁶⁵ Patients can use either commercially manufactured saline solutions or home-made normal saline: 1 teaspoon (5 g) rock or sea salt in 500 mL of water (preferably bottled or boiled).

There is not enough evidence to determine:

- whether solutions should be buffered or non-buffered, sterile or non-sterile
- whether various additives provide any advantage
- whether inhaling steam or an irritant decongestant (e.g. eucalyptus, menthol) before saline irrigation provides any extra benefit. However, patients are more likely to adhere to simple and convenient regimens, regardless of theoretical advantages. Caution is required with steam inhalation to avoid burns.

If patients are using both saline irrigation and an intranasal corticosteroid or intranasal H₁-antihistamine, they should perform saline irrigation first. Saline can be used again after waiting at least an hour after using an intranasal corticosteroid.

Young children are unlikely to tolerate nasal irrigation.

Surgical turbinate reduction

Turbinate reduction surgery can be considered when nasal obstruction is due to turbinate hypertrophy and symptoms do not respond to medical treatment. It should not be performed in young children except after thorough investigation and review.

Inferior turbinate hypertrophy secondary to inflammation is a common cause of nasal obstruction in patients with allergic rhinitis.⁶⁶ Several surgical procedures are available to correct this problem.⁶⁷ The ideal surgical reduction should preserve the mucosa and physiological function.⁶⁶

Short-term adverse outcomes of inferior turbinate reduction include nasal bleeding, scarring and crusting. Rarely, it may worsen symptoms when patients have non-specific rhinitic conditions or sino-nasal somatisation disorders ('empty nose syndrome').⁶⁷ There is no evidence that turbinate surgery creates these conditions, but sino-nasal surgery may exacerbate the symptoms.

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Managing allergic rhinitis in people with asthma

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Managing allergic rhinitis in children with asthma

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Managing allergic rhinitis in adults and adolescents with asthma

Recommendations

Prescribe or recommend intranasal corticosteroids for adults and adolescents with persistent allergic rhinitis or moderate-to-severe intermittent allergic rhinitis, even if the person is already taking regular inhaled corticosteroids for asthma. Intranasal corticosteroids can be used alone or in combination with an intranasal antihistamine (e.g. azelastine or levocabastine).

Table. Classification of allergic rhinitis

Pattern of symptoms				
Intermittent	Persistent			
Either of:	Both of:			
 symptoms present <4 days per week symptoms present <4 consecutive weeks 	 symptoms present ≥4 days per week symptoms present ≥4 consecutive weeks 			
Severity				
Mild	Moderate-to-severe			
No features of moderate-to-severe allergic rhinitis	Any of:			

• sleep disturbance

• impairment of school or work

troublesome symptoms

• impairment of daily activities, leisure, physical activity

Source: Bousquet J, Khaltaev N, Cruz AA et al. Allergic rhinitis and its impact on asthma (ARIA) 2008. Allergy 2008; 63(Suppl 86): 7-160. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1398-9995.2007.01620.x/full

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Figure. Management of allergic rhinitis in adults and adolescents

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/106



How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Seidman *et al*, 2015¹
- Bousquet et al, 2008²
- Brożek *et al*, 2010³

- Lohia *et al*, 2013⁴
- Bousquet et al, 2016⁵
- Wallace et al, 2008⁶
- Berger and Meltzer, 2015⁷

If symptoms are troublesome to the patient, consider initially adding an agent with a more rapid onset of action, e.g. or al H_1 - antihistamine, intranasal H_1 - antihistamine or short-term (maximum 5 days) intranasal decongestant.

Note: Warn patients not to take intranasal decongestants for more than 5 days, and only occasionally.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Bachert and Maspero, 2011⁸
- Bousquet *et al.* 2008²
- Brożek *et al.* 2010³
- Howarth, 1999⁹
- Kaliner *et al.* 2011¹⁰
- Wallace et al. 2008⁶

For adults and adolescents with mild intermittent allergic rhinitis, consider starting treatment with an intranasal H_1 -antihistamine or second-generation less sedating oral H_1 -antihistamine. Do not use sedating antihistamines.

If symptoms do not improve significantly within 2 weeks, switch to an intranasal corticosteroid.

For those with seasonal allergic rhinitis, montelukast can be considered as an alternative to antihistamines.

• Advise patients and parents about potential adverse psychiatric effects of montelukast in young people

 $\ensuremath{\bigcirc}$ How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Seidman et al, 2015¹
- Bousquet et al, 2008²
- Brożek *et al*, 2010³
- Lohia et al, 2013⁴
- Bousquet et al, 2016⁵
- Wallace et al, 2008⁶
- Berger & Meltzer, 2015⁷
- Bachert & Maspero, 2001⁸

Advise patients that intranasal corticosteroids, intranasal antihistamines or oral antihistamines will often relieve eye itching and redness associated with allergic rhinitis without the need for eye drops.

If ocular symptoms are troublesome, consider initial use of topical H₁-antihistamines (e.g. azelastine, ketotifen, levocabastine or olopatadine).

If long-term treatment for ocular symptoms is necessary, consider a topical mast-cell stabiliser (e.g. cromoglycate or lodoxamide). Explain that onset of therapeutic effect may take up to 2–4 weeks.

Avoid topical alpha agonist vasoconstrictors (including in combination with antihistamines) because they can cause conjunctivitis medicamentosa.

Note: People who wear contact lenses should consult their pharmacist about which products are suitable.



Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Seidman *et al*, 2015¹¹
- Bousquet et al, 2008²
- Brożek *et al*, 2010³
- Wallace et al, 2008⁶
- Hong et al, 2011¹²
- Castillo et al, 2015¹³

Provide an allergic rhinitis treatment plan.

► Go to: ASCIA's <u>Allergic rhinitis treatment plan template</u>



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If allergic rhinitis symptoms do not resolve within 3-4 weeks:

- review the diagnosis
- check adherence and intranasal administration technique
- consider allergy testing.

O, How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If the response to an intranasal corticosteroid alone is inadequate despite regular daily use and correct spray technique, add an intranasal antihistamine and continue intranasal corticosteroid.



How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Seidman *et al*, 2015¹
- Bousquet et al, 2016⁵

For patients with asthma who need long-term regular medication for allergic rhinitis, explain that effective management of allergic rhinitis is part of their overall respiratory care. Emphasise the need to take intranasal corticosteroids consistently, and reassure patients that these medicines have a good safety profile when taken long term.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Demonstrate correct technique for using intranasal sprays and check patients' technique regularly.



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specialist referral for patients with allergic rhinitis who have:

- poorly controlled asthma, despite appropriate treatment, good adherence and good inhaler technique
- other significant allergic disease (e.g. food allergies or severe eczema)
- symptoms that suggest an alternative diagnosis (e.g. unilateral nasal symptoms, persistent nasal obstruction that does not respond to intranasal corticosteroids, or suspected chronic sinusitis).

, How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

In pharmacies, advise people with co-occurring asthma and allergic rhinitis to consult their GP for thorough investigation if:

- rhinitis symptoms are not well controlled by self-management with over-the-counter medicines (e.g. S2 intranasal corticosteroids, oral antihistamines)
- they need to take rhinitis treatment for more than 4 weeks at a time
- there are any complications (e.g. pain, loss of hearing or sense of smell, persistent cough).

O How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

At each review, check adherence to medications and topical therapy technique, as for asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Inspect nasal mucosa one month after starting treatment then every 6 months for resolution of turbinate hypertrophy and any evidence of local crusting or bleeding. Consider referral to an ear, nose and throat surgeon for review if the patient is bothered by nasal obstruction, and turbinate hypertrophy has not responded to 12 months of regular intranasal corticosteroid treatment.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If allergic rhinitis symptoms are uncontrolled despite regular use of an intranasal corticosteroid alone or in combination with an intranasal antihistamine, consider specialist referral.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Advise patients with allergic rhinitis to avoid tobacco smoke. Explain that smoking worsens both asthma and allergic rhinitis, and can reduce the effectiveness of treatment.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider nasal irrigation with saline solution or saline nasal sprays as well as drug treatment.

Note: If patients are using saline irrigation or saline nasal spray and an intranasal medication (corticosteroid or H₁-antihistamine) at the same time, they should use the saline first and wait approximately 10 minutes before using the medication. Saline can be used again after waiting at least an hour after using an intranasal corticosteroid.



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specific allergen immunotherapy in patients with allergic rhinitis or allergic asthma who have a history of proven, clinically important sensitisation to a particular allergen that cannot feasibly be avoided and for which specific allergen immunotherapy is available.

Note: Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV₁) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.

Note: Make sure the patient or parents understand that treatment must be long term (3–5 years), and understand the cost and risks of the treatment.



Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Virchow et al, 2016¹⁴
- Mosbech *et al*, 2014¹⁵
- Cox, 2016¹⁶
- Meadows et al, 2013¹⁷
- Durham et al, 2016¹⁸
- Passalacqua et al, 2014¹⁹
- Chelladurai et al, 2013²⁰
- Brożek *et al*, 2010³
- Erekosima et al, 2014²¹
- Calderon *et al*, 2015²²
- Radulovic et al, 2010²³
- Canonica *et al*, 2009²⁴

Warn people with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) that they may be at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before.



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to named source(s):

- Thien et al. 2018²⁵
- O'Hehir et al. 2018²⁶
- Lee et al. 2017²⁷
- Davies. 2017²⁸
- Girgis et al. 2000²⁹

• Marks et al. 2001³⁰

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For all patients at risk of thunderstorm-triggered asthma (e.g. because they have seasonal allergic rhinitis and/or asthma with grass pollen allergy, and are living in or travelling to an area with high grass pollen levels), provide advice on:

- continual or prophylactic seasonal use of inhaled corticosteroids for asthma, as indicated (see recommendation below)
- prophylactic seasonal use of intranasal corticosteroid for allergic rhinitis (see recommendation below)
- asthma first aid for those without known asthma, including how to recognise asthma symptoms, how to get and use a reliever inhaler (ideally with spacer), and when to call an ambulance
- avoidance warn against being outdoors just before and during thunderstorms in spring and early summer, especially in wind gusts that precede the rain front.



O How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• NACA, 2017³¹

For people with seasonal allergic rhinitis who do not use intranasal corticosteroid treatment all year, advise intranasal corticosteroid starting 6 weeks before the pollen season (or exposure) and continuing until pollen levels abate (e.g. in Victoria, ideally 1 September-31 December).

Note: Refer to ASCIA's Pollen calendar

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• NACA. 2017³²

For people with asthma who are at risk of thunderstorm asthma:

- prescribe regular inhaled corticosteroids for continuous use if indicated (most adults and older adolescents with asthma)
- for patients for whom preventer therapy is not otherwise indicated, prescribe regular inhaled corticosteroids for at least 2 weeks before and throughout the pollen season (e.g. in Victoria, ideally 1 September–31 December)
- provide training in correct inhaler technique, and check technique and adherence regularly
- advise patients to carry a reliever inhaler and replace it before the expiry date
- provide an up-to-date written asthma action plan that includes thunderstorm advice and instructs the person to increase doses of both inhaled preventer and reliever (as well as starting oral corticosteroids, if indicated) in response to flare-ups.

Notes: Most adults and older adolescents with asthma should be using a regular inhaled corticosteroid long term.

People with asthma are particularly at risk of thunderstorm asthma if they have seasonal (springtime) allergic rhinitis (i.e. allergic to ryegrass pollen), and live in or are travelling to an area with high grass pollen levels. People with allergy to ryegrass pollen without known asthma are also at risk of thunderstorm asthma.

For people with seasonal allergic rhinitis who do not use intranasal corticosteroid treatment all year, advise intranasal corticosteroid starting 6 weeks before the pollen season (or exposure) and continuing until pollen levels abate (e.g. in Victoria, ideally 1 September-31 December).

Refer to ASCIA's <u>Pollen calendar</u> for information on local high-risk periods.



How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• NACA, 2017³³

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More information

Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.^{3,5,6,8,9}

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.^{3, 5} Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.³

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.^{1, 9, 10}

Data from thunderstorm as thma epidemics suggest that the risk of as thma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known as thma).³

The worst outcomes are seen in people with poorly controlled asthma.¹ Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.⁵

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.¹¹

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.⁴

► Go to: National Asthma Council Australia's <u>Epidemic thunderstorm asthma</u> information paper Go to: ASCIA's <u>Pollen calendar</u> Go to: <u>Vic Emergency's Thunderstorm asthma forecast</u> (Victoria only)

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Links between allergic rhinitis and asthma

Prevalence, aetiology and symptoms

Asthma and allergic rhinitis frequently coexist. At least 75% of patients with asthma also have rhinitis, although estimates vary widely.³ Patients with asthma may have both allergic and non-allergic rhinitis.

Allergic rhinitis that starts early in life is usually due to a classical IgE hypersensitivity. Adult-onset asthma or inflammatory airway conditions typically have more complex causes. Chronic rhinosinusitis with nasal polyps is not a simple allergic condition and generally needs specialist care.³⁴

Symptoms and signs of allergic rhinitis can be local (e.g. nasal discharge, congestion or itch), regional (e.g. effects on ears, eyes, throat or voice), and systemic (e.g. sleep disturbance and lethargy). Most people with allergic rhinitis experience nasal congestion or obstruction as the predominant symptom. Ocular symptoms (e.g. tearing and itch) in people with allergic rhinitis are usually due to coexisting allergic conjunctivitis.³⁵

Patients may mistake symptoms of allergic rhinitis for asthma and vice versa. Allergic rhinitis is sometimes more easily recognised only after asthma has been stabilised.

► Go to: National Asthma Council Australia's Managing allergic rhinitis in people with asthma information paper

Effects on asthma

Allergic rhinitis is an independent risk factor for developing asthma in children and adults.^{36, 37, 38, 39, 40} However, the use of antihistamines in children has not been shown to prevent them developing asthma.³

The presence of allergic rhinitis is associated with worse asthma control in children and adults.^{41, 42, 43, 44} The use of intranasal corticosteroids in patients with concommitant allergic rhinitis and asthma may improve asthma control in patients who are not already taking regular inhaled corticosteroids.⁴

Both rhinitis and asthma can be triggered by the same factors, whether allergic (e.g. house dust mite, pet allergens, pollen, cockroach) or non-specific (e.g. cold air, strong odours, environmental tobacco smoke).

Food allergies do not cause allergic rhinitis. Most people with allergic rhinitis are sensitised to multiple allergens (e.g. both pollens and house dust mite), so symptoms may be present throughout the year.

Pollens (e.g. grasses, weeds, trees) and moulds are typically seasonal allergens in southern regions, but can be perennial in tropical northern regions.⁴⁵ However, ryegrass is not found in tropical regions (see <u>Thunderstorm asthma</u>).

Pollen calendars provide information on when airborne pollen levels are likely to be highest for particular plants.

Thunderstorm asthma

Seasonal allergic rhinitis, which in Australia is typically associated with sensitisation to perennial ryegrass (*Lolium perenne*), is an important risk factor for thunderstorm asthma.⁴⁶

Go to: ASCIA's Pollen calendar

Go to: National Asthma Council Australia's Epidemic thunderstorm asthma information paper

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Treatment of allergic rhinitis in adults and adolescents

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/102

Intranasal corticosteroids

If continuous treatment is required, an intranasal corticosteroid is the first-choice treatment unless contraindicated. Intranasal corticosteroids are more effective in the treatment of allergic rhinitis than other drug classes including oral H₁-antihistamines, intranasal H₁-antihistamines and montelukast.^{4, 3, 5} Intranasal corticosteroid are most effective when taken continuously.⁴

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in adults and adolescents with allergic rhinitis.^{4, 3} They are also effective for ocular symptoms.¹²

All available intranasal corticosteroids appear to be equally effective.⁴

The onset of action is between 3 and 36 hours after first dose and, in practice, the full therapeutic effect takes a few days.¹⁸

The addition of an oral H_1 -antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more effective than intranasal corticosteroid monotherapy.⁵

Intranasal corticosteroids are well tolerated. Common (>1%) adverse effects include nasal stinging, itching, nosebleed, sneezing, sore throat, dry mouth, cough.⁴⁷ Nose bleeds are usually due to poor spray technique or crusting. Evidence from studies mainly in adults suggests that intranasal corticosteroids do not cause atrophy of nasal epithelium.⁴⁸

Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects when given in recommended doses.^{4, 6} Studies in adults evaluating effects on the hypothalamic-pituitary axis using morning cortisol concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion show no adverse effects with beclomethasone dipropionate, budesonide, ciclesonide, fluticasone propionate, fluticasone furoate, or triamcinolone acetonide.⁴

In patients with asthma already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be taken into account when calculating the total daily corticosteroid dose. Drug-drug interactions (e.g. with CYP3A4 inhibitors such as such as erythromycin, clarithromycin, ritonavir and itraconazole) may change the metabolism or increase absorption of corticosteroids administered by any route, increasing the risk of adrenal suppression.⁴⁷

Combination intranasal corticosteroid plus intranasal antihistamines

Combined intranasal fluticasone propionate and azelastine hydrochloride in a single device is more effective than fluticasone propionate alone for a range of nasal and ocular symptoms.^{4, 5, 46}

The onset of therapeutic action is approximately 30 minutes after dosing.⁴⁶

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.¹⁴

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and

ocular symptoms.^{5, 8} They can provide adequate relief for some individuals when taken continuously or intermittently.⁴ Available agents appear to be equally effective.⁶

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{4, 2} In adults with allergic rhinitis, oral antihistamines usually produce no further improvement when added to intranasal corticosteroid treatment.⁴

Common (>1%) adverse effects include drowsiness, fatigue, headache, nausea and dry mouth.⁴⁷ Oral antihistamines can also cause ocular dryness.⁴⁹

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H₁-antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.³

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.⁴ They have a rapid onset of action (15–30 minutes).⁴

The most common (>1%) adverse effect is local irritation.⁴⁷ Bitter taste is more common intranasal antihistamines than with intranasal corticosteroids.⁴

Montelukast

Leukotriene receptor antagonists are no more effective than oral H_1 -antihistamines.^{3, 5} Montelukast is less effective than intranasal corticosteroid in the treatment of allergic rhinitis.^{4, 3} In most studies, adding montelukast to an intranasal corticosteroid was not more effective than intranasal corticosteroid alone.⁵

Montelukast is approved by TGA for treatment of in adults with asthma or seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{50, 51, 52, 53, 54} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares, depression, and aggression.⁵⁴ Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.⁵⁴

Other nasal sprays

Ipratropium bromide spray is effective in managing persistent rhinorrhoea in patients with allergic rhinitis, but not blockage or itch.³ It is indicated for use in adults and adolescents over 12 years old.

Intranasal sodium cromoglycate is less effective than intranasal corticosteroids, but is effective in some patients for prevention and treatment of allergic rhinitis and is associated with minimal adverse effects.⁶

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Non-recommended medications for allergic rhinitis

Intranasal decongestants have a limited role in the management of allergic rhinitis because they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa (rhinitis medicamentosa), which can lead to dose escalation by patients, with a risk of atrophic rhinitis. Intranasal decongestants can be considered for a patient with severe nasal congestion to gain rapid relief of symptoms until the full effect of intranasal corticosteroids is achieved.

Oral decongestants (e.g. pseudoephedrine or phenylephrine) should not generally be used in the management of allergic rhinitis. They are indicated for short-term use only (e.g. acute infectious rhinitis, or during air travel by a patient with symptomatic rhinitis, as a single tablet taken one hour before landing). They are associated with adverse effects including palpitations, tachycardia and insomnia.

Oral corticosteroids should be avoided as a treatment for allergic rhinitis. In exceptional circumstances, their use might be considered in consultation with an allergy specialist.

Topical ocular alpha agonist vasoconstrictors (including in combination with antihistamines) should not be used for allergic conjunctivitis because they can cause conjunctivitis medicamentosa.

Smoking and allergic rhinitis

Smoking may worsen both asthma and rhinitis, and exposure to tobacco smoke can reduce the effectiveness of treatment in adults and

Nasal saline irrigation for allergic rhinitis

Nasal irrigation (via a syringe, rinse bottle, spray or other device) can improve nasal symptoms, mucociliary clearance, and quality of life.⁵⁷ Saline administered by spray or other devices was used at least twice daily in most studies that showed a benefit.⁵⁷

Isotonic solution is preferable to hypertonic solution because it supports optimal mucociliary clearance.⁵⁷ Isotonic saline is solution is inexpensive and has no known adverse effects.⁵⁷ Patients can use either commercially manufactured saline solutions or home-made normal saline: 1 teaspoon (5 g) rock or sea salt in 500 mL of water (preferably bottled or boiled).

There is not enough evidence to determine:

- whether solutions should be buffered or non-buffered, sterile or non-sterile
- whether various additives provide any advantage
- whether inhaling steam or an irritant decongestant (e.g. eucalyptus, menthol) before saline irrigation provides any extra benefit. However, patients are more likely to adhere to simple and convenient regimens, regardless of theoretical advantages. Caution is required with steam inhalation to avoid burns.

If patients are using both saline irrigation and an intranasal corticosteroid or intranasal H₁-antihistamine, they should perform saline irrigation first. Saline can be used again after waiting at least an hour after using an intranasal corticosteroid.

Young children are unlikely to tolerate nasal irrigation.

Specific allergen immunotherapy (desensitisation)

• Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV₁) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.^{58, 59} For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered. These patients will need specialist supervision during treatment.

Options available in Australia

Two forms of specific allergen immunotherapy are available:

- sublingual immunotherapy
- subcutaneous immunotherapy.

Both forms of specific allergen immunotherapy require 3-5 years of treatment. Specific allergy immunotherapy can be repeated.

Although some specific allergen therapies can be prescribed by primary care health professionals, it is recommended that they are initiated under the care of an allergy specialist (allergist or clinical immunologist), where possible.

Commercial allergen preparations for immunotherapy are available in Australia for aeroallergens including house dust mite, pollens (e.g. grass, tree and weed pollens), animal dander and moulds.

► Go to: ASCIA's <u>Allergen Immunotherapy</u> fact sheet for patients Go to: ASCIA's <u>Allergen immunotherapy e-training for health professionals</u>

Overview of efficacy

There is strong evidence that allergen immunotherapy is effective in the treatment of seasonal and perennial allergic rhinitis.^{60, 7, 5} There is less evidence supporting specific allergen immunotherapy in children than in adults.⁷ Specific allergen immunotherapy in children with seasonal allergic rhinoconjunctivitis might prevent development of asthma.^{34, 61, 62}

Single-allergen specific allergen immunotherapy is effective in patients sensitised to one allergen and those sensitised to multiple allergens.^{32, 63, 64} In selected cases more than one allergen may be administered as separate extracts. There is weak evidence for the efficacy of allergen mixes.⁶⁵

A systematic review of studies directly comparing subcutaneous immunotherapy and sublingual immunotherapy in the treatment of allergic rhinoconjunctivitis and asthma found:²⁰

- low-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing asthma symptoms and for reducing a combined measure of rhinitis symptoms and medication use
- moderate-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing nasal and/or eye symptoms.

Sublingual immunotherapy is associated with a lower rate of severe adverse effects (anaphylaxis and death) than subcutaneous immunotherapy, based on indirect comparison.^{3, 21, 22}

Sublingual immunotherapy

Sublingual immunotherapy (self-administered at home) is effective for the treatment of allergic rhinitis in adults and children.^{23, 24} The greatest benefits have been demonstrated in those with allergies to temperate grass pollens or house dust mite.²⁴ Therapeutic Goods Administration (TGA)-approved indications for commercially available preparations vary according to age group.

The extract must be held under the tongue without swallowing for 2 minutes (liquid extracts) or 1 minute (tablets).

Sublingual immunotherapy is generally well tolerated.²³ Local adverse effects are common in children receiving sublingual immunotherapy.³ Systemic adverse reactions, such as anaphylaxis, are very rare.³ The majority of adverse events occur soon after beginning treatment.²⁴

TGA-approved indications

Asthma: Acarizax (house dust mite) is indicated for adults 18-65 years with house dust mite allergic asthma that is not well controlled by inhaled corticosteroids and is associated with mild-to-severe house dust mite allergic rhinitis.⁶⁶ It is contraindicated in patients with FEV₁ <70% predicted after adequate treatment, and for patients who have experienced a severe flare-up within the previous 3 months.⁶⁶

Allergic rhinitis: Several commercial preparations of aeroallergens for sublingual immunotherapy in patients with allergic rhinitis are used in Australia, including:

- Acarizax (house dust mite) indicated for adults 18–65 years with persistent moderate to severe house dust mite allergic rhinitis despite symptomatic treatment.⁶⁶
- Actair (house dust mite) indicated for the treatment of house dust mite allergic rhinitis with or without conjunctivitis in adults and adolescents over 12 years diagnosed with house dust mite allergy.⁶⁷
- *Grazax* (Timothy grass [*Phleum pratense*] pollen extract) indicated for adults, adolescents and children older than 5 years with allergic rhinitis induced by Timothy grass⁶⁸
- Oralair tablets (mix of grass pollens) indicated for adults and children over 5 years with grass pollen allergic rhinitis.⁶⁹

Various single allergens and/or multiple allergen mixes are available for use as advised by the treating allergist, available as liquid extracts. Age restrictions vary between products.

Note: PBS status as at October 2016: Treatment with sublingual immunotherapy specific allergen preparations is not subsidised by the PBS.

Subcutaneous immunotherapy

Subcutaneous immunotherapy involves injections in which the dose is gradually increased at regular intervals (usually weekly), or until a therapeutic/maintenance dose is reached. This can take approximately 3–6 months.⁷⁰ Treatment is then continued for a further 3–5 years.

Subcutaneous immunotherapy is generally not suitable for younger children (e.g. less than 7 years) because they may not be able to tolerate frequent injections.

Several commercial preparations of aeroallergens for subcutaneous immunotherapy are available in Australia, including various single allergens and/or multiple allergen mixes for use as advised by the treating allergist. Age restrictions vary between products.

Subcutaneous immunotherapy is effective for the treatment of allergic rhinitis and asthma, particularly when single-allergen immunotherapy regimens are used.²¹ There is strong evidence that it reduces asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life, in comparison to placebo or usual care.²¹ There is also moderate evidence that subcutaneous immunotherapy reduces rhinitis/rhinoconjunctivitis medication usage.²¹

Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects.^{3, 24} The most common systemic reactions are respiratory symtoms. There have been few reports of anaphylaxis.³

Note: PBS status as at March 2019: Treatment with subcutaneous specific allergen immunotherapy preparations is not subsidised by the PBS. *Last reviewed version 2.0*

Surgical turbinate reduction

Turbinate reduction surgery can be considered when nasal obstruction is due to turbinate hypertrophy and symptoms do not respond to medical treatment. It should not be performed in young children except after thorough investigation and review.

Inferior turbinate hypertrophy secondary to inflammation is a common cause of nasal obstruction in patients with allergic rhinitis.⁷¹ Several surgical procedures are available to correct this problem.¹ The ideal surgical reduction should preserve the mucosa and physiological function.⁷¹

Short-term adverse outcomes of inferior turbinate reduction include nasal bleeding, scarring and crusting. Rarely, it may worsen symptoms when patients have non-specific rhinitic conditions or sino-nasal somatisation disorders ('empty nose syndrome').¹ There is no evidence that turbinate surgery creates these conditions, but sino-nasal surgery may exacerbate the symptoms.

Montelukast for adults and adolescents: psychiatric effects

Post-marketing surveillance reports led to concerns about a possible association between leukotriene receptor antagonist use and suicide risk.⁵⁰ A recent case-control study reported a statistically significant association between the use of leukotriene receptor antagonists and suicide attempts in people aged 19–24 years. However, this association was no longer statistically significant after adjusting for potential confounding factors, including previous exposure to other asthma medicines and previous exposure to other medicines associated with suicide.⁵⁰

► Go to: <u>TGA alert</u>

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Managing allergic rhinitis in children with asthma

Recommendations

In school-aged children with persistent or moderate-to-severe intermittent symptoms, prescribe or recommend an intranasal corticosteroid (even if the child is already using regular inhaled corticosteroids for asthma).

If symptoms do not improve significantly within 3-4 weeks:

- review the diagnosis
- check adherence and intranasal administration technique
- consider allergy testing.

Figure. Management of allergic rhinitis in children under 12 years

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How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Seidman *et al*, 2015⁶⁶
- Bousquet et al, 200838
- Brożek et al, 2010²¹
- Lohia et al, 2013¹
- Bousquet et al, 2016²
- Wallace *et al*, 2008³⁶
- Berger & Meltzer, 2015³
- Bachert & Maspero, 2011⁴

In school-aged children with mild intermittent symptoms, consider starting treatment with an intranasal H1-antihistamine, second-generation (less sedating) or al H_1 -antihistamine or montelukast. Do not use sedating antihistamines.

Montelukast can be considered as an alternative to antihistamines in children with seasonal allergic rhinitis.

If symptoms do not improve significantly within 2-4 weeks, switch to an intranasal corticosteroid.

• Advise parents about potential adverse psychiatric effects of montelukast

Figure. Management of allergic rhinitis in children under 12 years

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Based on selected evidence

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- Seidman *et al*, 2015⁵
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- Bousquet et al, 2016⁷

- Wallace et al, 200836
- Berger & Meltzer, 2015⁸
- Bachert & Maspero, 2011⁴
- Nasser *et al*, 2010⁹

In preschool-aged children or children who will not tolerate intranasal medication, start treatment with a second-generation (less sedating) oral H₁-antihistamine approved for use in this age-group (e.g. cetirizine, desloratadine, fexofenadine, loratadine). Do not use sedating antihistamines.

Montelukast can be considered as an alternative to antihistamines.

If symptoms do not improve significantly within 2-4 weeks, switch to an intranasal corticosteroid if possible.

• Advise parents about potential adverse psychiatric effects of montelukast

Figure. Management of allergic rhinitis in children under 12 years

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Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Provide an allergic rhinitis treatment plan.

► Go to: ASCIA's <u>Allergic rhinitis treatment plan template</u>



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

In children of any age in whom allergic rhinitis symptoms are uncontrolled despite regular use of intranasal corticosteroids, review the diagnosis and consider specialist referral.

Adenoid hypertrophy should be suspected in children who do not respond to treatment within 4 weeks.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

For children who are taking an inhaled corticosteroid for asthma and who have persistent allergic rhinitis symptoms despite treatment with an intranasal corticosteroid, consider adding montelukast.

• Advise parents about potential adverse psychiatric effects of montelukast



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

At each review, check adherence to medications and topical therapy technique, as for asthma.

How this recommendation was developed Consensus



Inspect nasal mucosa one month after starting treatment then every 6 months for improvement in symptoms, resolution of turbinate hypertrophy, and any evidence of local crusting or bleeding. Refer to an ear, nose and throat surgeon for review if symptoms do not improve and turbinate hypertrophy does not respond to medical intervention.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Consider specific allergen immunotherapy in children with allergic rhinitis who have a history of proven, clinically important sensitisation to a particular allergen that cannot feasibly be avoided and for which for specific allergen immunotherapy is available.

Note: Specific allergen immunotherapy should not be started in children with asthma unless asthma is stable. For those able to perform spirometry, this includes spirometry-demonstrated forced expiratory volume in 1 second (FEV₁) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.

Note: Make sure parents understand that treatment must be long term (3-5 years), and understand the cost and risks of the treatment.

Note: TGA-approved indications for commercially available preparations vary according to age group. As at October 2017, the only product approved by TGA for use in children under 12 years is a mixed grass pollen preparation indicated for children over 5 years with allergic rhinitis.



How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

- Cox, 2016¹⁰
- Meadows et al, 2013¹¹
- Durham et al. 2016¹²
- Passalacqua et al, 2014¹³
- Chelladurai et al, 2013¹⁴
- Brożek et al, 2010²¹
- Erekosima et al, 2014¹⁵
- Calderon *et al*, 2015¹⁶
- Radulovic *et al*, 2010¹⁷
- Canonica *et al*, 2009¹⁸
- Jacobsen et al, 2007¹⁹
- Paino et al. 2017²⁰

Advise parents to provide a smoke-free environment for children with allergic rhinitis.



How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

More information

Links between allergic rhinitis and asthma

Prevalence, aetiology and symptoms

Asthma and allergic rhinitis frequently coexist. At least 75% of patients with asthma also have rhinitis, although estimates vary widely.²¹ Patients with asthma may have both allergic and non-allergic rhinitis.

Allergic rhinitis that starts early in life is usually due to a classical IgE hypersensitivity. Adult-onset asthma or inflammatory airway conditions typically have more complex causes. Chronic rhinosinusitis with nasal polyps is not a simple allergic condition and generally

needs specialist care.²²

Symptoms and signs of allergic rhinitis can be local (e.g. nasal discharge, congestion or itch), regional (e.g. effects on ears, eyes, throat or voice), and systemic (e.g. sleep disturbance and lethargy). Most people with allergic rhinitis experience nasal congestion or obstruction as the predominant symptom. Ocular symptoms (e.g. tearing and itch) in people with allergic rhinitis are usually due to coexisting allergic conjunctivitis.²³

Patients may mistake symptoms of allergic rhinitis for asthma and vice versa. Allergic rhinitis is sometimes more easily recognised only after asthma has been stabilised.

► Go to: National Asthma Council Australia's Managing allergic rhinitis in people with asthma information paper

Effects on asthma

Allergic rhinitis is an independent risk factor for developing asthma in children and adults.^{24, 25, 26, 27, 28} However, the use of antihistamines in children has not been shown to prevent them developing asthma.²¹

The presence of allergic rhinitis is associated with worse asthma control in children and adults.^{29, 30, 31, 32} The use of intranasal corticosteroids in patients with concommitant allergic rhinitis and asthma may improve asthma control in patients who are not already taking regular inhaled corticosteroids.¹

Both rhinitis and asthma can be triggered by the same factors, whether allergic (e.g. house dust mite, pet allergens, pollen, cockroach) or non-specific (e.g. cold air, strong odours, environmental tobacco smoke).

Food allergies do not cause allergic rhinitis. Most people with allergic rhinitis are sensitised to multiple allergens (e.g. both pollens and house dust mite), so symptoms may be present throughout the year.

Pollens (e.g. grasses, weeds, trees) and moulds are typically seasonal allergens in southern regions, but can be perennial in tropical northern regions.³³ However, ryegrass is not found in tropical regions (see <u>Thunderstorm asthma</u>).

Pollen calendars provide information on when airborne pollen levels are likely to be highest for particular plants.

Thunderstorm asthma

Seasonal allergic rhinitis, which in Australia is typically associated with sensitisation to perennial ryegrass (*Lolium perenne*), is an important risk factor for thunderstorm asthma.³⁴

Go to: ASCIA's Pollen calendar

Go to: National Asthma Council Australia's Epidemic thunderstorm asthma information paper

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Treatment of allergic rhinitis in children

Table. Overview of efficacy of allergic rhinitis medicines for specific symptoms

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Intranasal corticosteroids

Intranasal corticosteroids are effective in reducing congestion, rhinorrhoea, sneezing and itching in school-aged children with allergic rhinitis.^{1, 21} However, there is weaker evidence to support their efficacy in children than in adults.²¹ There is limited evidence to guide the treatment of allergic rhinitis in preschool children.²

The addition of an oral H_1 -antihistamine or leukotriene receptor antagonist to an intranasal corticosteroid is generally no more effective than intranasal corticosteroid monotherapy.²

TGA-approved indications vary between age groups. Intranasal corticosteroids indicated for children aged under 12 years include fluticasone furoate (age 2 years and over), mometasone furoate (age 3 years and over), and budesonide (age 6 years and over).

Intranasal corticosteroids are well tolerated. Evidence from studies mainly in adults suggests that they do not cause atrophy of nasal epithelium.³⁵ Intranasal corticosteroids are not generally associated with clinically significant systemic adverse effects in children when given in recommended doses.¹³⁶ Studies in children evaluating effects on the hypothalamic-pituitary axis using morning cortisol concentrations, cosyntropin stimulation, and 24-hour urinary free cortisol excretion showed no adverse effects with ciclesonide, fluticasone propionate, fluticasone furoate, mometasone furoate, or triamcinolone acetonide.¹ One knemometry study showed reduced lower leg growth rate in children using intranasal budesonide.¹ In studies using stadiometry over 12 months, higher-than-recommended doses of intranasal beclomethasone dipropionate were associated with growth suppression, but fluticasone propionate and mometasone furoate showed no effects on growth compared with placebo.¹

In children already taking inhaled corticosteroids, both the intranasal corticosteroid dose and the inhaled corticosteroid dose should be

taken into account when calculating the total daily corticosteroid dose.

Oral antihistamines

Second-generation (less sedating) antihistamines (e.g. cetirizine, desloratadine, fexofenadine or loratadine) should be used in preference to older, more sedating antihistamines. Cetirizine is the most likely of the less sedating antihistamines to cause sedation, while fexofenadine and loratadine appear to be the least sedating.³⁷

These antihistamines can be taken long term by children. Eighteen months of treatment with cetirizine was well tolerated in a large, prospective, multi-country, randomised controlled trial in infants with atopic dermatitis aged 12–24 months.¹

Less sedating oral H₁-antihistamines are effective in managing allergic rhinitis symptoms of rhinorrhoea, sneezing, nasal itching and ocular symptoms,^{2, 4} including in preschool children. ² They can provide adequate relief for some individuals when taken continuously or intermittently.¹ Available agents appear to be equally effective.³⁶

However, oral antihistamines are less effective than continuous intranasal corticosteroids, especially for nasal congestion.^{1, 38} The addition of oral antihistamines to intranasal corticosteroids has not been demonstrated to be an effective strategy in children.³⁹

TGA-approved indications vary between age groups. Less sedating oral antihistamines indicated for children under 12 years include cetirizine (1 year and over), loratatidine (1 year and over), desloratadine (6 months and over), and fexofenadine (6 months and over).

Intranasal antihistamines

Intranasal antihistamines are at least equally effective as second-generation, less sedating oral H_1 -antihistamines for the treatment of allergic rhinitis, but are generally less effective than intranasal corticosteroids.²¹

Intranasal antihistamines are more effective than oral antihistamines for reducing nasal congestion.¹ They have a rapid onset of action (15–30 minutes).¹

Montelukast

Leukotriene receptor antagonists are no more effective than oral H_1 -antihistamines.^{21, 2} Montelukast is less effective than intranasal corticosteroid in the treatment of allergic rhinitis.^{1, 21} In most studies, adding montelukast to an intranasal corticosteroid was not more effective than intranasal corticosteroid alone.²

Montelukast is approved by TGA for the treatment of asthma in children over 2 years, and for the treatment of seasonal allergic rhinitis.

It is generally very well tolerated, but has been infrequently associated with neuropsychiatric adverse effects, including suicidal ideation, in children and young people.^{40, 41, 42, 43} A recent analysis of databases of adults and children taking montelukast suggests it is associated with nightmares (especially in children), depression, and aggression (especially in children).⁴⁴ Allergic granulomatous angiitis has also been reported, but a causal relationship has not been established.⁴⁴

The potential association of montelukast with behaviour-related adverse events should be mentioned to parents when commencing treatment, and treatment should be stopped if such adverse events are suspected.

Specific allergen immunotherapy

Specific allergen immunotherapy (desensitisation) is effective in reducing allergic rhinitis symptoms (see separate topic).

► Go to: National Asthma Council Australia's <u>Allergic rhinitis and asthma</u> information paper Go to: National Asthma Council Australia's information on intranasal delivery technique, including <u>How-to videos</u> Go to: National Asthma Council Australia's <u>Allergic rhinitis treatments chart</u>

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Non-recommended medications for allergic rhinitis

Intranasal decongestants have a limited role in the management of allergic rhinitis because they should only be used for very short courses (up to 5 days maximum). Repeated or long-term use can cause rebound swelling of nasal mucosa (rhinitis medicamentosa), which can lead to dose escalation by patients, with a risk of atrophic rhinitis. Intranasal decongestants can be considered for a patient with severe nasal congestion to gain rapid relief of symptoms until the full effect of intranasal corticosteroids is achieved.

Oral decongestants (e.g. pseudoephedrine or phenylephrine) should not generally be used in the management of allergic rhinitis. They are indicated for short-term use only (e.g. acute infectious rhinitis, or during air travel by a patient with symptomatic rhinitis, as a single tablet taken one hour before landing). They are associated with adverse effects including palpitations, tachycardia and insomnia.

Oral corticosteroids should be avoided as a treatment for allergic rhinitis. In exceptional circumstances, their use might be considered in consultation with an allergy specialist.

Topical ocular alpha agonist vasoconstrictors (including in combination with antihistamines) should not be used for allergic conjunctivitis because they can cause conjunctivitis medicamentosa.

Montelukast for children: behavioural and/or neuropsychiatric adverse effects

Montelukast is generally very well tolerated. Behavioural and psychiatric adverse effects were rare in clinical trials.^{31, 43} However, postmarketing surveillance reports have identified behavioural and/or neuropsychiatric adverse effects associated with montelukast use in some children.⁴⁵

Behavioural treatment-associated effects are difficult to assess in young children. No factors have been identified to predict which children are at risk.

Reported adverse events include nightmares, sleep disturbance, anxiety, irritability, aggression and depression. 45, 46, 47, 48

Suicidal ideation has been reported in adolescents and adults taking montelukast.⁴⁸ A nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts.⁴⁹

Reported adverse effects are usually mild.⁴⁷ The majority occur within 7–14 days of starting montelukast,^{45, 47} but some may appear after several months.⁴⁸

Behavioural and/or neuropsychiatric adverse effects typically disappear within 4 days of stopping montelukast treatment.⁴⁷ There is no evidence of long term effects.

The TGA recommends that clinicians treating children with montelukast should educate caregivers about these potential adverse effects and should consider providing them with the CMI. Advise them to seek medical advice if they have any concerns.

► Go to: TGA's 2018 safety review of montelukast

Last reviewed version 2.0

Smoking and allergic rhinitis

Smoking may worsen both asthma and rhinitis, and exposure to tobacco smoke can reduce the effectiveness of treatment in adults and children.^{50, 51}

Nasal saline irrigation for allergic rhinitis

Nasal irrigation (via a syringe, rinse bottle, spray or other device) can improve nasal symptoms, mucociliary clearance, and quality of life.⁴⁶ Saline administered by spray or other devices was used at least twice daily in most studies that showed a benefit.⁴⁶

Isotonic solution is preferable to hypertonic solution because it supports optimal mucociliary clearance.⁴⁶ Isotonic saline is solution is inexpensive and has no known adverse effects.⁴⁶ Patients can use either commercially manufactured saline solutions or home-made normal saline: 1 teaspoon (5 g) rock or sea salt in 500 mL of water (preferably bottled or boiled).

There is not enough evidence to determine:

- whether solutions should be buffered or non-buffered, sterile or non-sterile
- whether various additives provide any advantage
- whether inhaling steam or an irritant decongestant (e.g. eucalyptus, menthol) before saline irrigation provides any extra benefit. However, patients are more likely to adhere to simple and convenient regimens, regardless of theoretical advantages. Caution is required with steam inhalation to avoid burns.

If patients are using both saline irrigation and an intranasal corticosteroid or intranasal H_1 -antihistamine, they should perform saline irrigation first. Saline can be used again after waiting at least an hour after using an intranasal corticosteroid.

Young children are unlikely to tolerate nasal irrigation.

Specific allergen immunotherapy (desensitisation)

• Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV₁) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.^{52, 53} For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered. These patients will need specialist supervision during treatment.

Options available in Australia

Two forms of specific allergen immunotherapy are available:

- sublingual immunotherapy
- subcutaneous immunotherapy.

Both forms of specific allergen immunotherapy require 3-5 years of treatment. Specific allergy immunotherapy can be repeated.

Although some specific allergen therapies can be prescribed by primary care health professionals, it is recommended that they are initiated under the care of an allergy specialist (allergist or clinical immunologist), where possible.

Commercial allergen preparations for immunotherapy are available in Australia for aeroallergens including house dust mite, pollens (e.g. grass, tree and weed pollens), animal dander and moulds.

► Go to: ASCIA's <u>Allergen Immunotherapy</u> fact sheet for patients Go to: ASCIA's <u>Allergen immunotherapy e-training for health professionals</u>

Overview of efficacy

There is strong evidence that allergen immunotherapy is effective in the treatment of seasonal and perennial allergic rhinitis.^{54, 3, 2} There is less evidence supporting specific allergen immunotherapy in children than in adults.³ Specific allergen immunotherapy in children with seasonal allergic rhinoconjunctivitis might prevent development of asthma.^{22, 55, 56}

Single-allergen specific allergen immunotherapy is effective in patients sensitised to one allergen and those sensitised to multiple allergens.^{57, 58, 59} In selected cases more than one allergen may be administered as separate extracts. There is weak evidence for the efficacy of allergen mixes.⁶⁰

A systematic review of studies directly comparing subcutaneous immunotherapy and sublingual immunotherapy in the treatment of allergic rhinoconjunctivitis and asthma found:¹⁴

- low-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing asthma symptoms and for reducing a combined measure of rhinitis symptoms and medication use
- moderate-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing nasal and/or eye symptoms.

Sublingual immunotherapy is associated with a lower rate of severe adverse effects (anaphylaxis and death) than subcutaneous immunotherapy, based on indirect comparison.^{21, 15, 16}

Sublingual immunotherapy

Sublingual immunotherapy (self-administered at home) is effective for the treatment of allergic rhinitis in adults and children.^{17, 18} The greatest benefits have been demonstrated in those with allergies to temperate grass pollens or house dust mite.¹⁸ Therapeutic Goods Administration (TGA)-approved indications for commercially available preparations vary according to age group.

The extract must be held under the tongue without swallowing for 2 minutes (liquid extracts) or 1 minute (tablets).

Sublingual immunotherapy is generally well tolerated.¹⁷ Local adverse effects are common in children receiving sublingual immunotherapy.²¹ Systemic adverse reactions, such as anaphylaxis, are very rare.²¹ The majority of adverse events occur soon after beginning treatment.¹⁸

TGA-approved indications

Asthma: Acarizax (house dust mite) is indicated for adults 18-65 years with house dust mite allergic asthma that is not well controlled by inhaled corticosteroids and is associated with mild-to-severe house dust mite allergic rhinitis.⁶¹ It is contraindicated in patients with FEV₁ <70% predicted after adequate treatment, and for patients who have experienced a severe flare-up within the previous 3 months.⁶¹

Allergic rhinitis: Several commercial preparations of aeroallergens for sublingual immunotherapy in patients with allergic rhinitis are used in Australia, including:

- Acarizax (house dust mite) indicated for adults 18–65 years with persistent moderate to severe house dust mite allergic rhinitis despite symptomatic treatment.⁶¹
- Actair (house dust mite) indicated for the treatment of house dust mite allergic rhinitis with or without conjunctivitis in adults and adolescents over 12 years diagnosed with house dust mite allergy.⁶²
- *Grazax* (Timothy grass [*Phleum pratense*] pollen extract) indicated for adults, adolescents and children older than 5 years with allergic rhinitis induced by Timothy grass⁶³
- Oralair tablets (mix of grass pollens) indicated for adults and children over 5 years with grass pollen allergic rhinitis.⁶⁴

Various single allergens and/or multiple allergen mixes are available for use as advised by the treating allergist, available as liquid extracts. Age restrictions vary between products.

Note: PBS status as at October 2016: Treatment with sublingual immunotherapy specific allergen preparations is not subsidised by the PBS.

Subcutaneous immunotherapy

Subcutaneous immunotherapy involves injections in which the dose is gradually increased at regular intervals (usually weekly), or until a therapeutic/maintenance dose is reached. This can take approximately 3–6 months.⁶⁵ Treatment is then continued for a further 3–5 years.

Subcutaneous immunotherapy is generally not suitable for younger children (e.g. less than 7 years) because they may not be able to tolerate frequent injections.

Several commercial preparations of aeroallergens for subcutaneous immunotherapy are available in Australia, including various single allergens and/or multiple allergen mixes for use as advised by the treating allergist. Age restrictions vary between products.

Subcutaneous immunotherapy is effective for the treatment of allergic rhinitis and asthma, particularly when single-allergen immunotherapy regimens are used.¹⁵ There is strong evidence that it reduces asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life, in comparison to placebo or usual care.¹⁵ There is also moderate evidence that subcutaneous immunotherapy reduces rhinitis/rhinoconjunctivitis medication usage.¹⁵

Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects.^{21, 18} The most common systemic reactions are respiratory symtoms. There have been few reports of anaphylaxis.²¹

Note: PBS status as at March 2019: Treatment with subcutaneous specific allergen immunotherapy preparations is not subsidised by the PBS. *Last reviewed version 2.0*

Surgical turbinate reduction

Turbinate reduction surgery can be considered when nasal obstruction is due to turbinate hypertrophy and symptoms do not respond to medical treatment. It should not be performed in young children except after thorough investigation and review.

Inferior turbinate hypertrophy secondary to inflammation is a common cause of nasal obstruction in patients with allergic rhinitis.⁴⁷ Several surgical procedures are available to correct this problem.⁶⁶ The ideal surgical reduction should preserve the mucosa and physiological function.⁴⁷

Short-term adverse outcomes of inferior turbinate reduction include nasal bleeding, scarring and crusting. Rarely, it may worsen symptoms when patients have non-specific rhinitic conditions or sino-nasal somatisation disorders ('empty nose syndrome').⁶⁶ There is no evidence that turbinate surgery creates these conditions, but sino-nasal surgery may exacerbate the symptoms.

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Considering allergen avoidance where feasible

Recommendations

Advise patients who are at risk of thunderstorm asthma to:

- check grass pollen counts for their region during spring and early summer (if available)
- on high grass pollen days, avoid exposure to outdoor air when a thunderstorm is approaching, especially during wind gusts just before the rain front hits (e.g. by going indoors with windows closed and air conditioner off or on recirculation mode, or shutting car windows and recirculating air).

Notes: People with asthma are particularly at risk of thunderstorm asthma if they have seasonal (springtime) allergic rhinitis (i.e. allergic to ryegrass pollen), and live in or are travelling to an area with high grass pollen levels.

People without known asthma (or previous symptoms of asthma) who have springtime allergic rhinitis and are sensitised to allergy to ryegrass pollen are also at risk of thunderstorm asthma.

Pollen counts are available during spring and summer (dates vary) for <u>Melbourne</u>, <u>Sydney</u>, <u>Brisbane</u>, <u>Canberra</u>, <u>Adelaide</u> and <u>Tasmania</u>. Phone apps are available for some areas.

► Go to: pollenforecast.com.au

O_A How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

• NACA, 2017¹

Last reviewed version 2.0

Advise allergen avoidance or reduction measures only if all the following apply:

- the patient has proven sensitivity to the allergen
- the allergen is a clinically significant asthma trigger
- the patient or carer is motivated to apply reduction measures long term and can afford them.

Note: With the exception of thunderstorm asthma prevention measures, which should be advised for all at-risk patients who are living in or travelling to a region with high grass pollen levels.

O How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Advise patient or parents that single interventions to reduce exposure to house dust mites are unlikely to be effective in improving asthma symptoms or control.



How this recommendation was developed

Evidence-based recommendation (Grade C)

Based on systematic literature review.

Clinical question for literature search:

Is allergen avoidance effective in improving asthma control? Which allergen avoidance strategies are most effective in controlling symptoms of asthma?

Key evidence considered:

- Gøtzsche and Johansen, 2008²
- van den Bemt *et al.* 2007³
- Brehler and Kniest, 2006⁴

Advise patient or parents that a combination of allergen reduction strategies may improve asthma symptoms or control for some patients sensitised to house dust mites.



How this recommendation was developed

Evidence-based recommendation (Grade C)

Based on systematic literature review.

Clinical question for literature search:

Is allergen avoidance effective in improving asthma control? Which allergen avoidance strategies are most effective in controlling symptoms of asthma?

Key evidence considered:

- Gøtzsche and Johansen, 2008²
- Hayden *et al.* 1997⁵

Explain that the use of mite allergen-impermeable covers for bedding (e.g. mattress covers, pillow covers, doona covers) was a component of some of the multi-component strategies for reducing house dust mite exposure that have been shown to be effective for improving asthma symptoms or control.

O How this recommendation was developed

Evidence-based recommendation (Grade C)

Based on systematic literature review.

Clinical question for literature search:

Is allergen avoidance effective in improving asthma control? Which allergen avoidance strategies are most effective in controlling symptoms of asthma?

Key evidence considered:

- Dorward *et al.* 1988⁶
- Hayden *et al.* 1997⁵
- Shapiro *et al.* 1999⁷
- Walshaw and Evans, 1986⁸

If a person has proven allergy to an animal, and symptoms that correlate with exposure to the particular animal, advise avoidance of the animal. If it is not possible to avoid the animal, consider premedicating with an antihistamine 20–30 minutes before predicted exposure.



Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

If the trigger animal is a family pet, advise removal of the pet from the home. If this is not feasible, advise keeping the pet outside or in a limited part of the house, and not allowing the pet into the allergic person's bedroom.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Advise patients who are sensitised to pollens (or parents) that some people try pollen avoidance measures during pollen season, but there is no reliable evidence that these are effective.

Strategies that may be helpful include:

- staying indoors during and after thunderstorms
- staying indoors on high-pollen days and windy days, if possible
- wearing sunglasses (which may help prevent allergens from depositing onto the conjunctivae)
- washing and drying clothing inside to help prevent deposition of pollen allergen on clean clothes
- keeping windows closed where possible.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Advise patients or parents to focus mould avoidance measures on reducing or preventing dampness of the home to prevent mould growth.

O How this recommendation was developed

Based on selected evidence

Based on a limited structured literature review or published systematic review, which identified the following relevant evidence:

• Sauni et al. 2011⁹

More information

Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause lifethreatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.^{3,5,6,8,9}

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.^{3, 5} Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.³

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.^{1, 9, 10}

Data from thunderstorm as thma epidemics suggest that the risk of as thma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known as thma).³

The worst outcomes are seen in people with poorly controlled asthma.¹ Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.⁵

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal

corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.¹¹

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.⁴

► Go to: National Asthma Council Australia's <u>Epidemic thunderstorm asthma</u> information paper Go to: ASCIA's <u>Pollen calendar</u> Go to: <u>Vic Emergency's Thunderstorm asthma forecast (Victoria only)</u>

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Allergy tests in adults with asthma

Allergy tests have a very limited role in the clinical investigation of asthma. They may be useful to guide management if the patient is sensitised to aeroallergens that are avoidable and avoidance has been shown to be effective, or in the investigation of suspected occupational asthma.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) recommends skin prick testing as the first-choice method for investigating allergies in a person with asthma.¹⁰

Patients who need allergy tests are usually referred to a specialist for investigation. GPs with appropriate training and experience can also perform skin prick tests for inhalent allergens, if facilities to treat potential systemic allergic reactions are available, or arrange for allergy tests (skin prick testing or blood tests) to be performed by an appropriate provider. Skin prick testing for food allergens should only be performed in specialist practices.

Asthma, particularly uncontrolled or unstable asthma, may be a risk factor for anaphylaxis during skin prick testing;¹⁰ however, anaphylaxis due to skin prick testing is extremely rare. As a precaution, ASCIA advises that skin prick testing in people with severe or unstable asthma should be performed only in specialist practices.¹⁰ ASCIA's manual on skin prick testing lists other risk factors.¹⁰

Go to: Australasian Society of Clinical Immunology and Allergy Skin Prick Testing Working Party's <u>Skin prick testing for the diagnosis of allergic disease. A manual for practitioners</u>
 Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

House dust mite

Exposure to house dust mite (mainly *Dermatophagoides pteronyssinus*) is a major asthma trigger in Australia.¹¹ These microscopic mites live indoors, feed on skin scales, and thrive in temperate and humid climates such as coastal Australia.

Strategies that have been proposed for reducing exposure to house dust mites include:¹¹

- encasing bedding (pillows, mattresses and doonas) in mite-impermeable covers
- weekly washing bed linen (pillow cases, sheets, doona covers) in a hot wash (> 55°C)
- using pillows manufactured with anti-microbial treatments that suppress fungal growth and dust mites
- removing unnecessary bedding such as extra pillows and cushions where dust mites might live and breed
- removing soft toys, or washing them in a hot wash (> 55°C) every week
- vacuuming rugs and carpets weekly using a vacuum with a high-efficiency particulate air (HEPA) filter, while allergic person is absent
- cleaning hard floors weekly with a damp or antistatic cloth, mop or a steam mop and dusting weekly using a damp or antistatic cloth
- regularly washing curtains or replacing curtains with cleanable blinds
- spraying the area with chemicals that kill mites (acaricides), such as benzyl benzoate spray or liquid nitrogen. Acaricide sprays are not commonly used in Australia.

Some clinical trials assessing the dust mite avoidance strategies (e.g. the use of allergen-impermeable mattress and pillow covers, acaricide sprays, air filters, or combinations of these) have reported a reduction in levels of house dust mite.^{12, 13, 14, 15, 16, 6, 17, 18, 19, 20, 21, 4} However, reduced exposure may not improve symptoms.

Overall, clinical trials assessing dust mite avoidance for patients with asthma do not show that these strategies are effective in improving asthma symptoms, improving lung function or reducing asthma medication requirements in adults or children, compared with sham interventions or no interventions.² The use of allergen-impermeable mattress covers, as a single mite-reduction intervention in adults, is unlikely to be effective in improving asthma.²²

Use of mite allergen-impermeable covers for bedding (e.g. mattress covers, pillow covers, doona covers) was a component of some of the multi-component strategies for reducing house dust mite exposure that have been shown to be effective for improving asthma symptoms or control.

► Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

Pet allergens

Contact with pets (e.g. cats, dogs and horses) can trigger asthma, mainly due to sensitisation to allergens in sebum or saliva. Exposure can trigger flare-ups or worsen symptoms.¹¹

The amount of allergen excreted differs between breeds.¹¹ Although some breeders claim that certain breeds of dogs are less likely to trigger asthma ('hypoallergenic' breeds), allergen levels have not been shown to be lower in the animal's hair or coat,²³ or in owner's homes²⁴ with these breeds than other breeds.

Cat allergens easily spread on clothing and are found in places where cats have never been.¹¹

The most effective method of allergen avoidance for people with asthma who are allergic to cats or dogs is to not have these pets in the home. However, the allergen can persist for many months, or even years, after the pet has been removed.¹¹

There is not enough clinical trial evidence to determine whether or not air filtration units are effective to reduce allergen levels in the management of pet-allergic asthma.²⁵

Other strategies for reducing exposure to pet allergens include:

- washing hands and clothes after handling pets
- washing clothes and pet bedding in hot water (> 55°C)
- frequent vacuuming of the home using a vacuum with a HEPA filter
- cleaning hard floors with a damp/antistatic cloth or a steam mop, and cleaning air-conditioning or heating ducts
- grooming pets regularly (where possible, the patient should be absent while this occurs), and washing pets regularly, but no more than the vet recommends.

► Go to: National Asthma Council Australia's <u>Asthma and allergy</u> information paper

Pollens

Allergy to airborne pollen grains from certain grasses, weeds and trees is common in people with asthma in Australia.¹¹ The highest pollen counts occur on calm, hot, sunny days in spring or early summer, or during the dry season in tropical regions.

Exposure to pollen:^{11, 26}

- may worsen asthma symptoms during the pollen season
- can cause outbreaks of asthma flare-ups after thunderstorms
- is usually caused by imported grasses, weeds and trees (which are wind pollinated) the pollen can travel many kilometres from its source
- is not usually caused by Australian native plants (although there are exceptions, such as Cypress Pine)
- is not usually caused by highly flowered plants as they produce less pollen (which is transported by bees) than wind pollinated plants.

Completely avoiding pollen can be difficult during the pollen season. Strategies that have been proposed for avoiding exposure to pollens include:¹¹

- avoiding going outdoors on days with high pollen counts (particularly 7-9 am and 4-6 pm), on windy days or after thunderstorms
- keeping car windows closed, ensuring the vehicle has a pollen cabin air filter and setting the cabin air to recirculate
- showering (or washing face and hands thoroughly) after being outside with exposure to pollen
- drying bed linen indoors during the pollen season
- holidaying out of the pollen season or at the seaside
- not mowing the grass, and staying inside when it is being mown
- wearing a facemask and/or glasses in special situations where pollen can't be avoided, e.g. if mowing is unavoidable
- removing any plants the patient is sensitive to from their garden.

Daily pollen indices and forecasts are available from news media websites (e.g. www.weatherzone.com.au).

Moulds

Building repairs to reduce dampness in homes (e.g. leak repair, improvement of ventilation, removal of water-damaged materials) may reduce asthma symptoms and the use of asthma medicines.⁹ A systematic review and meta-analysis found that damp remediation of houses reduced asthma-related symptoms including wheezing in adults, and reduced acute care visits in children.⁹ In children living in mouldy houses, remediation of the home may reduce symptoms and flare-ups, compared with cleaning advice about moulds.²⁷

Other strategies that have been proposed for avoiding exposure to moulds include:¹¹

- removing visible mould by cleaning with bleach or other mould reduction cleaners (patients should avoid breathing vapours)
- using high-efficiency air filters
- removing indoor pot plants

- drying or removing wet carpets
- treating rising damp as soon as it is detected
- avoiding the use of organic mulches and compost.
- See: <u>Asthma triggers</u>

Triggers in the workplace

A wide range of occupational allergens has been associated with work-related asthma. Investigation of work-related asthma is complex and typically requires specialist referral.

Table. Examples of common sensitising agents and occupations associated with exposure

Agent	Occupations			
Low molecular weight agents				
Wood dust (e.g. western red cedar, redwood, oak)	 Carpenters Builders Model builders Sawmill workers Sanders 			
Isocyanates	 Automotive industry workers Adhesive workers Chemical industry Mechanics Painters Polyurethane foam production workers 			
Formaldehyde	 Cosmetics industry Embalmers Foundry workers Hairdressers Healthcare workers Laboratory workers Tanners Paper, plastics and rubber industry workers 			
Platinum salts	 Chemists Dentists Electronics industry workers Metallurgists Photographers 			

Agent	Occupations		
Low molecular weight agents			
Latex	 Food handlers Healthcare workers Textile industry workers Toy manufacturers 		
Flour and grain dust	 Bakers Combine harvester drivers Cooks Farmers Grocers Pizza makers 		
Animal allergens (e.g. urine, dander)	 Animal breeders Animal care workers Jockeys Laboratory workers Pet shop workers Veterinary surgery workers 		

Source: Adapted from Hoy R, Abramson MJ, Sim MR. Work related asthma. *Aust Fam Physician* 2010; 39: 39-42. Available from: http://www.racgp.org.au/afp/201001/35841

Asset ID: 45

See: Work-related asthma

Multi-allergen avoidance strategies

Studies assessing interventions designed to reduce exposure to multiple allergens, including studies of individualised allergen avoidance advice after allergy testing, have reported inconsistent findings.^{28, 29, 30, 31}

A non-blinded randomised controlled clinical trial in 937 children with allergic asthma reported small reductions in symptoms and emergency department visits during a 1-year multi-component intervention and over a follow-up year, compared with no intervention. The intervention involved a combination of environmental tobacco smoke avoidance with a range of allergen avoidance strategies tailored to the child's sensitisation profile, including measures to reduce exposure to dust mites (allergen-impermeable covers for mattresses, pillows and bed springs, provision of high-efficiency particulate air-filter vacuum cleaner, installation of high-efficiency particulate air-filter in child's bedroom), cockroaches (professional pest control), pets (high-efficiency particulate air-filter in child's bedroom), rodents, and moulds.³⁰

A single-blinded randomised controlled clinical trial in 214 adults with asthma reported an increase in lung function among patients who underwent individualised allergen avoidance, compared with the control group.²⁸

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