



CME Article

Allergic rhinitis

Andrew S. Kemp*

Department of Allergy and Immunology, The Children's Hospital at Westmead and University of Sydney, Sydney, NSW 2145, Australia

EDUCATIONAL AIMS

- To discuss the diagnosis and management of childhood allergic rhinitis
- To provide information on appropriate pharmacotherapy
- To illustrate the benefits and limitations of allergen avoidance and
- To highlight the conclusions of evidence based medicine with regard to childhood allergic rhinitis

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SUMMARY

Childhood rhinitis may be classified into non-allergic and allergic. Allergic rhinitis is further divided into seasonal and perennial. Seasonal rhinitis is a disease particularly of teenagers and young adults and appears to be less common in primary and pre school age children. In seasonal rhinitis, with relevant grass pollen sensitization, the link between the allergen exposure and rhinitis is clear cut. However, in other situations such as perennial rhinitis and house dust mite allergen sensitization, the link between symptoms and allergen exposure is less certain. Avoidance of allergens often proves to be difficult in practice. Intranasal steroids are the treatment of choice for persistent moderate-severe allergic rhinitis and are more effective than antihistamines for relief of nasal obstruction. Antihistamines are effective for control of histamine related symptoms such as itching, rhinorrhoea and sneezing. The use and benefits of sublingual or injectable immunotherapy in children are controversial.

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INTRODUCTION

Allergic rhinitis (AR) affects both adolescents and younger children. AR may be regarded by parents as an irritation rather than as a significant disease and is often under-diagnosed and under-treated.¹ As AR is not life-threatening many patients or parents do not seek medical treatment or may choose to medicate with over-the-counter preparations. However, AR has a deleterious impact on quality of life² with significant effects on sleep, cognitive and psychomotor function, participation in social activities, and can result in learning impairment. AR is frequently associated with other childhood atopic diseases such as eczema and asthma. In one study 59% of children with asthma also had AR.³ Health service utilization and costs for asthma are greater for asthmatic children with associated AR. Associated asthma may be exacerbated by AR and treatment of the rhinitis can improve outcomes for asthma.⁴

CLASSIFICATION

Rhinitis may be classified into non-allergic and allergic; AR is further divided into seasonal ("hay fever") and perennial (all year round) (Table 1). The allergic inflammatory process may involve different mediators in seasonal and perennial AR. While this classification is useful as it indicates the possibilities for specific management steps, such as allergen avoidance and immunotherapy, in practice non-allergic and AR often co-exist.⁵ As inhalant allergen skin prick tests can be positive in a third of the childhood population⁶, it can be difficult to determine whether a positive test is related to a determinant of the AR. An alternative classification system based on symptom severity and frequency has been proposed and is useful in decisions regarding pharmacotherapy (Fig. 1).⁷

CLINICAL FEATURES

Rhinitis symptoms are characteristically nasal obstruction and rhinorrhoea, with AR also featuring sneezing, itchy nose, eyes and throat. The presentation can be non-specific, with features such as "fuzzy" head, tiredness and daytime sleepiness, constant "colds", sniffing, blinking and eye rubbing, speech problems, snoring and

* Tel.: +61 2 9845 3416; Fax: +61 2 9845 3421.

E-mail address: andrewk5@chw.edu.au.

Table 1
Types of childhood rhinitis and characteristic features

Rhinitis type	Key features
Allergic Rhinitis	
Seasonal allergic rhinitis “hayfever”	Associated with spring and early summer. Triggered by pollens, timing dependent on plant species and geographical location
Perennial allergic rhinitis	Symptoms occur year round. Triggered by house dust mite, pollens and pet animals
Non-allergic Rhinitis	
Idiopathic	Triggered by strong smells and changes in temperature
Infective	Most commonly repeated viral infections, causing episodes every 4–8 weeks of a nasal discharge lasting 5–7 days.
Vasomotor rhinitis	Sudden onset and offset of watery discharge.
Non-allergic with eosinophilia (NARES)	Negative allergy tests but greater than 20% eosinophils on nasal smears
Drug induced	β blockers, chlorpromazine, oral contraceptives, aspirin, rebound symptoms from topical decongestants

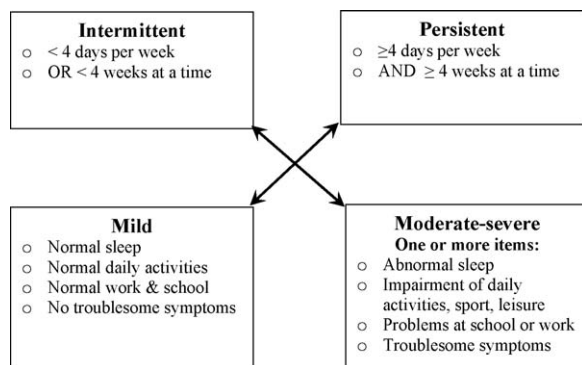


Figure 1. Functional classification of allergic rhinitis. In 2002, the WHO Allergic Rhinitis and its Impact on Asthma Workshop (ARIA) formulated this clinically relevant grading of rhinitis symptoms.⁷

dark circles under the eyes. Once AR is suspected, a directed history is required to assess the patient's environment and likely exposure to allergens and irritants, the type and timing of symptoms and their relationship to exposure, and the effect of symptoms on quality of life.⁸ The history will underpin decisions about investigations and future management.

RHINITIS AT DIFFERING AGES

Acquisition of sensitization to inhaled allergens occurs progressively throughout childhood and into adult life.⁹ Seasonal AR (hay fever) is a disease particularly of teenagers and young adults and appears to be less common in primary and pre school age children. At this age perennial rhinitis with the prominent symptom of nasal blockage is more common.¹⁰ The pattern of rhinitis (seasonal or perennial) will also be dictated by the climatic environment (temperate or tropical).

ROLE OF ALLERGENS AND ALLERGY TESTING

The role of allergens is complex. Sensitisation to an inhaled allergen does not necessarily mean that that allergen is the cause of the rhinitis. In some situations e.g. seasonal rhinitis with relevant grass pollen sensitization the link between the allergen exposure and symptoms of AR is clear cut however in other situations (e.g. perennial rhinitis and house dust mite allergen sensitization) the link between allergen and symptoms of rhinitis may be less clear. The relevant allergens may vary significantly according to geographic location.

Skin prick tests are the principal investigation for assessing the allergic basis of symptoms. A positive skin test (a wheal ≥ 3 mm) does not necessarily prove that the allergen is causing the patients' symptoms, only that there is sensitization with the production of IgE antibodies to the allergen. It is important to limit the allergens to be tested to what appears to be likely or to what can be excluded, as the indiscriminate ordering of “panels” with large numbers of allergens can lead to confusion and unnecessary attempts at allergen avoidance. The results of allergen testing must be interpreted together with the history. For example, symptoms restricted to early spring with negative tests to rye grass and positive tests to house dust mite may suggest that symptoms are non-allergic as house dust mite is a year round allergen. A mismatch between test results and history, or failure to respond to treatment should prompt consideration of other diagnoses such as non-allergic rhinitis, adenoidal hypertrophy, a deviated nasal septum, nasal polyps or a foreign body.

TREATMENT

Table 2 lists Cochrane reviews and their conclusions relevant to treatment of allergic rhinitis in children. Evidence based guidelines conclude that parent or patient education improves treatment effectiveness and quality of life, intranasal steroids are the treatment

Table 2
Cochrane Reviews relating to childhood allergic rhinitis

Title and reference	Year	Conclusions
Sublingual immunotherapy for allergic rhinitis. ⁴⁹	2003	SLIT is a safe treatment which significantly reduces symptoms and medication requirements.
Allergen injection immunotherapy for seasonal allergic rhinitis. ⁵⁰	2007	Specific allergen injection immunotherapy in suitably selected patients with seasonal allergic rhinitis results in a significant reduction in symptom scores and medication use.
Topical nasal steroids for intermittent and persistent allergic rhinitis in children. ²¹	2007	The three included trials provided some weak and unreliable evidence for the effectiveness of Beconase® and flunisolide used topically intranasally for the treatment of intermittent and persistent allergic rhinitis in children.
House dust mite avoidance measures for perennial allergic rhinitis. ¹¹	2007	The results of these studies suggest that use of acaricides and extensive bedroom based environmental control programmes may be of some benefit in reducing rhinitis symptoms.

of choice, and that immunotherapy (“desensitization”) is highly effective in selected cases.⁸

The chronic or recurrent nature of many cases of AR and the need for parent or, in the case of adolescents, self management emphasizes the importance of parent and patient education. This should cover the practical implications of test results, in particular the relevance of allergen avoidance measures, benefits, risks and side effects of treatments and techniques for administering topical medications.

ALLERGEN AVOIDANCE

Rhinitis symptoms due to inhaled allergens may resolve in the absence of allergen (e.g. the resolution of hay fever symptoms outside the pollen season). Consequently, if triggering allergens are identified, avoidance of these is a logical step. However, in practice this often proves to be difficult as, for example, grass pollens or their submicron fragments can be widely dispersed by the wind many kilometers from the site of production. Attempted pollen avoidance strategies such as staying indoors in an air conditioned environment or wearing a mask outdoors have low acceptability and are generally impractical.

There have been a number of trials of house dust mite avoidance measures which in some but not all cases have suggested that symptoms of asthma, eczema and rhinitis are improved. However, in perennial rhinitis attempts at dust mite allergen avoidance have not provided consistent benefit. In 2007, Sheikh et al found there were only 7 published trials on the effect of HDM avoidance for perennial rhinitis and, only two studies investigating the effectiveness of mite impermeable bedding covers were considered to be of good quality.¹¹ It was concluded that avoidance measures might reduce the symptoms of allergic rhinitis, but more research is needed. As the upper airway is in intimate contact with bedding, which is a major reservoir of dust mite allergen, it might be expected that reduction in dust mite allergen exposure in the bed would be of benefit in AR associated with dust mite sensitisation. A major problem with attempts at dust mite elimination by use of impermeable mattress pillows and doona covers is that although a reductions of the order of 50–70% can be obtained¹² the residual allergen may be enough to trigger symptoms. What may be required is total elimination of the allergen which is generally impossible to achieve. In addition, dust mite allergens are not only encountered in the bedding but are found in furniture and carpeted floors throughout the home. The decision to implement avoidance strategies such as impermeable covers, replacement of soft furnishings, high filtration vacuum cleaners and frequent washing of the bedding will be influenced by the severity of symptoms, the motivation of the family and the cost.

It is potentially possible to avoid pet allergens by removal of the pet however it should be recognised that allergens from pets, cats in particular, can persist in homes at significant levels for many months after pet removal.¹³

ANTIHISTAMINES

Oral and topical antihistamines are effective in allergic rhinoconjunctivitis for histamine related symptoms such as itching, rhinorrhoea and sneezing.¹⁴ Antihistamines have little effect on nasal blockage, as other mediators such as kinins are involved.¹⁵ Ideally antihistamines should be given before allergen exposure. Impairment in learning and concentration have been demonstrated with older (first generation) antihistamines, therefore newer, “non-sedating” oral formulations (cetirizine, loratadine, fexofenadine) should be utilised.¹⁴ In addition to the antihistamine effect these newer preparations may also have

additional anti-inflammatory properties which contribute to their therapeutic activity. First-generation antihistamines should not be administered to children because of their sedative properties, which can worsen learning problems associated with allergic rhinitis.² Intranasal antihistamines (levocabastine, azelastine) are as effective as oral antihistamines and have a rapid onset of action.

The most complete safety data on the use of antihistamines in young children is for the second generation antihistamine cetirizine. In toddlers and young children the safety of cetirizine when administered on a daily basis in an allergy prevention trial for a period of one to 2 years has been comprehensively evaluated in a multicentre study.¹⁶ No significant increase in adverse effects, including sedation, was observed as compared with placebo. In the treatment of AR cetirizine seemed equally efficacious in young 2–6 year old as older 6–12 year old children. With respect to other second generation antihistamines a pooled analysis of 3 trials found fexofenadine to be effective and safe in 6–11 year old children AR.¹⁷

Whether antihistamines can provide additional benefit to inhaled corticosteroids is unclear. Some trials have indicated that for seasonal AR the use of antihistamine plus intranasal steroid has no superiority over the administration of intranasal steroid alone.¹⁸ In seasonal AR, therapy with mometasone furoate and loratadine provided benefits similar to treatment with mometasone furoate alone.¹⁹ In contrast antihistamine (azelastine) nasal spray when combined with fluticasone nasal spray provided significant additional benefit as compared with fluticasone alone in seasonal allergic rhinitis.²⁰

INTRANASAL STEROIDS

Intranasal steroids are the treatment of choice for persistent moderate-severe AR and may also improve non-allergic rhinitis. Intranasal steroids appear safe for long-term use although it is prudent to use the lowest dose that will control symptoms.²¹ As stated above nasal steroids are particularly effective at relieving nasal obstruction.²² Interestingly following nasal steroid use ocular symptoms of AR may also be improved.^{23,24} The majority of studies of efficacy of nasal steroids have been on adolescents or adults and there is less data on school and preschool age children. Fokkens et al. (2004) compared intranasal fluticasone propionate and the antihistamine ketotifen in the treatment of 2–4-year-old children with perennial rhinitis. Although the numbers were small the steroid appeared to be more effective than the antihistamine.²⁵

Systemic absorption of inhaled nasal steroids occurs. Triamcinolone, budesonide, fluticasone, and mometasone have lower systemic bioavailability²⁶ which reduces the potential for adverse effects. Potential adverse effects of concern are hypothalamic-pituitary-adrenal axis suppression, osteoporosis or changes in bone mineral density, growth retardation, cataracts, and glaucoma. Significant issues in children are the possible effects on growth and adrenal function suppression by long term nasal steroid use. In prepubertal children with perennial rhinitis budesonide aqueous nasal spray, 64 microgram once daily, for one year did not suppress growth velocity compared with placebo.²⁷ While beclomethasone used for one year had some effect on growth, this has not been demonstrated with fluticasone²⁸ or mometasone.^{28,29} Concerning the possibility of adrenal suppression, budesonide aqueous nasal spray for 6 weeks had no measurable suppressive effects on HPA axis function in rhinitis patients aged 2 to 5 years.³⁰ Long-term (12-month) administration of fluticasone furoate 110 microgram once daily in adolescents was not associated with adrenal function suppression.³¹

A common reason for treatment failure is non-adherence. This may be exacerbated local side effects such as dryness, irritation and epistaxis. If it proves difficult to use steroid sprays on a daily

basis, intermittent “prn” dosing over the short term (4–6 weeks) has been shown effective for beclomethasone and fluticasone.³² Where there is significant obstruction saline nasal sprays may be a useful adjunct to clear mucus before steroid administration. The short term use (5–7) days of a nasal vasoconstrictor spray prior to the administration of steroid will allow better entry of the steroid spray into the nasal air passages in this situation.

LEUKOTRIENE RECEPTORS ANTAGONISTS (LTRA)

Cysteinyl leukotrienes are important inflammatory mediators in AR. Drugs that block the binding of leukotriene to cellular leukotriene receptors are widely used to treat childhood asthma and in addition have been investigated for their effect on childhood AR. LTRA are administered orally on a once daily basis. There are four published paediatric studies in children aged between 2 and 14 years. Following nasal allergen challenge montelukast significantly reduced sneezing and nasal obstruction scores.³³ However, cetirizine was better than monteleukast in improving nasal symptoms scores.³⁴ Another study found that montelukast significantly improved nasal and eye symptoms scores when compared to placebo.³⁵ In young children aged 2–6, cetirizine was more effective than moneteleukast in control of nasal symptoms (itch sneeze rhinorrhoea and congestion), although moneteleukast was associated with better sleep quality.³⁴ Thus, LTRA appear to be more effective than placebo but not as effective as antihistamines in childhood AR. It has been suggested that when LTRA are prescribed for rhinitis they should be used in conjunction with antihistamines. As moneteleukast may benefit concurrent asthma this is also a factor to consider when selecting a treatment for allergic rhinitis.³³

IMMUNOTHERAPY

Allergen-specific immunotherapy is a treatment which offers the prospect of a cure or substantial modification of the natural history. Immunotherapy may conceivably be administered by subcutaneous, oral mucosal, gastrointestinal or inhaled routes.

Subcutaneous immunotherapy in children has the drawback of multiple injections and the risk of serious or life threatening reactions if the child has significant asthma. The development of oral methods of allergen administration offers a desirable alternative.

Systematic reviews of randomised controlled trials have demonstrated the effectiveness of immunotherapy by injection in improving symptoms and medication use in AR. Most of the evidence is derived from studies involving adolescents or adults and the benefits particularly related to younger children are somewhat more controversial.³⁶ The decision to start immunotherapy should be carefully considered as 3–5 years of treatment is required for sustained effects. Immunotherapy may be recommended where symptoms are severe and medications have been ineffective, inappropriate or have intolerable side effects. In paediatric AR subcutaneous immunotherapy (SCIT), doses have been administered every 6 weeks mostly with aluminium-adsorbed preparations. The duration of therapy is frequently about 5 years and symptom reduction may continue for many years following the cessation of treatment.

Oral or sublingual immunotherapy (SLIT) has been shown to be effective in AR in a number of studies involving both adults and children.³⁷ The efficacy in children is yet to be fully established.^{36,38–40} The allergens have been administered in tablet or liquid form. A study of 168 children aged 6–18 years with seasonal allergic rhinitis in a primary care setting showed no benefit from 2 years of SLIT.⁴¹ In contrast, Wahn et al. (2009) performed a study with tablets containing a freeze-dried allergen extract of 5 grass

pollens (orchard, meadow, perennial rye, sweet vernal, and timothy) in 266 children from 5–17 years with seasonal rhinitis starting 4 months before and continuing through the pollen season.⁴² There was significant symptom improvement and less use of rescue medications. In the first treatment season there was a reduction of 28% in the mean symptom score however there was a high incidence of non-compliance (18%). Roder et al (2008) found a similar incidence of non compliance (23%) in a trial in children of SLIT for seasonal AR.⁴³ In this study non compliance was defined as use of less than 80% of the prescribed medication. A recent systematic review identified 11 studies of SLIT in children and concluded there was no evidence of a positive effect and called for more randomised trials to establish efficacy.³⁶ van Wijk concluded “as long as evidence for effectiveness is weak, SLIT cannot be firmly recommended in clinical practice”.⁴⁴

While minor oral reactions following SLIT are not uncommon, systemic adverse reactions are rare. One study found 7 systemic reactions following 23,154 doses. All the systemic reactions were associated with wheezing or worsening of nasal symptoms.⁴⁵ Another study, restricted to children under 5 years, recorded adverse effects in 5.6% patients and 0.2/1000 doses.⁴⁶ An intriguing possibility is that SLIT might prevent the development of new sensitisation. An open study found that SLIT reduced the acquisition of new allergen sensitisations from 34% to 3% of subjects.⁴⁷ Further work in this area is required.

PROBIOTICS

Changes in antigen-induced production of cytokines have been observed in patients with seasonal AR following treatment with probiotics indicating that probiotic supplementation might modulate immune responses in allergic rhinitis. A recent systematic review identified 12 randomised trials examining the use of probiotics to treat AR and suggested that probiotics may have more effect on AR than on asthma and concluded that more good quality studies are required to resolve the issue.⁴⁸

CONCLUSION

Childhood AR is a common condition with significant morbidity. There are a number of treatment options which can improve symptoms and quality of life. The selection of the appropriate option plus education of the parents and child in the administration of the therapy is of critical importance. The identification of relevant inhalant allergen triggers and development of oral modes of immunotherapy if proven to be efficacious offer a potential alternative to the traditional pharmacotherapeutic approach for some patients. In the immediate future pharmacotherapy particularly with topical corticosteroids will continue to be the mainstay of therapy.

CONFLICT OF INTEREST

None

PRACTICE POINTS

- Allergic and non allergic rhinitis may coexist
- A positive inhalant allergy test does not necessarily prove that the allergen is causing the patient's symptoms
- Antihistamines are less effective than topical steroids at relieving nasal obstruction
- Intranasal steroids are the treatment of choice for persistent moderate-severe AR

RESEARCH DIRECTIONS

- The efficacy of sublingual immunotherapy
- Whether immunotherapy can prevent the development of new sensitisation
- The role of probiotics in the management of allergic rhinitis

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CME SECTION

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Educational questions

Answer true or false to the following questions:

1. With regard to seasonal allergic rhinitis in children which one of the following is correct?
 - a. It is less common in school age children than adolescents
 - b. A positive allergen skin test proves that the allergen is a cause of the rhinitis
 - c. It often coexists with non allergic rhinitis
 - d. House dust mite is the most common provoking allergen
 - e. Allergen avoidance is usually successful in management
2. With regard to sublingual immunotherapy for childhood allergic rhinitis which one of the following is correct?
 - a. Life threatening adverse effects are common
 - b. A typical duration of treatment is 6 months
 - c. The benefits do not persist once the treatment is ceased
 - d. All systematic reviews have concluded it is highly effective
 - e. Has been utilised with both grass pollens and house dust mite allergens
3. Concerning the use of antihistamines for childhood seasonal allergic rhinitis which one of the following is correct?
 - a. Sedation is a common side effect with second generation antihistamines
 - b. There is no safety data for antihistamine use in children under 2 years of age
 - c. They are of benefit in preventing both the early and late inflammation induced by allergen challenge
 - d. They do not influence the results of allergy skin testing
 - e. They are effective when administered topically
4. Concerning the use of topical steroids for childhood rhinitis which one of the following is correct?
 - a. They can improve non-allergic rhinitis
 - b. Systemic absorption of inhaled nasal steroids does not occur
 - c. Ocular symptoms are not affected
 - d. There is extensive safety data in preschool age children
 - e. They are of equal efficacy with oral antihistamines in relieving nasal obstruction
5. Concerning the use of leukotriene receptor antagonists for childhood allergic rhinitis which one of the following is correct?
 - a. They act in allergic rhinitis by binding to circulating soluble leukotriene receptors
 - b. They are administered only once a day
 - c. When used at dosage recommended for allergic rhinitis does not affect associated asthma
 - d. They are as effective as topical steroids in symptom relief
 - e. They are more effective than antihistamines in symptom relief