

## GUIDELINES

## BSACI guidelines for the management of allergic and non-allergic rhinitis

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## Clinical and Experimental Allergy

### Summary

This guidance for the management of patients with allergic and non-allergic rhinitis has been prepared by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI). The guideline is based on evidence as well as on expert opinion and is for use by both adult physicians and paediatricians practicing in allergy. The recommendations are evidence graded. During the development of these guidelines, all BSACI members were included in the consultation process using a web-based system. Their comments and suggestions were carefully considered by the SOCC. Where evidence was lacking, consensus was reached by the experts on the committee. Included in this guideline are clinical classification of rhinitis, aetiology, diagnosis, investigations and management including subcutaneous and sublingual immunotherapy. There are also special sections for children, co-morbid associations and pregnancy. Finally, we have made recommendations for potential areas of future research.

**Keywords** allergen, allergy, antihistamine, anti-leukotriene, aspirin, asthma, BSACI, cat allergen, child, corticosteroid, cromoglicate, decongestant, guideline, house dust mite, IgE, immunotherapy, ipratropium bromide, lactation, nitric oxide, occupational, pregnancy, rhinitis, rhinosinusitis, sinusitis, skin prick test, sublingual immunotherapy, surgery

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### Introduction

Rhinitis significantly reduces quality of life (QOL) [1], interferes with both attendance and performance at school and work [2, 3] and results in substantial NHS costs [4]. The nose is the gateway to the respiratory tract and rhinitis is associated with symptoms arising from the sinuses [5], middle ear [6], the nasopharynx and lower airways [7]. Occupational rhinitis often precedes the development of occupational asthma. Both allergic rhinitis (AR) and non-AR are risk factors for the development of asthma [7]. Rhinosinusitis can also be the presenting complaint of potentially severe systemic disorders such as Wegener's granulomatosis, sarcoidosis and Churg–Strauss syndrome [8]. Therefore, all patients presenting with nasal symptoms require appropriate treatment based on an accurate diagnosis. Separate British Society for Allergy and Clinical Immunology (BSACI) guidelines on rhinosinusitis and nasal polyposis will also be published.

These guidelines for the management of patients with rhinitis are intended for use by physicians treating allergic conditions. Evidence for the recommendations was obtained by using electronic literature searches using the primary key words – rhinitis and non-AR. Further searches were carried out by combining these search terms with allergy, asthma, immunotherapy, sublingual immunotherapy (SLIT), corticosteroid, antihistamine, anti-leukotriene, ipratropium bromide, decongestant, cromoglicate, cat, house dust mite (HDM), anti-IgE, child, pregnancy, lactation, surgery and aspirin. Each article was reviewed for suitability for inclusion in the guideline. The recommendations were evidence graded at the time of preparation of these guidelines. The grades of recommendation and the levels of evidence are defined as in our previous guideline on urticaria [9]. During the development of these guidelines, a web-based system was used to allow consultation with all BSACI members. The draft guidelines were amended by the Standards of Care Committee (SOCC) after careful consideration of all

comments and suggestions. Where evidence was lacking, a consensus was reached among the experts on the committee. Conflicts of interests were recorded by the SOCC; none jeopardized unbiased guideline development.

## Executive summary and recommendations

### *Allergic rhinitis*

- Is common and affects over 20% of the UK population.
- Affects QOL, school and work attendance and performance.
- Is diagnosed by history and examination backed up by specific allergy tests.
- Is a risk factor for the development of asthma.
- Topical nasal corticosteroids are the treatment of choice for moderate to severe disease. (*Grade of recommendation = A*)
- Standardized allergy education improves disease-specific QOL. (*Grade of recommendation = C*)
- Treatment failure may be related to poor technique in the use of nasal sprays and drops and therefore appropriate training is imperative. (*Grade of recommendation = C*)
- Treatment of rhinitis is associated with benefits for asthma. (*Grade of recommendation = A*)
- Immunotherapy is highly effective in selected cases. (*Grade of recommendation = A*)
- Occupational rhinitis often precedes the development of occupational asthma.

### *Non-allergic rhinitis*

- Has a multifactorial aetiology.
- Is a risk factor for the development of asthma.
- If eosinophilic, usually responds to treatment with corticosteroids.
- May be a presenting complaint for systemic disorders such as Wegener's granulomatosis, Churg–Strauss and sarcoidosis.

### *Infective rhinitis*

- Can be caused by viruses, and less commonly by bacteria, fungi and protozoa.
- Is often more severe in allergic patients especially if infection occurs at the time of allergen exposure.

## Definitions

Rhinitis describes inflammation of the nasal mucosa but is clinically defined by symptoms of nasal discharge, itching, sneezing and nasal blockage or congestion. As the

sinus linings are also usually involved, the term rhinosinusitis is more accurate, but is conventionally reserved for more severe disease. Rhinitis can be classified into allergic, non-allergic and infective. However, acute viral upper respiratory infections are not considered in detail in this document.

## Classification and aetiology of rhinitis

### *Allergic rhinitis*

The prevalence of AR has increased over the last three decades [10, 11]. At most risk are those with atopy, with a family history of rhinitis, first-born children and immigrants [12–14]. AR is the predominant form in children, but accounts for about a third of rhinitis cases in adults.

In AR, the immediate reaction resulting from IgE-mediated mast cell degranulation and mediator release is rapid and leads to sneezing, rhinorrhoea, itch and nasal blockage. The late-phase reaction involves inflammation, with an eosinophilic infiltrate [15–17]. Symptoms are chronic obstruction, hyposmia, post-nasal mucous discharge and nasal hyper-reactivity. Figure 1 illustrates the mechanisms leading to AR. Table 1 lists the common allergic triggers for rhinitis, and Table 2 specifies the common causes of occupational rhinitis.

The WHO ARIA workshop 'Allergic Rhinitis and its impact on Asthma' [18] suggested a new classification of AR based on frequency and severity of symptoms as these are the major factors involved in determining treatment; see Fig. 2. These recommendations have been validated subsequently [19]. A clinical classification of seasonal and perennial rhinitis is useful in UK practice, especially for diagnosis and immunotherapy, and can be used alongside the ARIA classification.

The ARIA recommendations emphasized the concept of treating 'one airway, one disease' with a similar unified therapeutic approach to the management of co-morbidities such as asthma, sinusitis, otitis media and conjunctivitis [20].

### *Infective rhinitis*

Any cause of congestion of the nasal mucosa can lead to occlusion of the sinus ostia, predisposing to facial pain, sinusitis and/or eustachian tube dysfunction. The causes and disease patterns of infective rhinitis are summarized in Table 3.

### *Non-allergic rhinitis*

The numerous diagnoses in this category need to be borne in mind for patients with negative skin prick tests (SPTs). Table 4 summarizes the causes and disease patterns of non-AR.

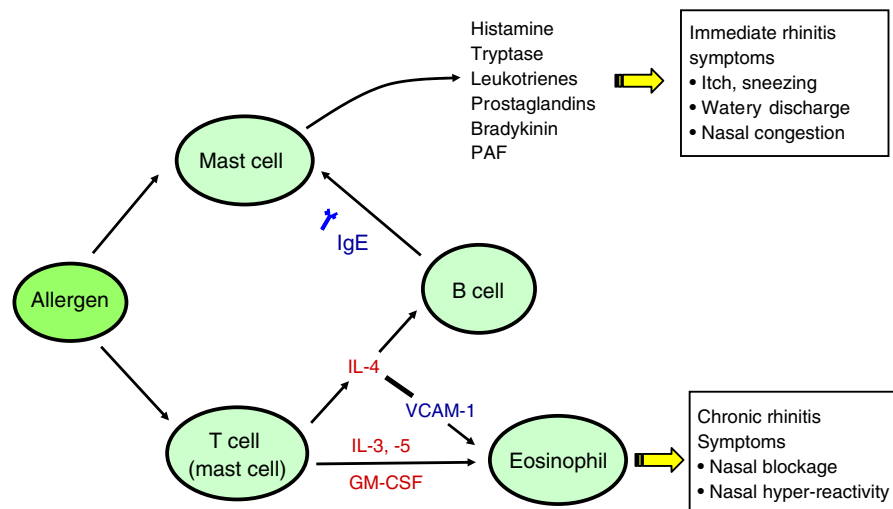


Fig. 1. Mechanism of allergic rhinitis. Sensitized patients with allergic rhinitis have IgE antibodies for specific allergen(s) bound to receptors on the surface of mast cells. On re-exposure to the specific allergen(s), cross-linking of adjacent IgE molecules occurs, and mast cell degranulation (rupture) takes place, releasing a variety of chemical mediators that may be preformed (e.g. histamine) or newly synthesized (e.g. leukotrienes, prostaglandins). These chemicals give rise to the typical immediate symptoms experienced by the patient. In many patients, there is also a late-phase reaction in which T helper type 2 cytokines induce an eosinophilic inflammatory infiltrate, similar to that seen in asthma. This results in chronic, less obvious symptoms. GM, granulocyte macrophage; CSF, cerebrospinal fluid; PAF, platelet-activating factor.

Table 1. Allergic triggers for rhinitis

Trigger types	Origin/specific example of trigger	Type of rhinitis caused
Mites	House dust mite, storage mites, allergen in mite fecal pellets	Major causes of perennial rhinitis
Pollens	Trees, grasses, shrubs, weeds	Main causes of seasonal rhinitis; cross-reactivity among pollens
Animals	Cats, dogs, horses Mice, rats	Allergen in sebaceous glands and saliva Allergen mainly in urine
Fungi (moulds)	Alternaria, Cladosporium, Aspergillus	Seasonal and/or perennial symptoms
Occupational induced (see also Table 2)	Flour, latex, laboratory animals, wood dust, enzymes, other airborne proteins	Reversible with early diagnosis and avoidance but becomes chronic and irreversible if exposure is prolonged [206] May progress to asthma. Diagnosis based on symptom diary cards and provocation tests (Table 4)
Occupation aggravated	Smoke, cold air, formaldehyde, sulphur dioxide, ammonia, glues, solvents, etc. [204, 205]	Pre-existing rhinitis can be aggravated by work-place irritants

## Diagnosis of rhinitis

### History

A detailed history is vital for an accurate diagnosis. The patient is asked to list their main symptoms in order of priority and this usually produces a short list of differential diagnoses.

### Symptoms

*Sneezing, itchy nose, itchy palate.* AR is likely and further refinement of the diagnosis is aided by asking whether the symptoms are intermittent or persistent although this is not a substitute for specific allergen testing.

- Seasonal at the same time each year? – pollens or mould spores.
- At home? – pets or HDM.
- At work? – occupational allergens.
- On holiday? – remission suggests an environmental cause.

*Rhinorrhoea.* Rhinorrhoea is either anterior or leads to post-nasal drip:

- Clear – infection unlikely.
- Unilateral – is uncommon and cerebrospinal fluid (CSF) leak should be excluded [21].
- Coloured
  - yellow – allergy or infection
  - green – usually infection
  - blood tinged

**Table 2.** Common causes of occupational rhinitis

Agents	High MW	Low MW	Industry
Animal proteins	Mouse, rat, guinea pig, crabs, etc. urinary and epithelial proteins		Laboratory research, animal breeding [207–209], crab processing industry [210]
Vegetable proteins	Wheat and other cereal flours and grains, latex [51]		Baking [211], milling, food processing, hospital workers
Enzymes	Protease, amylase, cellulase, lipase		Food processing, detergent manufacture, pharmaceuticals
Pharmaceuticals	Antibiotics, morphine, cimetidine		Pharmaceutical manufacture and dispensing
Chemicals		Diisocyanates, colophony fumes, (trimellitic) acid anhydrides (TMA) [212], cyanoacrylates, epoxy resins, alkyd/polyunsatu- rated polyester resins [213]	Spray painting, electronic soldering, plastics and paint manufacture, vinyl flooring, resin production

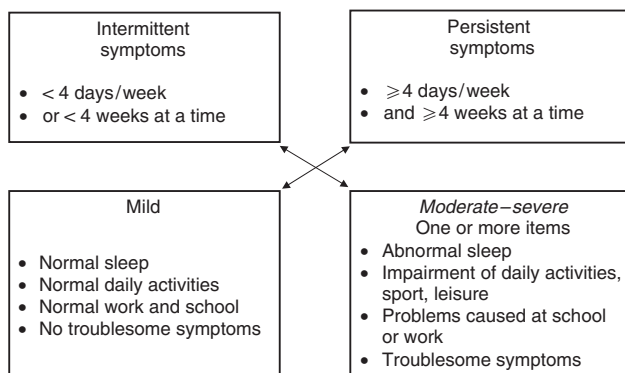


Fig. 2. Classification of allergic rhinitis. Each box may be further sub-classified into seasonal or perennial.

- unilateral – tumour, foreign body, nose picking or misapplication of nasal spray
- bilateral – misapplication of nasal spray, granulomatous disorder, bleeding diathesis or nose picking.

#### Nasal obstruction

- Unilateral – usually septal deviation but also consider foreign body, antrochoanal polyp and tumours.
- Bilateral – may be septal (sigmoid) deviation but more likely rhinitis or nasal polyps.
- Alternating – generalized rhinitis exposing the nasal cycle [22].

#### Nasal crusting

- Severe nasal crusting especially high inside the nose is an unusual symptom and requires further investigation. Consider nose picking, Wegener's granulomatosis, sarcoidosis, other vasculitides, ozaena (wasting

away of the bony ridges and mucous membranes inside the nose), non-invasive ventilation and chronic rhinosinusitis [23].

- Rarely, topical steroids may cause crusting.

*Eye symptoms.* Eye symptoms associated with AR and particularly with seasonal rhinitis include intense itching, hyperaemia, watering, chemosis and periorbital oedema. Symptoms typically resolve within 24 h if removed from the allergen source.

*Other symptoms.* Other symptoms such as snoring, sleep problems, repeated sniffing or a nasal intonation of the voice can be caused or exacerbated by nasal obstruction and rhinorrhoea from any cause. In some patients with seasonal allergic rhinitis (SAR), oral allergy syndrome is triggered by ingestion of cross-reacting antigens in some fruits, vegetables and nuts [24].

#### Lower respiratory tract symptoms

- Cough, wheeze, being short of breath.
- Disorders of the upper and lower respiratory tract often coexist:
- Most asthmatics have rhinitis – see 'Co-morbid association' on rhinitis and asthma.
  - In asthma with aspirin sensitivity – 36–96% have nasal polyps with rhinosinusitis [25].

*Family history.* A family history of atopy, seasonal rhinitis or asthma makes the diagnosis of AR more likely [26].

*Social history.* In order to assess possible allergen and irritant exposure, a full history of housing conditions, pets, occupation or schooling and, in young children, feeding details should be obtained.

Table 3. Infective causes of rhinitis

Infective agent type	Examples of infective agent	Caused disease pattern
Viruses	Common cold viruses, e.g. rhinovirus, coronaviruses, RSV, etc.	Sinus changes on CT scan remain for up to 6 weeks after the infection [214] 0.5–2% become superinfected by bacteria [215] 'Colds' may exacerbate asthma and COPD [216, 217] Children average 6–8 'colds' per year [218]
Bacteria	Streptococcus, Haemophilus, Moraxella, Staphylococcus, Mycobacteria	Acute infection causes nasal obstruction, facial pain, crusting, purulent discharge Can progress to rhinosinusitis
Fungi and other opportunistic infections	Aspergillus	Rarely cause symptoms; mainly affect immunosuppressed individuals [219]

COPD, chronic obstructive pulmonary disease; CT, computed tomography; RSV, respiratory syncytial virus.

**Drugs.** A detailed drug history is vital as drugs such as topical sympathomimetics,  $\alpha$ -blockers and other anti-hypertensives as well as aspirin and non-steroidal anti-inflammatory drugs may cause rhinitis symptoms (see Table 4). It is important to enquire about the efficacy of previous treatments for rhinitis and details of how they were used and for how long.

**Occupation.** Exposure to occupationally related triggers is common and may have to be addressed in order to improve rhinitis symptoms.

### Examination

#### Visual assessment

- Horizontal nasal crease across the dorsum of the nose – supports a diagnosis of AR.
- Depressed nasal bridge – post-surgery, Wegener's granulomatosis or cocaine misuse.
- Widened bridge; polyps (see also BSACI guideline on rhinosinusitis and nasal polyposis).
- Purple tip in lupus pernio due to sarcoidosis.
- An assessment of nasal airflow – (e.g. metal spatula misting in young children).

#### Anterior rhinoscopy

- Appearance of the turbinates.
- The presence/absence of purulent secretions.
- The presence/absence of nasal polyps, but it may not be possible to see a small ones. Larger polyps can be seen at the nares and are distinguishable from the inferior turbinate by their lack of sensitivity, yellowish grey colour and the ability to get between them and the side wall of the nose.
- Yellow sub-mucosal nodules with a cobblestone appearance suggest sarcoidosis [27].
- Crusting and granulations raise the possibility of vasculitis.

- Septal perforation may occur after septal surgery, due to chronic vasoconstriction (cocaine,  $\alpha$ -agonists), Wegener's granulomatosis, nose picking and very rarely steroid nasal sprays.

### Investigations

**Objective measures of nasal airway.** Objective measurements of the nasal airway are not made in routine clinical practice but can be useful when allergen or aspirin challenges are undertaken and may be helpful when septal surgery or turbinate reduction are being contemplated.

**Peak nasal inspiratory flow.** Measurement of peak nasal inspiratory flow provides a simple and inexpensive method for determining nasal airway patency using a nasal inspiratory flow meter. The results are reproducible and correlate with rhinoscopic evidence of rhinitis but not with symptom scores [28]. The technique is most useful for comparing changes in airway patency within the same subject, although some normative data are now available [29].

**Acoustic rhinometry.** Acoustic rhinometry can be used to measure changes in mucosal congestion using reflected sound. The technique is based on the physical principle that sound in the nasal cavity is reflected by changes in acoustic impedance caused by changes in cavity dimensions. The change in acoustic impedance between the incident wave and reflected sound waves is proportional to the cross-sectional area. The method requires standardization and considerable experience to interpret and obtain reproducible results. Guidelines for its use are published [30].

**Rhinomanometry.** Rhinomanometry allows an estimation of nasal resistance from pressure–flow relationships and is difficult to perform reproducibly but is still regarded by some as the most accurate measure of nasal airway patency. With anterior rhinomanometry, the pressure

**Table 4.** Types and possible triggers of non-allergic rhinitis

Type	Suggested triggers/cause	Signs/symptoms
Eosinophilic or non-allergic rhinitis with eosinophilia syndrome (NARES)	50% develop aspirin sensitive disease with asthma and nasal polyposis later in life [220]	Skin tests negative but nasal smears show eosinophilia Perennial symptoms with paroxysmal episodes. About 50% have bronchial hyper-reactivity [220]
Autonomic (vasomotor)	Triggered by physical/chemical agents	More common in middle age with clear rhinorrhoea especially in the morning. Less favourable course than allergic. Possibly caused by parasympathetic hyperactivity [221]
Drugs	$\alpha$ -adrenergic blockers, ACE inhibitors, chlorpromazine Cocaine Nasal decongestants (with prolonged use)	Nasal blockage Rhinorrhoea, crusting, pain and nasal septum perforation reduced olfaction [222] Rhinitis medicamentosa with chronic nasal blockage [126]
Hormonal	Aspirin/NSAIDs Pregnancy [157], puberty, HRT, contraceptive pill [223, 224] Possibly hypothyroidism, acromegaly [225, 226]	Acute rhinitis symptoms $\pm$ asthma All can cause nasal blockage and/or rhinorrhoea
Food	Alcohol, spicy foods, pepper, sulphites	Rhinorrhoea, facial flushing Gustatory rhinorrhoea
Atrophic	Klebsiella Ozonae [227] or secondary to trauma, surgery, radiation	Foul-smelling odour, crusting, hyposmia, nasal blockage [228]
Primary mucus defect	Cystic fibrosis	Children with polyps must be screened for cystic fibrosis [229]
Primary ciliary dyskinesias Systemic/inflammatory	Kartagener and Young syndromes Sjogren, SLE, rheumatoid arthritis, Churg–Strauss [230]	Rhinosinusitis, bronchiectasis and reduced fertility Nasal blockage
Immunodeficiency	Antibody deficiency	Polyps, sinusitis, asthma, eosinophilia Chronic infective sinusitis
Malignancy	Lymphoma, melanoma, squamous cell carcinoma	Bloody, purulent discharge, pain and nasal blockage – symptoms may be unilateral
Granulomatous diseases	Sarcoidosis Wegener's disease [231]	External nasal swelling or collapse, sinusitis, swelling, crusting, bleeding, septal perforation
Structural abnormalities	Nasal septal deviation	Unilateral nasal obstruction unlikely to present unless additional cause, e.g. rhinitis
Idiopathic	Unknown cause – diagnosis of exclusion	May respond to topical capsaicin [232–234]

ACE, angiotensin-converting enzyme; HRT, hormone replacement therapy; NSAID, non-steroidal anti-inflammatory drugs; SLE, systemic lupus erythematosus.

sensor is placed at the tip of each nostril and resistance is measured in each nostril separately. With posterior rhinomanometry, the pressure sensor is placed in the back of the nasal cavity and total nasal airway resistance is determined. The technique requires expensive equipment and considerable experience in interpretation [31].

**Nasal endoscopy.** Used in specialist centres, this is more specific than rhinoscopy and alters the diagnosis in up to a fifth of patients with nasal disease [32].

**Allergen-specific immunoglobulin E.** Allergen-specific IgE can be detected with SPTs or by a serum immunoassay.

**Skin prick tests.** SPTs should be carried out routinely in all cases in order to determine whether the rhinitis is

allergic or non-allergic. Injectable adrenaline should be available, but is unlikely to be needed.

- Must be interpreted in the light of the clinical history. At least 15% of people with a positive SPT do not develop symptoms on exposure to the relevant allergen [33].
- Have a high negative predictive value.
- Suppressed by antihistamines, tricyclic antidepressants and topical but not oral steroids [34].
- Are inadvisable outside specialist allergy clinics if the patient has a history of anaphylaxis.

**Serum total and specific immunoglobulin E.** Serum-specific IgE may be requested when skin tests are not possible or when the SPT, together with the clinical history, give equivocal results.

- Total IgE alone can be misleading but may aid interpretation of specific IgE.
- Allergen-specific IgE correlates with the results of SPTs and nasal challenges although there are exceptions.
- Currently available SPTs and immunoassays show similar sensitivity for HDM, but SPTs are more sensitive to other inhalant allergens such as cat epithelium, mould and grass pollen [35].

*Routine laboratory investigations.* Other investigations to help with the initial management of patients with rhinitis are guided by the findings from the history, examination and results of SPTs. Examples of routine laboratory investigations include:

- Full blood count and differential white cell count.
- C-reactive protein.
- Nasal smear/brushing for eosinophils.
- Microbiological examination of sputum and sinus swabs.
- Nasal secretions – CSF asialotransferrin for CSF rhinorrhoea.
- Urine toxicology when cocaine abuse is suspected.

*Olfactory tests.* The University of Pennsylvania Smell Identification Test is well validated, can identify malingerers [36] and is accepted for legal cases.

*Cytology.* The techniques for obtaining cells for cytology in secretions, lavage, scraping, cotton pledgetts or brushings have not been standardized, nor have the criteria for evaluating cell counts [37]. Nevertheless, the presence of eosinophils implies inflammation and may be helpful in predicting response to corticosteroids.

*Exhaled nitric oxide.* Exhaled nitric oxide (FeNO, fractional exhaled nitric oxide) measurement can be useful clinically in the diagnosis and monitoring of asthma. Normal levels are <20 p.p.b., but become elevated in eosinophilic lower respiratory tract inflammation [38].

#### *Nasal challenge*

- Is not routinely available outside specialist centres.
- There is no standardized methodology.
- Asthmatic reactions can occur.
- May be useful to confirm aspirin sensitivity.
- May be useful in patients with an unclear history and negative or equivocal tests for allergen-specific IgE or when the trigger is not IgE mediated.
- Has a role in occupational AR, where there is a discrepancy between history and when there are potentially important occupational implications.

*Tests for asthma.* Measurements of lung function should be considered in all patients with persistent rhinitis e.g.

peak expiratory flow rate and spirometry as detailed in the British Thoracic Society guidelines on the management of asthma [39].

#### **Treatment of rhinitis**

Figure 3 shows an algorithm for the treatment of rhinitis. Grades of recommendation are given in Table A4.

#### *Education*

- Standardized allergy education of health personnel improves disease-specific QOL [40]. (*Grade of recommendation = C*)
- The patient or parents of children should be informed about the nature of the disease, causes and mechanisms of rhinitis, the symptoms and available treatments.
- Education on means of allergen avoidance and drug therapy, including safety and potential side effects, should be provided.
- Treatment failure may be related to poor technique in the use of nasal sprays and drops and therefore appropriate training is imperative (Figs 4a and b) [41, 42].
- It is important to provide patients with education on the complications of rhinitis including sinusitis and otitis media, and comorbid conditions such as asthma and nasal polyps. They should be aware of how such complications are recognized and treated.
- Patients should be made aware of the potential negative impact of rhinitis on their QOL and benefits of complying with therapeutic recommendations.
- Patients should be provided with realistic expectations for the results of therapy and should understand that complete cures do not usually occur in the treatment of chronic diseases, including rhinitis, and that long-term treatment may be needed.

#### *Allergen avoidance*

Allergen avoidance decisions are complicated and the clinician's task of providing advice to patients is not facilitated by the paucity of available evidence. Avoidance is clearly beneficial in allergy to domestic pets, horses and certain occupational allergens (laboratory animals, latex), where clinical trials are unnecessary. However, a number of measures designed to reduce mite exposure have not shown the expected results. The appendix to this document includes several tables providing advice on allergen avoidance (see Tables A1–A3).

*House dust mite.* HDM is the most common indoor allergen causing rhinitis. It is logical to assume that reduction

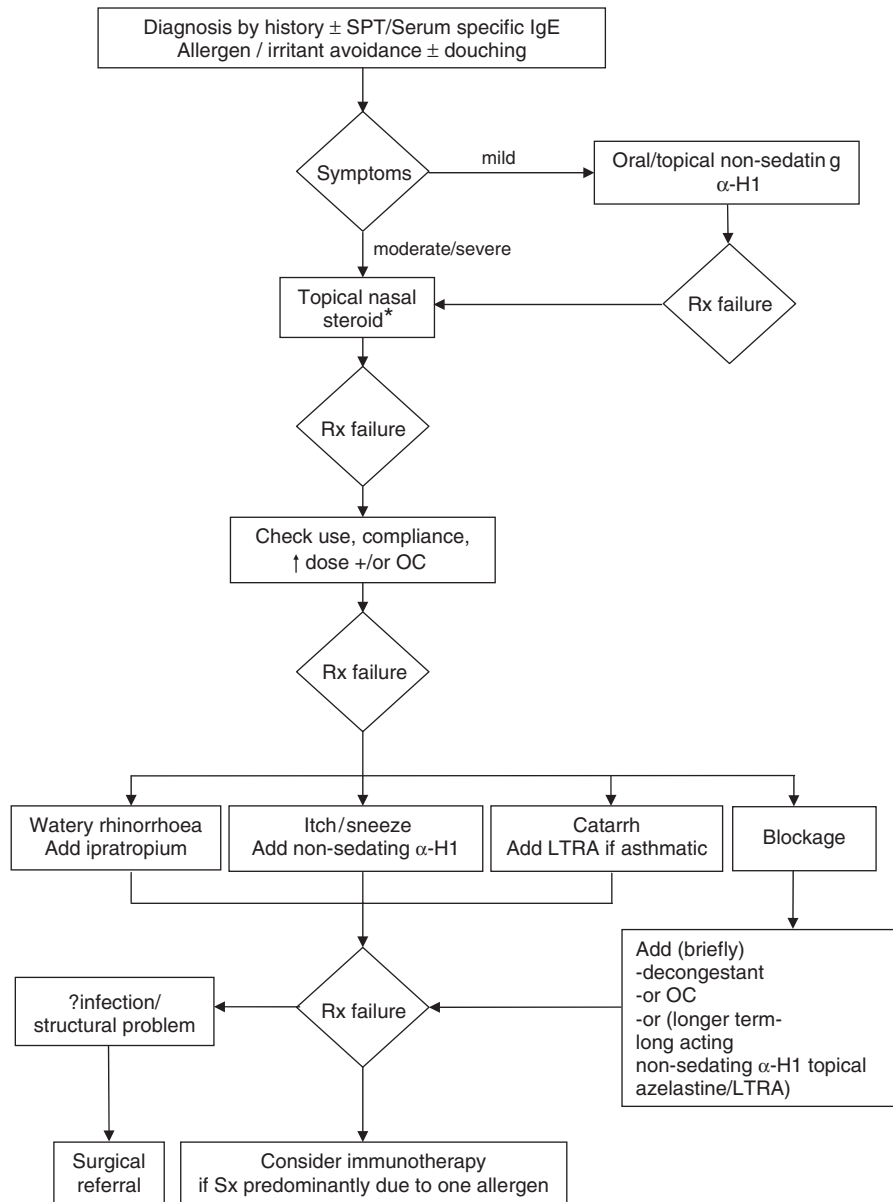


Fig. 3. Algorithm for the treatment of rhinitis. \*Spray or drops. OC, oral corticosteroids;  $\alpha$ -H1, antihistamines; LTRA, leukotriene receptor antagonist; Sx, symptoms; Rx, treatment; SPT, skin prick test.

of allergens such as HDM would reduce symptoms in sensitized patients. However, the evidence to refute or confirm this hypothesis is lacking. Use of mite-proof bed covers as a single intervention in mite-allergic adults or children is not of proven value according to a number of placebo-controlled trials [43, 44]. A Cochrane meta-analysis in 2001 [45] addressed the potential benefit of HDM avoidance measures for perennial allergic rhinitis. It was found that the benefit of using a single measure to improve symptoms of perennial rhinitis was questionable. Efforts to obtain maximal mite elimination may lead to clinical benefits in selected highly motivated patients, and clinical benefits are most likely with multiple interventions [46].

**Pollen avoidance in seasonal allergic rhinitis.** Nasal filters have been shown to reduce symptoms of AR and allergic conjunctivitis significantly during the ragweed and grass pollen seasons [47]. A number of other measures are often recommended to patients with pollen allergy to minimize symptoms but these are based on expert consensus rather than clinical trial data (Table A2).

**Cat allergen.** There are no trials examining whether measures to minimize cat allergen levels lead to clinical improvement in rhinitis as it takes several months for cat allergens to disappear from a home once the cat has been removed. Therefore, trials of brief cat removal are ineffective [48]. However, it is likely that cat removal will



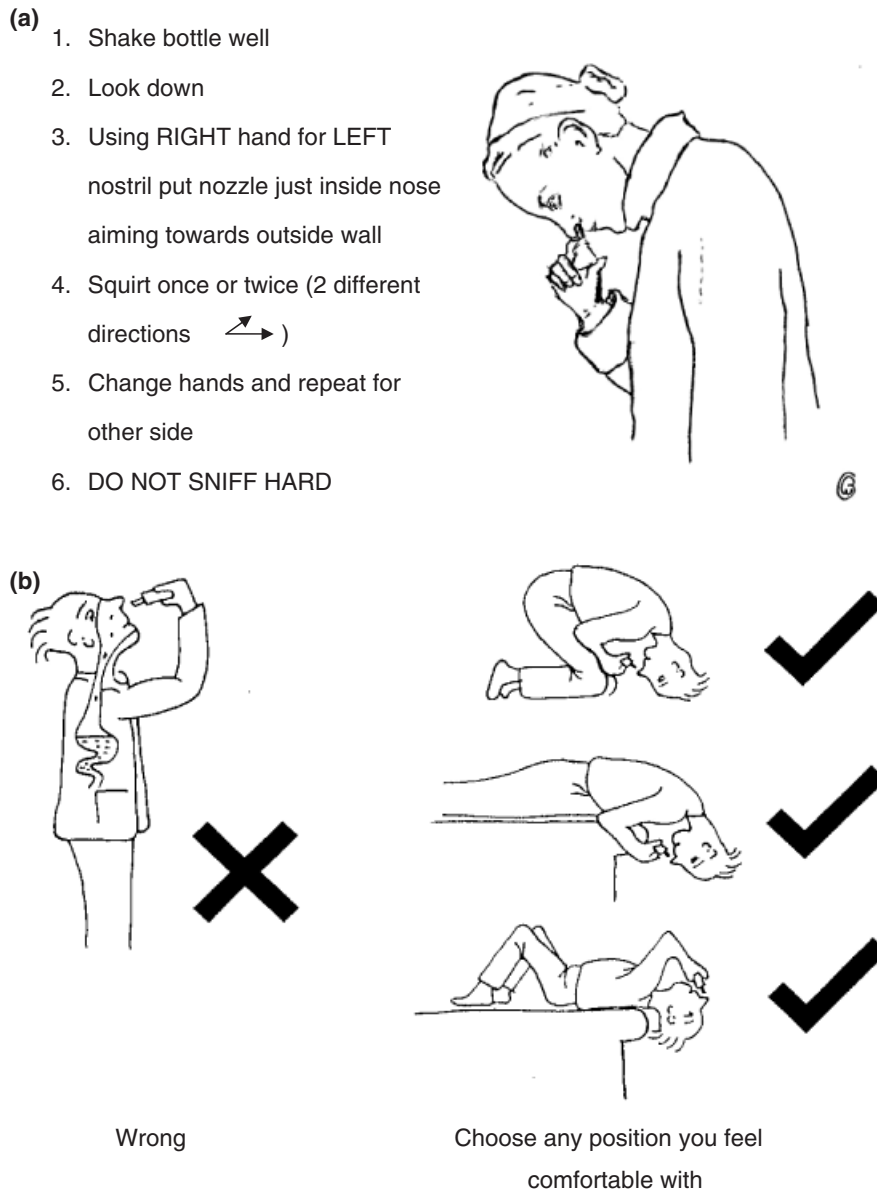


Fig. 4. (a) Correct procedure for the application of nasal sprays. (b) Correct procedure for the installation of nasal drops.

produce an improvement in symptoms, and a number of measures to minimize cat allergen levels at home are recommended (Table A3).

**Occupational allergens.** Rhinitis may be induced by workplace exposure to a respiratory sensitizing agent ('occupational rhinitis'), Table 2. Where pre-existing disease is provoked by an (irritant) occupational agent, it is described as 'work-exacerbated' rhinitis. The agents that can give rise to occupational rhinitis, numbering over 300, are the same as those that induce occupational asthma. Particle size is probably important in determining the site of disease. Occupational rhinitis is as much as three times more frequent than occupational asthma but the two conditions frequently occur together [49, 50].

An understanding of those occupations that incur relevant exposures and a detailed history of such exposures and their relationship with the onset and pattern of symptoms are essential for identification of occupational rhinitis. If a diagnosis of occupational rhinitis is established, then avoidance of further exposure to the causative agent may lead to cure. Symptoms caused by continuing exposure may be very difficult to treat.

- Occupational rhinitis generally precedes, and may be a risk factor for, occupational asthma. The risk of occupational asthma is the highest in the year after the development of occupational rhinitis [49, 51]. (Level of evidence = 2 –)

- The early identification of a causative occupational agent and the avoidance of exposure are important measures for the management of occupational rhinitis and prevention of progression to occupational asthma [47, 48, 52, 53]. (*Level of evidence = 2++*; *grade of recommendation = B*)
- Prevention of latex allergy by removing powdered gloves or substituting non-latex ones is essential. All healthcare environments should have a latex policy [53, 54]. (*Level of evidence = 2+ and 4*; *Grade of recommendation = D, C for adults and children with perennial rhinitis or adults and children with latex allergy*.)

**Irritant avoidance.** Many patients with active rhinitis exhibit nasal hyper-reactivity to substances such as smoke, pollutants, perfume and dust and to temperature change. In many cases, it is likely that improved management of rhinitis will lead to an improvement in symptoms of nasal hyper-reactivity. (*Grade of recommendation = D*)

#### *Nasal douching and drops*

In mainland Europe, nasal douching is a more commonly used therapy than in the United Kingdom. Saline douching reduced symptoms in children and adults with seasonal rhinitis [55, 56] (*Grade of recommendation = A*). It is a safe, inexpensive treatment.

#### *Adverse events*

- Sodium load should be considered in hypertensive patients.

#### *Place in therapy*

- Additional to therapy in rhinitis.

- Effective in children with seasonal and other forms of AR in combination with conventional treatment [55, 57].
- Sterile saline eyedrops are a simple, non-toxic and effective addition for seasonal allergic conjunctivitis [58].

#### *Pharmacotherapy*

Despite allergen and trigger avoidance, many rhinitis sufferers continue to have persistent symptoms, the nature of which should determine the selection of medication. Available treatments and their effects on individual symptoms are detailed in Table 5. (All have a *grade of recommendation = A*)

#### *Oral H1-antihistamines (Table 6)*

- Reduce total nasal symptom scores by a mean of 7% (5–9%) more than placebo [59].
- Effective predominantly on neurally mediated symptoms of itch, sneeze and rhinorrhoea.
- Desloratadine, fexofenadine, cetirizine and levocetirizine have modest effects on nasal blockage [60–65].
- Improve allergic symptoms at sites other than the nose such as the conjunctiva, palate, skin and lower airways [66–68].
- Regular therapy is more effective than 'as-needed' use in persistent rhinitis [69].
- Can significantly improve QOL [70].

#### *Adverse events*

- First-generation antihistamines, e.g. chlorphenamine, diphenhydramine, cause sedation and reduce academic and/or work performance and should be avoided [71, 72].
- Second-generation antihistamines, e.g. acrivastine, cetirizine, desloratadine, fexofenadine levocetirizine,

**Table 5.** Effect of therapies on rhinitis symptoms (adapted from [235])

	Sneezing	Rhinorrhoea	Nasal obstruction	Nasal itch	Eye symptoms
<b>H1-antihistamines</b>					
Oral	++	++	+	+++	++
Intranasal	++	++	+	++	0
Eye drops	0	0	0	0	+++
<b>Corticosteroids</b>					
Intranasal	+++	+++	+++	++	++
<b>Chromones</b>					
Intranasal	+	+	+	+	0
Eye drops	0	0	0	0	++
<b>Decongestants</b>					
Intranasal	0	0	++++	0	0
Oral	0	0	+	0	0
Anticholinergics	0	++	0	0	0
Anti-leukotrienes	0	+	++	0	++

Table 6. Oral antihistamines licensed in the UK according to age

Age	Non-sedating antihistamine	Sedating antihistamine
>6 months		Alimemazine (trimeprazine)
>1 year	Desloratadine	Hydroxyzine hydrochloride Clemastine Chlorphenamine
>2 years	Cetirizine hydrochloride (SAR only) Loratadine Levocetirizine hydrochloride	Cyproheptadine hydrochloride Promethazine hydrochloride Ketotifen
>6 years	Fexofenadine hydrochloride (SAR only) Cetirizine hydrochloride	
>12 years	Acrivastine Mizolastine Fexofenadine hydrochloride	

SAR, seasonal allergic rhinitis

loratadine and mizolastine are less sedating in most patients, with fexofenadine the least sedating [73, 74].

In addition, they

- do not cause significant QT prolongation at normal therapeutic doses
- have few major drug interactions, except for increased risk of ventricular arrhythmias, when mizolastine is co-administered with some anti-arrhythmics, antibiotics and  $\beta$ -blockers.

#### *H<sub>1</sub>-antihistamines – topical nasal*

- Azelastine – therapeutic effects superior to oral antihistamines for rhinitis symptoms [75, 76].
- Do not improve symptoms due to histamine at other sites, such as the eye, pharynx, lower airways and skin.
- Fast onset of action within 15 min [75] – useful as rescue therapy.

#### *Adverse events*

- Local irritation.
- Taste disturbance with azelastine.

#### *Place in therapy – oral and topical antihistamines*

- First-line therapy for mild to moderate intermittent and mild persistent rhinitis.
- Additional to intranasal steroids for moderate/severe persistent rhinitis uncontrolled on topical intranasal corticosteroids alone [77–79].

#### *Topical intranasal corticosteroids*

- Meta-analysis shows that intranasal corticosteroids (INS) are superior to antihistamines [80, 81].
- Act by suppression of inflammation at multiple points in the inflammatory cascade [82].
- Reduce all symptoms of rhinitis by about 17% greater than placebo, with a variable effect on associated allergic conjunctivitis [59].

- Onset of action is 6–8 h after the first dose, clinical improvement may not be apparent for a few days and maximal effect may not be apparent until after 2 weeks [81].
- Starting treatment 2 weeks before a known allergen season improves efficacy [83].
- Similar clinical efficacy for all INS but bioavailability varies considerably.
- Systemic absorption negligible with mometasone and fluticasone, modest for the remainder and high for betamethasone and dexamethasone – these should be used short term only [84–86].
- Long-term growth studies in children using fluticasone, mometasone and budesonide have reassuring safety data, unlike beclomethasone [87–91].
- Concomitant treatment with CYP3A inhibitors such as itraconazole or ritonavir may increase systemic bioavailability of intranasal corticosteroids [92, 93].

#### *Adverse events*

- Local nasal irritation, sore throat and epistaxis affect around 10% of users.
- Benzalkonium chloride is used as a preservative in all topical corticosteroids, except Rhinocort<sup>®</sup> (Astrazeneca International, London, UK) nasal spray and Flixonase<sup>®</sup> nasules, and may irritate the nose, but does not adversely affect mucociliary clearance [94].
- Reduction of local adverse effects can probably be achieved by correct use; see Fig. 4a. (*Grade of recommendation = D*)
- Nasal drops are useful for severe obstruction and should be used in the ‘head upside down’ position in order to reach the ostiomeatal complex; see Fig. 4b.
- Hypothalamic–pituitary axis suppression may occur when multiple sites are treated with topical corticosteroids in the same person (e.g. skin, nose and chest). It is advisable to monitor growth in children [95] (see also Table 7).

**Table 7.** Nasal corticosteroids licensed for use in the United Kingdom according to age

Age (years)	Drug	Good safety data	Availability
>4	Fluticasone propionate spray	Yes	Over the counter
>5	Flunisolide	–	Prescription only
	Dexamethasone isonicotinate with Tramazoline hydrochloride	–	Prescription only
>6	Mometasone furoate	Yes	Prescription only
	Triamcinolone acetonide	–	Prescription only
	Beclomethasone dipropionate	–	Over the counter
>12	Budesonide	Yes	Prescription only
	Betamethasone	–	Prescription only

- Raised intra-ocular pressure has been described with INS [96], and patients with a history of glaucoma should be monitored more closely.

#### *Place in therapy*

- First-line therapy for moderate to severe persistent symptoms and treatment failures with antihistamines alone [18, 81].
- Topical steroid drops should be used initially in nasal polyposis and severe obstruction.

#### *Systemic glucocorticosteroids*

- Rarely indicated in the management of rhinitis, except for:
  - severe nasal obstruction
  - short-term rescue medication for uncontrolled symptoms on conventional pharmacotherapy
  - important social or work-related events, e.g. examinations, weddings
- Oral corticosteroids should be used briefly and always in combination with a topical nasal corticosteroid. A suggested regime for adults is 0.5 mg/kg given orally in the morning with food for 5–10 days.

#### *Injectable corticosteroids*

- Injected preparations are not recommended unless under exceptional circumstances [97, 98].
- Compared with other available treatments, the risk-benefit profile for intramuscular corticosteroids is poor [97].

#### *Anti-leukotrienes*

- Anti-leukotrienes are of two kinds: (i) receptor antagonists (LTRAs, e.g. montelukast and zafirlukast) [99] and (ii) synthesis inhibitors, e.g. zileuton (unavailable in the United Kingdom).
- There is a spectrum of individual responsiveness to LTRAs that is currently not predictable [100–102].
- Therapeutic profile similar to antihistamines, with efficacy comparable to loratadine in SAR [103]. How-

ever, the response is less consistent than that observed with antihistamines. A study found that LTRAs reduced the mean daily rhinitis symptom scores by 5% more than placebo [59].

- Anti-leukotrienes are less effective than topical nasal corticosteroids [103–106].
- Anti-leukotriene plus antihistamine combinations do not improve efficacy to a clinically relevant extent compared with either drug used alone [107–110], and their use in rhinitis is thus disputed [111].
- The combination of antihistamine and anti-leukotriene is no more effective than topical corticosteroid alone [112, 113].
- May have a place in patients with SAR and asthma [114].

#### *Adverse events*

- Usually well tolerated; occasional headache, gastrointestinal symptoms or rashes.
- Occasional reports of Churg–Strauss syndrome that may relate more to steroid withdrawal rather than a direct effect of the drug, although further long-term evaluation is needed.

#### *Place in therapy*

- Montelukast is licensed in the United Kingdom for those with SAR who also have concomitant asthma (UK license for age >6 months; Zafirlukast UK license >12 years).
- May be useful in patients with asthma and persistent rhinitis.
- Some patients with aspirin sensitivity appear to show marked improvement [115], although at present, it is not possible to predict responders other than by use of a trial of therapy.

*Topical anti-cholinergic: ipratropium bromide (Rinatec<sup>®</sup>, Boehringer Ingelheim Ltd., Berkshire, UK)*

- Decreases rhinorrhoea but has no effect on other nasal symptoms [116–118].

- Needs to be used three times daily, mainly in the morning, e.g. before breakfast, after breakfast and after morning tea break (symptoms of rhinorrhoea occur mainly in the morning).
- Regular use may be effective, particularly:
  - In 'old man's drip'
  - As an 'add on' for AR when watery rhinorrhoea persists despite topical steroids and antihistamines
  - For autonomic rhinitis when the dominant symptom is profuse watery rhinorrhoea in response to irritant triggers or changes in temperature [119, 120]
- Also useful in the common cold.

#### Adverse events

- Dry nose and epistaxis [121].
- Systemic anti-cholinergic effects are unusual [122]
  - Urinary retention [123]
  - Glaucoma [124]
- Caution advised in the elderly.

#### Place in therapy

- Autonomic rhinitis.
- Persistent rhinorrhoea from other causes.

**Intranasal decongestants.** The  $\alpha$ 1-agonist ephedrine (as nasal drops) and  $\alpha$ 2-agonist xylometazoline (available as nasal drops or spray for adults and children over 3 months of age) are sympathomimetics that increase nasal vasoconstriction and are effective for nasal obstruction in both allergic and non-AR [125]. Oxymetazoline has an action that starts within 10 min and lasts up to 12 h.

#### Adverse events

- Regular use can lead to rhinitis medicamentosa with tachyphylaxis to the drug and marked chronic nasal obstruction [126].
- Nasal irritation.
- May increase rhinorrhoea.

#### Place in therapy

- Brief use of <10 days is advised in order to avoid rebound effect
  - for eustachian tube dysfunction when flying
  - in children with acute otitis media to relieve middle ear pain/pressure
  - post-URTI to reduce nasal/sinus congestion
  - to increase nasal patency before intranasal administration of nasal steroids

#### Oral decongestants (pseudoephedrine)

- Weakly effective in reducing nasal obstruction [127].
- Do not cause a rebound effect on withdrawal but are less effective than topical preparations for nasal obstruction [128].
- Effect lasts 30 min – 6 h or longer with slow-release preparations.

#### Side-effects

- Hypertension
- Interact with antidepressants
- Insomnia
- Agitation
- Tachycardia

#### Place in therapy

- Not generally recommended.

**Chromones [sodium cromoglicate (= cromolyn) and nedocromil sodium].** Sodium cromoglicate and nedocromil sodium inhibit the degranulation of sensitized mast cells, inhibiting the release of inflammatory and allergic mediators [129]. Sodium cromoglicate is weakly effective in rhinitis, with some effect on nasal obstruction [130, 131]. The spray needs to be used several times (three to four) per day.

#### Adverse events

- Local irritation
- Rarely transient bronchospasm
- Occasional taste perversion
- Headache

#### Place in therapy

Generally very well tolerated (pregnancy)

- Children and adults with mild symptoms only and sporadic problems in season or on limited exposure [132].
- Cromoglicate and nedocromil eyedrops are useful in conjunctivitis as topical therapy [133, 134].

#### Allergen immunotherapy

Allergen immunotherapy involves the repeated administration of an allergen extract in order to reduce symptoms and the need for rescue medication on subsequent exposure to that allergen [135]. Immunotherapy can be highly effective and is the only treatment that is able to modify the natural history of AR and offer the potential for long-term disease remission [136, 137] (*level of evidence = 1+*). Recent reviews include the 'ARIA Update'

[138] and 'Standards for Practical Immunotherapy' (European guideline) [139].

Whereas non-sedating anti-histamines and topical nasal corticosteroids remain first-line treatments for AR, immunotherapy is recommended in those subjects with IgE-mediated disease in whom allergen avoidance is either undesirable or not feasible and who fail to respond to optimal treatment [18]. The benefit to risk ratio should be considered in every case. The quality of allergen vaccines is important and only standardized extracts should be used. An optimal maintenance dose of 5–20 µg of major allergen per maintenance injection has been shown to correspond with clinical efficacy [135].

#### *Adverse events*

- Pain and swelling at the site of injection is seen in the majority of patients.
- Systemic reactions (particularly in patients with asthma [140]): including urticaria, angio-oedema, asthma and anaphylaxis.
- Chronic asthma is a contraindication in the United Kingdom [141].

For these reasons, immunotherapy should only be performed:

- under the supervision of a physician fully trained in the management of allergic disease
- with immediate access to adrenaline and other resuscitative measures
- patients should be observed for a minimum of 60 min (30 min in mainland Europe) following injections [141, 142]

#### *Place in therapy*

At present, within the United Kingdom, allergen injection immunotherapy is recommended in patients with:

- IgE-mediated seasonal pollen-induced rhinitis and/or conjunctivitis in patients whose symptoms respond inadequately to usual therapy [143, 144]. (*Level evidence = 1+; Grade of recommendation = A*)
- persistent symptoms despite a trial of medical therapy in carefully selected patients with an allergy to animals (e.g. cat) or HDM and where the allergen is not easily avoided e.g. occupational allergy in vets or public sector workers.
- systemic allergic reactions to stinging insect venom (wasp or bee).

#### *Sublingual immunotherapy*

SLIT has been proposed as an alternative to the subcutaneous route [145]. SLIT has been shown to be effective in

both rhinitis and asthmatic patients and to have a good safety profile (no anaphylactic reactions reported) [145, 146]. A recent Cochrane meta-analysis [147] concluded that 'SLIT is a safe treatment which significantly reduces symptoms and medication requirements in AR. The size of the benefit compared with that of other available therapies, particularly injection immunotherapy, is not clear, having been assessed directly in very few studies. Further research is required concentrating on optimizing allergen dosage and patient selection'.

Recent studies performed in large samples of patients have shown a clear dose effect of tablet-based SLIT in patients with grass pollen-induced rhinoconjunctivitis [148–150]. In one study in which subcutaneous and SLIT for seasonal rhinitis were compared, both were effective compared with placebo, although the study was underpowered to detect differences between treatments [151]. A further recent trial of grass allergen tablets for sublingual use demonstrated a 30–40% improvement in symptom and medication scores and an approximate 50% increase in the responder rate, compared with placebo [152]. A further follow-up for 5 years is planned in order to assess possible long-term benefits of SLIT as has already been confirmed for the subcutaneous route.

#### *Anti-immunoglobulin E*

At present, this is only licensed for severe allergic asthma in patients over 12 years of age. It is likely that associated AR would also improve in patients who respond with an improvement in their asthma control. Future use may include combined treatment with immunotherapy in high-risk patients.

#### *Surgery*

Surgery is required only for a small minority of cases. Indications for surgical intervention are:

- Drug-resistant inferior turbinate hypertrophy [153].
- Anatomical variations of the septum with functional relevance.
- Anatomical variations of the bony pyramid with functional relevance.

#### **Rhinitis and pregnancy**

Rhinitis affects at least 20% of pregnancies [154] and can start during any gestational week [155]. Although the pathogenesis is multifactorial, nasal vascular engorgement and placental growth hormone are likely to be involved [155, 156]. Informing the patient that pregnancy-induced rhinitis is a self-limiting condition is often reassuring.

Most medications cross the placenta, and should only be prescribed when the apparent benefit is greater than the risk to the foetus [157]. Regular nasal douching may be helpful. It is a good practice to start treatment with 'tried and tested' drugs [157]. Beclomethasone, fluticasone and budesonide appear to have good safety records as they are widely used in pregnant asthmatic women [158–160]. Chlorphenamine, loratadine and cetirizine may be added but decongestants should be avoided [161, 162]. Chromones have not shown teratogenic effects in animals and are the safest drug recommended in the first 3 months of pregnancy although they require multiple daily administrations. Patients already on immunotherapy may continue if they have already reached the maintenance phase but each case must be considered individually. However, initiation of immunotherapy and up dosing is contraindicated [154].

### Co-morbid association

#### *Rhinitis and asthma – the link*

Rhinitis and asthma are common diseases associated with substantial cost to patients, employers and health care systems. Asthma and rhinitis usually co-exist [163–168], with symptoms of rhinitis found in 75–80% of patients with asthma [163, 169]. Although the costs of rhinitis and asthma are independently high, medical care costs are higher in those with asthma and rhinitis compared with those with asthma alone [164].

Rhinitis is a risk factor for the development of asthma [165]. A number of allergens affect both the nose and the lungs [163] and allergy to HDM or cat dander is a risk factor for both asthma and rhinitis [170, 171]. Many patients with AR have increased non-specific bronchial reactivity [172, 173] during seasonal [174] and perennial [175] allergen exposure. Asthma [169] and bronchial hyperresponsiveness are more common and severe in perennial compared with seasonal rhinitis [175, 176]. Patients with SAR develop seasonal increases in non-specific bronchial responsiveness (BR) but not necessarily asthma symptoms, and these patients often have normal BR during the winter months [177]. BR is also increased in viral rhinitis [178, 179] and following nasal allergen challenge [180, 181]. These observations suggest that bronchial inflammation is associated with nasal inflammation, and is supported by the fact that bronchial hyper-reactivity is reversed by intranasal treatment with sodium cromoglycate [182] and corticosteroids [38, 183]. Nasal allergen challenge results in eosinophil ingress not only to the nose but also to the bronchi, and vice versa [184]. Segmental bronchoprovocation with allergen in AR patients leads to significant changes in mast cell and basophil numbers in both the nasal and bronchial mucosa [185]. A systemic link has been postulated with inhaled

allergen, causing a release of immature eosinophils from the bone marrow into the circulation, from where they migrate to the whole respiratory tract, not just to the site of allergen contact [186].

Allergen-specific immunotherapy for rhinitis has been shown to reduce the development of asthma in children [137] and to reduce non-specific bronchial hyper-reactivity and seasonal asthma in adults with seasonal rhinoconjunctivitis [177]. Patients with co-morbid asthma and rhinitis who are receiving treatment for AR have a significantly lower risk of hospitalizations or attending accident and emergency departments for asthma [187–191].

### Allergic rhinitis in children

Selection of treatment should be considered in the context of the child's needs and response to a given agent. Adherence issues are important because treatment is given chronically. It is essential to explain treatment options to parents [192].

#### *First-line treatments*

**Antihistamines.** Compliance with once-daily administration of a long-acting antihistamine is likely to be better than medication that requires multiple daily doses. Antihistamines are useful if the main symptoms are rhinorrhoea and sneezing, or if there are symptoms outside the nose such as conjunctivitis or rash. Desloratadine, cetirizine, levocetirizine and fexofenadine may also be beneficial for symptoms of nasal congestion [60, 61, 64, 65, 193]. For optimal results, they should be given continuously or prophylactically as opposed to 'as required' [194].

**Nasal steroids.** Nasal steroid with low systemic bioavailability should be used at the lowest possible dose to control symptoms and are useful for nasal congestion and obstruction. Intermittent use may be beneficial due to the rapid vasoconstrictor effect of corticosteroids [195, 196]. Compliance and efficacy is improved if the child is taught how to use the nasal spray, Fig. 4a [41].

#### *Second-line treatments*

- For relief of nasal congestion, short-term use (<14 days) of corticosteroid nose drops (e.g. betamethasone or fluticasone) and a topical decongestant may be helpful [197]. The best position for administration of nose drops is with the child lying, head back; see Fig. 4b [42]. A short course of oral steroids may be required to relieve nasal congestion with systemic symptoms in SAR. Surgical referral for submucosal resection of the

inferior turbinate bones may be indicated only if extensive medical treatment fails [153].

- For refractory rhinorrhoea, ipratropium bromide 0.03% may be helpful [120, 198].
- For SAR, saline nasal irrigation during the pollen season may improve symptoms and reduce antihistamine requirement [55].
- Leukotriene receptor antagonists may have a role if there is concomitant asthma [103].
- To treat underlying allergic disease, allergen immunotherapy is widely used in Europe but has yet to gain general acceptance in the United Kingdom [136, 137]. Efficacy has been demonstrated with both subcutaneous [137, 199] and SLIT [200–203] but is contraindicated in children with asthma.

### Future research

- SLIT, its safety, long-term effectiveness and ability to reduce disease progression.
- Utility of anti-IgE therapy in conjunction with specific immunotherapy.
- Value of extensive, multi-allergen avoidance measures – particularly HDM.
- Aetiological factors that can be altered to reduce the incidence of rhinitis.
- Prospective study examining whether early identification and effective therapy for rhinitis in children reduces progression to asthma.
- Prospective study examining whether effective therapy for rhinitis reduces asthma exacerbations and cost.

These *guidelines* inform the management of allergic and non-AR. Adherence to these guidelines does not constitute an automatic defence for negligence and conversely non-adherence is not indicative of negligence. It is anticipated that these guidelines will be reviewed 5 yearly.

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### References

- 1 Laforest L, Bousquet J, Pietri G *et al*. Quality of life during pollen season in patients with seasonal allergic rhinitis with or without asthma. *Int Arch Allergy Immunol* 2005; **136**: 281–6.
- 2 Blaiss MS. Allergic rhinitis and impairment issues in schoolchildren: a consensus report. *Curr Med Res Opin* 2004; **20**: 1937–52.
- 3 Cockburn IM, Bailit HL, Berndt ER, Finkelstein SN. Loss of work productivity due to illness and medical treatment. *J Occup Environ Med* 1999; **41**:948–53.
- 4 Blaiss MS. Cognitive, social, and economic costs of allergic rhinitis. *Allergy Asthma Proc* 2000; **21**:7–13.
- 5 Slavin RG. Complications of allergic rhinitis: implications for sinusitis and asthma. *J Allergy Clin Immunol* 1998; **101**: S357–60.
- 6 Doyle WJ. The link between allergic rhinitis and otitis media. *Curr Opin Allergy Clin Immunol* 2002; **2**:21–5.
- 7 Passalacqua G, Ciprandi G, Pasquali M, Guerra L, Canonica GW. An update on the asthma–rhinitis link. *Curr Opin Allergy Clin Immunol* 2004; **4**:177–83.
- 8 Barry B. Rhino-sinus manifestations of systemic diseases. *Rev Prat* 2000; **50**:1548–50.
- 9 Powell RJ, Du Toit GL, Siddique N *et al*. BSACI guidelines for the management of chronic urticaria and angio-oedema. *Clin Exp Allergy* 2007; **37**:631–50.
- 10 Aberg N, Hesselmar B, Aberg B, Eriksson B. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995; **25**:815–9.
- 11 Maziak W, Behrens T, Brasky TM *et al*. Are asthma and allergies in children and adolescents increasing? Results from ISAAC phase I and phase III surveys in Munster, Germany. *Allergy* 2003; **58**:572–9.
- 12 Kaiser HB. Risk factors in allergy/asthma. *Allergy Asthma Proc* 2004; **25**:7–10.
- 13 D'Amato G, Liccardi G, D'Amato M, Cazzola M. The role of outdoor air pollution and climatic changes on the rising trends in respiratory allergy. *Respir Med* 2001; **95**:606–11.
- 14 Peden DB. Effect of pollutants in rhinitis. *Curr Allergy Asthma Rep* 2001; **1**:242–6.
- 15 Park YJ, Baraniuk JN. Mechanisms of allergic rhinitis. *Clin Allergy Immunol* 2002; **16**:275–93.
- 16 Smurthwaite L, Durham SR. Local IgE synthesis in allergic rhinitis and asthma. *Curr Allergy Asthma Rep* 2002; **2**:231–8.
- 17 Hansen I, Klimek L, Mosges R, Hormann K. Mediators of inflammation in the early and the late phase of allergic rhinitis. *Curr Opin Allergy Clin Immunol* 2004; **4**:159–63.
- 18 Bousquet J, Van CP, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001; **108**:S147–334.
- 19 Demoly P, Allaert FA, Lecasble M, Bousquet J. Validation of the classification of ARIA (allergic rhinitis and its impact on asthma). *Allergy* 2003; **58**:672–5.
- 20 Bachert C, Vignola AM, Gevaert P, Leynaert B, Van CP, Bousquet J. Allergic rhinitis, rhinosinusitis, and asthma: one airway disease. *Immunol Allergy Clin North Am* 2004; **24**: 19–43.
- 21 Marshall AH, Jones NS, Robertson IJ. CSF rhinorrhoea: the place of endoscopic sinus surgery. *Br J Neurosurg* 2001; **15**:8–12.



- 22 Flanagan P, Eccles R. Spontaneous changes of unilateral nasal airflow in man. A re-examination of the 'nasal cycle'. *Acta Otolaryngol* 1997; 117:590–5.
- 23 Jennings CR, Jones NS, Dugar J, Powell RJ, Lowe J. Wegener's granulomatosis – a review of diagnosis and treatment in 53 subjects. *Rhinology* 1998; 36:188–91.
- 24 Ortolani C, Ispano M, Pastorello E, Bigi A, Ansaloni R. The oral allergy syndrome. *Ann Allergy* 1988; 61:47–52.
- 25 Settupane GA, Chafee FH. Nasal polyps in asthma and rhinitis. A review of 6,037 patients. *J Allergy Clin Immunol* 1977; 59:17–21.
- 26 Van Arsdel PP Jr, Motulsky AG. Frequency and heritability of asthma and allergic rhinitis in college students. *Acta Genet Stat Med* 1959; 9:101–14.
- 27 Fergie N, Jones NS, Havlat MF. The nasal manifestations of sarcoidosis: a review and report of eight cases. *J Laryngol Otol* 1999; 113:893–8.
- 28 Starling-Schwanz R, Peake HL, Salome CM *et al.* Repeatability of peak nasal inspiratory flow measurements and utility for assessing the severity of rhinitis. *Allergy* 2005; 60:795–800.
- 29 Ottaviano G, Scadding GK, Coles S, Lund VJ. Peak nasal inspiratory flow; normal range in adult population. *Rhinology* 2006; 44:32–5.
- 30 Hilberg O, Pedersen OF. Acoustic rhinometry: recommendations for technical specifications and standard operating procedures. *Rhinology* 2000; 16 (Suppl.):3–17.
- 31 Clement PA. Committee report on standardization of rhinometry. *Rhinology* 1984; 22:151–5.
- 32 Hughes RG, Jones NS. The role of nasal endoscopy in out-patient management. *Clin Otolaryngol Allied Sci* 1998; 23:224–6.
- 33 Droste JH, Kerhof M, de Monchy JG, Schouten JP, Rijcken B. Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. The Dutch ECRHS Group. *J Allergy Clin Immunol* 1996; 97:922–32.
- 34 Tabora-Barata L, Jacobson M, Walker S *et al.* Effect of cetirizine and prednisolone on cellular infiltration and cytokine mRNA expression during allergen-induced late cutaneous responses. *Clin Exp Allergy* 1996; 26:68–78.
- 35 Gleeson M, Cripps AW, Hensley MJ, Wlodarczyk JH, Henry RL, Clancy RL. A clinical evaluation in children of the Pharmacia ImmunoCAP system for inhalant allergens. *Clin Exp Allergy* 1996; 26:697–702.
- 36 Doty RL, Shaman P, Kimmelman CP, Dann MS. University of Pennsylvania Smell Identification Test: a rapid quantitative olfactory function test for the clinic. *Laryngoscope* 1984; 94:176–8.
- 37 Romero JN, Scadding G. Eosinophilia in nasal secretions compared to skin prick test and nasal challenge test in the diagnosis of nasal allergy. *Rhinology* 1992; 30:169–75.
- 38 Prieto L, Berto JM, Gutierrez V, Tornero C. Effect of inhaled budesonide on seasonal changes in sensitivity and maximal response to methacholine in pollen-sensitive asthmatic subjects. *Eur Respir J* 1994; 7:1845–51.
- 39 British Thoracic Society. British guideline on the management of asthma. *Thorax* 2003; 58 (Suppl. 1): i1–94.
- 40 Sheikh A, Khan-Wasti S, Price D, Smeeth L, Fletcher M, Walker S. Standardized training for healthcare professionals and its impact on patients with perennial rhinitis: a multi-centre randomized controlled trial. *Clin Exp Allergy* 2007; 37:90–9.
- 41 Gani F, Pozzi E, Crivellaro MA *et al.* The role of patient training in the management of seasonal rhinitis and asthma: clinical implications. *Allergy* 2001; 56:65–8.
- 42 Kayarkar R, Clifton NJ, Woolford TJ. An evaluation of the best head position for instillation of steroid nose drops. *Clin Otolaryngol Allied Sci* 2002; 27:18–21.
- 43 Recer GM. A review of the effects of impermeable bedding encasements on dust-mite allergen exposure and bronchial hyper-responsiveness in dust-mite-sensitized patients. *Clin Exp Allergy* 2004; 34:268–75.
- 44 Terreehorst I, Hak E, Oosting AJ *et al.* Evaluation of impermeable covers for bedding in patients with allergic rhinitis. *N Engl J Med* 2003; 349:237–46.
- 45 Sheikh A, Hurwitz B. House dust mite avoidance measures for perennial allergic rhinitis. *Cochrane Database Syst Rev* 2001; CD001563.
- 46 Eggleston PA, Butz A, Rand C *et al.* Home environmental intervention in inner-city asthma: a randomized controlled clinical trial. *Ann Allergy Asthma Immunol* 2005; 95:518–24.
- 47 O'Meara TJ, Sercombe JK, Morgan G, Reddel HK, Xuan W, Tovey ER. The reduction of rhinitis symptoms by nasal filters during natural exposure to ragweed and grass pollen. *Allergy* 2005; 60:529–32.
- 48 Colloff MJ, Ayres J, Carswell F *et al.* The control of allergens of dust mites and domestic pets: a position paper. *Clin Exp Allergy* 1992; 22 (Suppl. 2):1–28.
- 49 Karjalainen A, Martikainen R, Klaukka T, Saarinen K, Uitti J. Risk of asthma among Finnish patients with occupational rhinitis. *Chest* 2003; 123:283–8.
- 50 Siracusa A, Desrosiers M, Marabini A. Epidemiology of occupational rhinitis: prevalence, aetiology and determinants. *Clin Exp Allergy* 2000; 30:1519–34.
- 51 Cortona G, Pisati G, Dellabianca A, Moscato G. Respiratory occupational allergies: the experience of the hospital operative unit of occupational medicine in Lombardy from 1990 to 1998. *G Ital Med Lav Ergon* 2001; 23:64–70.
- 52 Kronqvist M, Johansson E, Pershagen G, Johansson SG, van Hage-Hamsten M. Risk factors associated with asthma and rhinoconjunctivitis among Swedish farmers. *Allergy* 1999; 54:1142–9.
- 53 Filon FL, Radman G. Latex allergy: a follow up study of 1040 healthcare workers. *Occup Environ Med* 2006; 63:121–5.
- 54 Hemery ML, Dhivert-Donnadieu H, Verdier R, Dujols P, Godard P, Demoly P. A clinical and serological follow-up study of health care workers allergic to natural rubber latex who had followed a latex avoidance programme. *Allergy* 2004; 59:1013–4.
- 55 Garavello W, Romagnoli M, Sordo L, Gaini RM, Di BC, Angriano A. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: a randomized study. *Pediatr Allergy Immunol* 2003; 14:140–3.
- 56 Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. *Laryngoscope* 2000; 110:1189–93.
- 57 Garavello W, Di BF, Romagnoli M, Sambataro G, Gaini RM. Nasal rinsing with hypertonic solution: an adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. *Int Arch Allergy Immunol* 2005; 137:310–4.

- 58 Joss JD, Craig TJ. Seasonal allergic conjunctivitis: overview and treatment update. *J Am Osteopath Assoc* 1999; **99**: S13–8.
- 59 Wilson AM, O'Byrne PM, Parameswaran K. Leukotriene receptor antagonists for allergic rhinitis: a systematic review and meta-analysis. *Am J Med* 2004; **116**:338–44.
- 60 Nayak AS, Schenkel E. Desloratadine reduces nasal congestion in patients with intermittent allergic rhinitis. *Allergy* 2001; **56**:1077–80.
- 61 Ciprandi G, Cosentino C, Milanese M, Mondino C, Canonica GW. Fexofenadine reduces nasal congestion in perennial allergic rhinitis. *Allergy* 2001; **56**:1068–70.
- 62 Ciprandi G, Cirillo I, Vizzaccaro A, Tosca MA. Levocetirizine improves nasal obstruction and modulates cytokine pattern in patients with seasonal allergic rhinitis: a pilot study. *Clin Exp Allergy* 2004; **34**:958–64.
- 63 van SJ, Clement PA, Beel MH. Comparison of five new antihistamines (H1-receptor antagonists) in patients with allergic rhinitis using nasal provocation studies and skin tests. *Allergy* 2002; **57**:346–50.
- 64 Patou J, De SH, Van CP, Bachert C. Pathophysiology of nasal obstruction and meta-analysis of early and late effects of levocetirizine. *Clin Exp Allergy* 2006; **36**:972–81.
- 65 Canonica GW, Tarantini F, Compalati E, Penagos M. Efficacy of desloratadine in the treatment of allergic rhinitis: a meta-analysis of randomized, double-blind, controlled trials. *Allergy* 2007; **62**:359–66.
- 66 Schwarzer G, Bassler D, Mitra A, Ducharme FM, Forster J. Ketotifen alone or as additional medication for long-term control of asthma and wheeze in children. *Cochrane Database Syst Rev* 2004; **CD001384**.
- 67 Portnoy JM, Dinakar C. Review of cetirizine hydrochloride for the treatment of allergic disorders. *Expert Opin Pharmacother* 2004; **5**:125–35.
- 68 Nelson HS. Prospects for antihistamines in the treatment of asthma. *J Allergy Clin Immunol* 2003; **112**:S96–100.
- 69 Leurs R, Church MK, Tagliabue M. H1-antihistamines: inverse agonism, anti-inflammatory actions and cardiac effects. *Clin Exp Allergy* 2002; **32**:489–98.
- 70 Bachert C, Bousquet J, Canonica GW *et al*. Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis. *J Allergy Clin Immunol* 2004; **114**:838–44.
- 71 Vuurman EF, van Veggel LM, Uiterwijk MM, Leutner D, O'Hanlon JF. Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy* 1993; **71**:121–6.
- 72 Sheikh A, Khan-Wasti S, Price D, Smeeth L, Fletcher M, Walker S. Structured allergy training for health professionals improves quality of life in patients with perennial rhinitis: randomised controlled trial. *J Allergy Clin Immunol* 2005; **115** (Suppl.): S42.
- 73 Hindmarch I, Shamsi Z, Kimber S. An evaluation of the effects of high-dose fexofenadine on the central nervous system: a double-blind, placebo-controlled study in healthy volunteers. *Clin Exp Allergy* 2002; **32**:133–9.
- 74 Howarth PH, Stern MA, Roi L, Reynolds R, Bousquet J. Double-blind, placebo-controlled study comparing the efficacy and safety of fexofenadine hydrochloride (120 and 180 mg once daily) and cetirizine in seasonal allergic rhinitis. *J Allergy Clin Immunol* 1999; **104**:927–33.
- 75 McNeely W, Wiseman LR. Intranasal azelastine. A review of its efficacy in the management of allergic rhinitis. *Drugs* 1998; **56**:91–114.
- 76 Portnoy JM, Van OT, Williams PB. Evidence-based strategies for treatment of allergic rhinitis. *Curr Allergy Asthma Rep* 2004; **4**:439–46.
- 77 Juniper EF, Kline PA, Hargreave FE, Dolovich J. Comparison of beclomethasone dipropionate aqueous nasal spray, astemizole, and the combination in the prophylactic treatment of ragweed pollen-induced rhinoconjunctivitis. *J Allergy Clin Immunol* 1989; **83**:627–33.
- 78 Simpson RJ. Budesonide and terfenadine, separately and in combination, in the treatment of hay fever. *Ann Allergy* 1994; **73**:497–502.
- 79 Ratner PH, van Bavel JH, Martin BG *et al*. A comparison of the efficacy of fluticasone propionate aqueous nasal spray and loratadine, alone and in combination, for the treatment of seasonal allergic rhinitis. *J Fam Pract* 1998; **47**:118–25.
- 80 Yanez A, Rodrigo GJ. Intranasal corticosteroids versus topical H1 receptor antagonists for the treatment of allergic rhinitis: a systematic review with meta-analysis. *Ann Allergy Asthma Immunol* 2002; **89**:479–84.
- 81 Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ* 1998; **317**:1624–9.
- 82 Fokkens WJ, Godthelp T, Holm AF, Klein-Jan A. Local corticosteroid treatment: the effect on cells and cytokines in nasal allergic inflammation. *Am J Rhinol* 1998; **12**:21–6.
- 83 Graft D, Aaronson D, Chervinsky P *et al*. A placebo- and active-controlled randomized trial of prophylactic treatment of seasonal allergic rhinitis with mometasone furoate aqueous nasal spray. *J Allergy Clin Immunol* 1996; **98**:724–31.
- 84 Homer JJ, Gazis TG. Cushing's syndrome induced by beta-methasone nose drops. In rhinological disease betamethasone should be regarded as systemic corticosteroid. *BMJ* 1999; **318**:1355.
- 85 Perry RJ, Findlay CA, Donaldson MD. Cushing's syndrome, growth impairment, and occult adrenal suppression associated with intranasal steroids. *Arch Dis Child* 2002; **87**:45–8.
- 86 Fowler PD, Gazis AG, Page SR, Jones NS. A randomized double-blind study to compare the effects of nasal fluticasone and betamethasone on the hypothalamo-pituitary-adrenal axis and bone turnover in patients with nasal polyposis. *Clin Otolaryngol Allied Sci* 2002; **27**:489–93.
- 87 Allen DB. Systemic effects of intranasal steroids: an endocrinologist's perspective. *J Allergy Clin Immunol* 2000; **106**: S179–90.
- 88 Salib RJ, Howarth PH. Safety and tolerability profiles of intranasal antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis. *Drug Saf* 2003; **26**:863–93.
- 89 Moller C, Ahlstrom H, Henricson KA, Malmqvist LA, Akerlund A, Hildebrand H. Safety of nasal budesonide in the long-term treatment of children with perennial rhinitis. *Clin Exp Allergy* 2003; **33**:816–22.
- 90 Schenkel EJ, Skoner DP, Bronsky EA *et al*. Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. *Pediatrics* 2000; **105**:E22.

- 91 Skoner DP, Rachelefsky GS, Meltzer EO *et al.* Detection of growth suppression in children during treatment with intranasal beclomethasone dipropionate. *Pediatrics* 2000; **105**: E23.
- 92 Johnson SR, Marion AA, Vrchoticky T, Emmanuel PJ, Lujan-Zilbermann J. Cushing syndrome with secondary adrenal insufficiency from concomitant therapy with ritonavir and fluticasone. *J Pediatr* 2006; **148**:386–8.
- 93 Skov M, Main KM, Sillesen IB, Muller J, Koch C, Lanng S. Iatrogenic adrenal insufficiency as a side-effect of combined treatment of itraconazole and budesonide. *Eur Respir J* 2002; **20**:127–33.
- 94 McMahon C, Darby Y, Ryan R, Scadding G. Immediate and short-term effects of benzalkonium chloride on the human nasal mucosa in vivo. *Clin Otolaryngol Allied Sci* 1997; **22**: 318–22.
- 95 Allen DB, Meltzer EO, Lemanske RF Jr *et al.* No growth suppression in children treated with the maximum recommended dose of fluticasone propionate aqueous nasal spray for one year. *Allergy Asthma Proc* 2002; **23**:407–13.
- 96 Bui CM, Chen H, Shyr Y, Joos KM. Discontinuing nasal steroids might lower intraocular pressure in glaucoma. *J Allergy Clin Immunol* 2005; **116**:1042–7.
- 97 Nasser SM, Ewan PW. Lesson of the week: depot corticosteroid treatment for hay fever causing avascular necrosis of both hips. *BMJ* 2001; **322**:1589–91.
- 98 Anonymous. Any place for depot triamcinolone in hay fever?. *Drug Ther Bull* 1999; **37**:17–8.
- 99 Bisgaard H, Olsson P, Bende M. Effect of leukotriene D4 on nasal mucosal blood flow, nasal airway resistance and nasal secretion in humans. *Clin Allergy* 1986; **16**:289–97.
- 100 Fowler SJ, Hall IP, Wilson AM, Wheatley AP, Lipworth BJ. 5-Lipoxygenase polymorphism and in-vivo response to leukotriene receptor antagonists. *Eur J Clin Pharmacol* 2002; **58**: 187–90.
- 101 Sampson AP, Siddiqui S, Buchanan D *et al.* Variant LTC(4) synthase allele modifies cysteinyl leukotriene synthesis in eosinophils and predicts clinical response to zafirlukast. *Thorax* 2000; **55** (Suppl. 2):S28–31.
- 102 Mastalerz L, Nizankowska E, Sanak M *et al.* Clinical and genetic features underlying the response of patients with bronchial asthma to treatment with a leukotriene receptor antagonist. *Eur J Clin Invest* 2002; **32**:949–55.
- 103 Philip G, Malmstrom K, Hampel FC *et al.* Montelukast for treating seasonal allergic rhinitis: a randomized, double-blind, placebo-controlled trial performed in the spring. *Clin Exp Allergy* 2002; **32**:1020–8.
- 104 Pullerits T, Praks L, Skoogh BE, Ani R, Lotvall J. Randomized placebo-controlled study comparing a leukotriene receptor antagonist and a nasal glucocorticoid in seasonal allergic rhinitis. *Am J Respir Crit Care Med* 1999; **159**:1814–8.
- 105 Ratner PH, Howland WC III, Arastu R *et al.* Fluticasone propionate aqueous nasal spray provided significantly greater improvement in daytime and nighttime nasal symptoms of seasonal allergic rhinitis compared with montelukast. *Ann Allergy Asthma Immunol* 2003; **90**:536–42.
- 106 Wilson AM, Dempsey OJ, Sims EJ, Lipworth BJ. A comparison of topical budesonide and oral montelukast in seasonal allergic rhinitis and asthma. *Clin Exp Allergy* 2001; **31**:616–24.
- 107 Meltzer EO, Malmstrom K, Lu S *et al.* Concomitant montelukast and loratadine as treatment for seasonal allergic rhinitis: a randomized, placebo-controlled clinical trial. *J Allergy Clin Immunol* 2000; **105**:917–22.
- 108 Nayak AS, Philip G, Lu S, Malice MP, Reiss TF. Efficacy and tolerability of montelukast alone or in combination with loratadine in seasonal allergic rhinitis: a multicenter, randomized, double-blind, placebo-controlled trial performed in the fall. *Ann Allergy Asthma Immunol* 2002; **88**:592–600.
- 109 Wilson AM, Orr LC, Sims EJ, Lipworth BJ. Effects of mono-therapy with intra-nasal corticosteroid or combined oral histamine and leukotriene receptor antagonists in seasonal allergic rhinitis. *Clin Exp Allergy* 2001; **31**:61–8.
- 110 Wilson AM, Orr LC, Coutie WJ, Sims EJ, Lipworth BJ. A comparison of once daily fexofenadine versus the combination of montelukast plus loratadine on domiciliary nasal peak flow and symptoms in seasonal allergic rhinitis. *Clin Exp Allergy* 2002; **32**:126–32.
- 111 Pawankar R. Exploring the role of leukotriene receptor antagonists in the management of allergic rhinitis and comorbid asthma. *Clin Exp Allergy Rev* 2003; **3**:74–80.
- 112 Pullerits T, Praks L, Ristioja V, Lotvall J. Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. *J Allergy Clin Immunol* 2002; **109**:949–55.
- 113 Di Lorenzo G., Pacor ML, Pellitteri ME *et al.* Randomized placebo-controlled trial comparing fluticasone aqueous nasal spray in mono-therapy, fluticasone plus cetirizine, fluticasone plus montelukast and cetirizine plus montelukast for seasonal allergic rhinitis. *Clin Exp Allergy* 2004; **34**:259–67.
- 114 Philip G, Nayak AS, Berger WE *et al.* The effect of montelukast on rhinitis symptoms in patients with asthma and seasonal allergic rhinitis. *Curr Med Res Opin* 2004; **20**: 1549–58.
- 115 Dahlen B, Nizankowska E, Szczeklik A *et al.* Benefits from adding the 5-lipoxygenase inhibitor zileuton to conventional therapy in aspirin-intolerant asthmatics. *Am J Respir Crit Care Med* 1998; **157**:1187–94.
- 116 Grossman J, Banov C, Boggs P *et al.* Use of ipratropium bromide nasal spray in chronic treatment of nonallergic perennial rhinitis, alone and in combination with other perennial rhinitis medications. *J Allergy Clin Immunol* 1995; **95**:1123–7.
- 117 Kaiser HB, Findlay SR, Georgitis JW *et al.* The anticholinergic agent, ipratropium bromide, is useful in the treatment of rhinorrhea associated with perennial allergic rhinitis. *Allergy Asthma Proc* 1998; **19**:23–9.
- 118 Tan R, Corren J. Optimum treatment of rhinitis in the elderly. *Drugs Aging* 1995; **7**:168–75.
- 119 Ostberg B, Winther B, Borum P, Mygind N. Common cold and high-dose ipratropium bromide: use of anticholinergic medication as an indicator of reflex-mediated hypersecretion. *Rhinology* 1997; **35**:58–62.
- 120 Bonadonna P, Senna G, Zanon P *et al.* Cold-induced rhinitis in skiers – clinical aspects and treatment with ipratropium bromide nasal spray: a randomized controlled trial. *Am J Rhinol* 2001; **15**:297–301.
- 121 Wood CC, Fireman P, Grossman J, Wecker M, MacGregor T. Product characteristics and pharmacokinetics of intranasal

- ipratropium bromide. *J Allergy Clin Immunol* 1995; **95**: 1111–6.
- 122 Bronsky EA, Druce H, Findlay SR *et al*. A clinical trial of ipratropium bromide nasal spray in patients with perennial nonallergic rhinitis. *J Allergy Clin Immunol* 1995; **95**:1117–22.
- 123 Pras E, Stienlauf S, Pinkhas J, Sidi Y. Urinary retention associated with ipratropium bromide. *Drug Intell Clin Pharmacol* 1991; **25**:939–40.
- 124 Hall SK. Acute angle-closure glaucoma as a complication of combined beta-agonist and ipratropium bromide therapy in the emergency department. *Ann Emerg Med* 1994; **23**:884–7.
- 125 Storms WW. Pharmacologic approaches to daytime and nighttime symptoms of allergic rhinitis. *J Allergy Clin Immunol* 2004; **114**:S146–53.
- 126 Scadding GK. Rhinitis medicamentosa. *Clin Exp Allergy* 1995; **25**:391–4.
- 127 Malm L. Pharmacological background to decongesting and anti-inflammatory treatment of rhinitis and sinusitis. *Acta Otolaryngol* 1994; **515** (Suppl.):53–5.
- 128 Naclerio RM. Optimizing treatment options. *Clin Exp Allergy* 1998; **28** (Suppl. 6):54–9.
- 129 Ratner PH, Ehrlich PM, Fineman SM, Meltzer EO, Skoner DP. Use of intranasal cromolyn sodium for allergic rhinitis. *Mayo Clin Proc* 2002; **77**:350–4.
- 130 James IG, Campbell LM, Harrison JM, Fell PJ, Ellers-Lenz B, Petzold U. Comparison of the efficacy and tolerability of topically administered azelastine, sodium cromoglycate and placebo in the treatment of seasonal allergic conjunctivitis and rhinoconjunctivitis. *Curr Med Res Opin* 2003; **19**:313–20.
- 131 Meltzer EO. Efficacy and patient satisfaction with cromolyn sodium nasal solution in the treatment of seasonal allergic rhinitis: a placebo-controlled study. *Clin Ther* 2002; **24**: 942–52.
- 132 Hadley JA. Cost-effective pharmacotherapy for inhalant allergic rhinitis. *Otolaryngol Clin North Am* 2003; **36**:825–36.
- 133 James IG, Campbell LM, Harrison JM, Fell PJ, Ellers-Lenz B, Petzold U. Comparison of the efficacy and tolerability of topically administered azelastine, sodium cromoglycate and placebo in the treatment of seasonal allergic conjunctivitis and rhinoconjunctivitis. *Curr Med Res Opin* 2003; **19**:313–20.
- 134 Owen CG, Shah A, Henshaw K, Smeeth L, Sheikh A. Topical treatments for seasonal allergic conjunctivitis: systematic review and meta-analysis of efficacy and effectiveness. *Br J Gen Pract* 2004; **54**:451–6.
- 135 Bousquet J, Lockey R, Malling HJ. Allergen immunotherapy: therapeutic vaccines for allergic diseases. A WHO position paper. *J Allergy Clin Immunol* 1998; **102**:558–62.
- 136 Durham SR, Walker SM, Varga EM *et al*. Long-term clinical efficacy of grass-pollen immunotherapy. *N Engl J Med* 1999; **341**:468–75.
- 137 Moller C, Dreborg S, Ferdousi HA *et al*. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). *J Allergy Clin Immunol* 2002; **109**:251–6.
- 138 Passalacqua G, Durham SR. Allergic rhinitis and its impact on asthma update: allergen immunotherapy. *J Allergy Clin Immunol* 2007; **119**:881–91.
- 139 Alvarez-Cuesta O, Bousquet J, Canonica GW, Durham SR, Malling HJ, Valovirta E. Standards for practical allergen-specific immunotherapy. *Allergy* 2006; **61** (Suppl. 82): 1–20.
- 140 Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TA. Survey of fatalities from skin testing and immunotherapy 1985–1989. *J Allergy Clin Immunol* 1993; **92**:6–15.
- 141 Medicines Control Agency Committee on Safety of Medicines. Desensitising vaccines: new advice. *Curr Probl Pharmacovigilance* 1994; **20**:5.
- 142 Youtlen LJ, Atkinson BA, Lee TH. The incidence and nature of adverse reactions to injection immunotherapy in bee and wasp venom allergy. *Clin Exp Allergy* 1995; **25**:159–65.
- 143 Frew AJ. Injection immunotherapy. British Society for Allergy and Clinical Immunology Working Party. *BMJ* 1993; **307**: 919–23.
- 144 Malling HJ. Immunotherapy in Europe. *Clin Exp Allergy* 1994; **24**:515–21.
- 145 Canonica GW, Passalacqua G. Noninjection routes for immunotherapy. *J Allergy Clin Immunol* 2003; **111**:437–48.
- 146 Gidaro GB, Marcucci F, Sensi L, Incorvaia C, Frati F, Ciprandi G. The safety of sublingual-swallow immunotherapy: an analysis of published studies. *Clin Exp Allergy* 2005; **35**:565–71.
- 147 Wilson DR, Lima MT, Durham SR. Sublingual immunotherapy for allergic rhinitis: systematic review and meta-analysis. *Allergy* 2005; **60**:4–12.
- 148 Durham SR, Yang WH, Pedersen MR, Johansen N, Rak S. Sublingual immunotherapy with once-daily grass allergen tablets: a randomized controlled trial in seasonal allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 2006; **117**:802–9.
- 149 Dahl R, Stender A, Rak S. Specific immunotherapy with SQ standardized grass allergen tablets in asthmatics with rhinoconjunctivitis. *Allergy* 2006; **61**:185–90.
- 150 Khinchi MS, Poulsen LK, Carat F, Andre C, Hansen AB, Malling HJ. Clinical efficacy of sublingual and subcutaneous birch pollen allergen-specific immunotherapy: a randomized, placebo-controlled, double-blind, double-dummy study. *Allergy* 2004; **59**:45–53.
- 151 Didier A, Melac M, Combebias A, Andre C. Efficacy and safety of sublingual immunotherapy (slit) tablets in patients with grass pollen rhinoconjunctivitis. *J Allergy Clin Immunol* 2006; **117**:721.
- 152 Dahl R, Kapp A, Colombo G *et al*. Efficacy and safety of sublingual immunotherapy with grass allergen tablets for seasonal allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 2006; **118**:434–40.
- 153 Passali D, Passali FM, Damiani V, Passali GC, Bellussi L. Treatment of inferior turbinate hypertrophy: a randomized clinical trial. *Ann Otol Rhinol Laryngol* 2003; **112**:683–8.
- 154 Keles N. Treatment of allergic rhinitis during pregnancy. *Am J Rhinol* 2004; **18**:23–8.
- 155 Ellegard EK. The etiology and management of pregnancy rhinitis. *Am J Respir Med* 2003; **2**:469–75.
- 156 Incaudo GA. Diagnosis and treatment of allergic rhinitis and sinusitis during pregnancy and lactation. *Clin Rev Allergy Immunol* 2004; **27**:159–77.
- 157 Gani F, Braida A, Lombardi C, Del GA, Senna GE, Passalacqua G. Rhinitis in pregnancy. *Allerg Immunol (Paris)* 2003; **35**: 306–13.
- 158 Demoly P, Piette V, Daures JP. Treatment of allergic rhinitis during pregnancy. *Drugs* 2003; **63**:1813–20.

- 159 Ellegard EK, Hellgren M, Karlsson NG. Fluticasone propionate aqueous nasal spray in pregnancy rhinitis. *Clin Otolaryngol Allied Sci* 2001; 26:394–400.
- 160 Mazzotta P, Loebstein R, Koren G. Treating allergic rhinitis in pregnancy. Safety considerations. *Drug Saf* 1999; 20:361–75.
- 161 Diav-Citrin O, Shechtman S, Aharonovich A *et al.* Pregnancy outcome after gestational exposure to loratadine or antihistamines: a prospective controlled cohort study. *J Allergy Clin Immunol* 2003; 111:1239–43.
- 162 Moretti ME, Caprara D, Coutinho CJ *et al.* Fetal safety of loratadine use in the first trimester of pregnancy: a multicenter study. *J Allergy Clin Immunol* 2003; 111:479–83.
- 163 Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. *Thorax* 1991; 46:895–901.
- 164 Yawn BP, Yunginger JW, Wollan PC, Reed CE, Silverstein MD, Harris AG. Allergic rhinitis in Rochester, Minnesota residents with asthma: frequency and impact on health care charges. *J Allergy Clin Immunol* 1999; 103:54–9.
- 165 Wright AL, Holberg CJ, Martinez FD, Halonen M, Morgan W, Taussig LM. Epidemiology of physician-diagnosed allergic rhinitis in childhood. *Pediatrics* 1994; 94:895–901.
- 166 Neukirch F, Pin I, Knani J *et al.* Prevalence of asthma and asthma-like symptoms in three French cities. *Respir Med* 1995; 89:685–92.
- 167 Huovinen E, Kaprio J, Laitinen LA, Koskenvuo M. Incidence and prevalence of asthma among adult Finnish men and women of the Finnish Twin Cohort from 1975 to 1990, and their relation to hay fever and chronic bronchitis. *Chest* 1999; 115:928–36.
- 168 Greisner WA III, Settignano RJ, Settignano GA. Co-existence of asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Asthma Proc* 1998; 19:185–8.
- 169 Leynaert B, Bousquet J, Neukirch C, Liard R, Neukirch F. Perennial rhinitis: An independent risk factor for asthma in nonatopic subjects: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 104:301–4.
- 170 Sears MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin Exp Allergy* 1989; 19:419–24.
- 171 Yssel H, Abbal C, Pene J, Bousquet J. The role of IgE in asthma. *Clin Exp Allergy* 1998; 28 (Suppl. 5):104–9.
- 172 Townley RG, Ryo UY, Kolotkin BM, Kang B. Bronchial sensitivity to methacholine in current and former asthmatic and allergic rhinitis patients and control subjects. *J Allergy Clin Immunol* 1975; 56:429–42.
- 173 Ramsdale EH, Morris MM, Roberts RS, Hargreave FE. Bronchial responsiveness to methacholine in chronic bronchitis: relationship to airflow obstruction and cold air responsiveness. *Thorax* 1984; 39:912–8.
- 174 Gerblich AA, Schwartz HJ, Chester EH. Seasonal variation of airway function in allergic rhinitis. *J Allergy Clin Immunol* 1986; 77:676–81.
- 175 Verdiani P, Di CS, Baronti A. Different prevalence and degree of nonspecific bronchial hyperreactivity between seasonal and perennial rhinitis. *J Allergy Clin Immunol* 1990; 86:576–82.
- 176 Prieto JL, Gutierrez V, Berto JM, Camps B. Sensitivity and maximal response to methacholine in perennial and seasonal allergic rhinitis. *Clin Exp Allergy* 1996; 26:61–7.
- 177 Walker SM, Pajno GB, Lima MT, Wilson DR, Durham SR. Grass pollen immunotherapy for seasonal rhinitis and asthma: a randomized, controlled trial. *J Allergy Clin Immunol* 2001; 107:87–93.
- 178 Lemanske RF Jr, Dick EC, Swenson CA, Vrtis RF, Busse WW. Rhinovirus upper respiratory infection increases airway hyper-reactivity and late asthmatic reactions. *J Clin Invest* 1989; 83:1–10.
- 179 Sterk PJ. Virus-induced airway hyperresponsiveness in man. *Eur Respir J* 1993; 6:894–902.
- 180 Corren J, Adinoff AD, Irvin CG. Changes in bronchial responsiveness following nasal provocation with allergen. *J Allergy Clin Immunol* 1992; 89:611–8.
- 181 Aubier M, Levy J, Clerici C, Neukirch F, Cabrieres F, Herman D. Protective effect of theophylline on bronchial hyperresponsiveness in patients with allergic rhinitis. *Am Rev Respir Dis* 1991; 143:346–50.
- 182 Lowhagen O, Rak S. Modification of bronchial hyperreactivity after treatment with sodium cromoglycate during pollen season. *J Allergy Clin Immunol* 1985; 75:460–7.
- 183 Sotomayor H, Badier M, Vervloet D, Orehek J. Seasonal increase of carbachol airway responsiveness in patients allergic to grass pollen. Reversal by corticosteroids. *Am Rev Respir Dis* 1984; 130:56–8.
- 184 Braunstahl GJ, Overbeek SE, Kleinjan A, Prins JB, Hoogsteden HC, Fokkens WJ. Nasal allergen provocation induces adhesion molecule expression and tissue eosinophilia in upper and lower airways. *J Allergy Clin Immunol* 2001; 107:469–76.
- 185 Braunstahl GJ, Overbeek SE, Fokkens WJ *et al.* Segmental bronchoprovocation in allergic rhinitis patients affects mast cell and basophil numbers in nasal and bronchial mucosa. *Am J Respir Crit Care Med* 2001; 164:858–65.
- 186 Sehmi R, Baatjes AJ, Denburg JA. Hemopoietic progenitor cells and hemopoietic factors: potential targets for treatment of allergic inflammatory diseases. *Curr Drug Targets Inflamm Allergy* 2003; 2:271–8.
- 187 Crystal-Peters J, Neslusan C, Crown WH, Torres A. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. *J Allergy Clin Immunol* 2002; 109:57–62.
- 188 Adams RJ, Fuhlbrigge A, Guilbert T, Lozano P, Martinez F. Inadequate use of asthma medication in the United States: results of the asthma in America national population survey. *J Allergy Clin Immunol* 2002; 110:58–64.
- 189 Corren J, Manning BE, Thompson SF, Hennessy S, Strom BL. Rhinitis therapy and the prevention of hospital care for asthma: a case-control study. *J Allergy Clin Immunol* 2004; 113:415–9.
- 190 Adams RJ, Fuhlbrigge AL, Finkelstein JA, Weiss ST. Intranasal steroids and the risk of emergency department visits for asthma. *J Allergy Clin Immunol* 2002; 109:636–42.
- 191 Corren J. The connection between allergic rhinitis and bronchial asthma. *Curr Opin Pulm Med* 2007; 13:13–8.
- 192 Clement PA, Bluestone CD, Gordts F *et al.* Management of rhinosinusitis in children. *Int J Pediatr Otorhinolaryngol* 1999; 49 (Suppl. 1):S95–100.
- 193 de Blic J, Wahn U, Billard E, Alt R, Pujazon MC. Levocetirizine in children: evidenced efficacy and safety in a 6-week

- randomized seasonal allergic rhinitis trial. *Pediatr Allergy Immunol* 2005; **16**:267–75.
- 194 Ciprandi G, Ricca V, Passalacqua G *et al*. Seasonal rhinitis and azelastine: long- or short-term treatment? *J Allergy Clin Immunol* 1997; **99**:301–7.
- 195 Dykewicz MS, Kaiser HB, Nathan RA *et al*. Fluticasone propionate aqueous nasal spray improves nasal symptoms of seasonal allergic rhinitis when used as needed (prn). *Ann Allergy Asthma Immunol* 2003; **91**:44–8.
- 196 Jen A, Baroody F, de TM, Haney L, Blair C, Naclerio R. As-needed use of fluticasone propionate nasal spray reduces symptoms of seasonal allergic rhinitis. *J Allergy Clin Immunol* 2000; **105**:732–8.
- 197 Serra HA, Alves O, Rizzo LF, Devoto FM, Ascierio H. Loratadine-pseudoephedrine in children with allergic rhinitis, a controlled double-blind trial. *Br J Clin Pharmacol* 1998; **45**:147–50.
- 198 Meltzer EO, Orgel HA, Biondi R *et al*. Ipratropium nasal spray in children with perennial rhinitis. *Ann Allergy Asthma Immunol* 1997; **78**:485–91.
- 199 Kuehr J, Brauburger J, Zielen S *et al*. Efficacy of combination treatment with anti-IgE plus specific immunotherapy in polysensitized children and adolescents with seasonal allergic rhinitis. *J Allergy Clin Immunol* 2002; **109**:274–80.
- 200 Moller C, Dreborg S, Lanner A, Bjorksten B. Oral immunotherapy of children with rhinoconjunctivitis due to birch pollen allergy. A double blind study. *Allergy* 1986; **41**:271–9.
- 201 Vourdas D, Syrigou E, Potamianou P *et al*. Double-blind, placebo-controlled evaluation of sublingual immunotherapy with standardized olive pollen extract in pediatric patients with allergic rhinoconjunctivitis and mild asthma due to olive pollen sensitization. *Allergy* 1998; **53**:662–72.
- 202 LaRosa M., Ranno C, Andre C, Carat F, Tosca MA, Canonica GW. Double-blind placebo-controlled evaluation of sublingual-swallow immunotherapy with standardized *Parietaria judaica* extract in children with allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 1999; **104**:425–32.
- 203 Yuksel H, Tanac R, Gousseinov A, Demir E. Sublingual immunotherapy and influence on urinary leukotrienes in seasonal pediatric allergy. *J Investig Allergol Clin Immunol* 1999; **9**:305–13.
- 204 Shusterman D. Toxicology of nasal irritants. *Curr Allergy Asthma Rep* 2003; **3**:258–65.
- 205 Drake-Lee A, Ruckley R, Parker A. Occupational rhinitis: a poorly diagnosed condition. *J Laryngol Otol* 2002; **116**:580–5.
- 206 Petrick MM, Slavin RG. Occupational rhinitis. *Immunol Allergy Clin North Am* 2003; **23**:193–203, vi.
- 207 Cullinan P, Cook A, Gordon S *et al*. Allergen exposure, atopy and smoking as determinants of allergy to rats in a cohort of laboratory employees. *Eur Respir J* 1999; **13**:1139–43.
- 208 Gautrin D, Infante-Rivard C, Ghezzi H, Malo JL. Incidence and host determinants of probable occupational asthma in apprentices exposed to laboratory animals. *Am J Respir Crit Care Med* 2001; **163**:899–904.
- 209 Gautrin D, Ghezzi H, Infante-Rivard C, Malo JL. Natural history of sensitization, symptoms and occupational diseases in apprentices exposed to laboratory animals. *Eur Respir J* 2001; **17**:904–8.
- 210 Cartier A, Malo JL, Forest F *et al*. Occupational asthma in snow crab-processing workers. *J Allergy Clin Immunol* 1984; **74**:261–9.
- 211 Houba R, Heederik D, Doekes G. Wheat sensitization and work-related symptoms in the baking industry are preventable. An epidemiologic study. *Am J Respir Crit Care Med* 1998; **158**:1499–503.
- 212 Grammer LC, Ditto AM, Tripathi A, Harris KE. Prevalence and onset of rhinitis and conjunctivitis in subjects with occupational asthma caused by trimellitic anhydride (TMA). *J Occup Environ Med* 2002; **44**:1179–81.
- 213 Wernfors M, Nielsen J, Schutz A, Skerfving S. Phthalic anhydride-induced occupational asthma. *Int Arch Allergy Appl Immunol* 1986; **79**:77–82.
- 214 Gwaltney JM. Clinical significance and pathogenesis of viral respiratory infections. *Am J Med* 2002; **112** (Suppl. 6A):13S–8S.
- 215 Gwaltney JM Jr. Acute community acquired bacterial sinusitis: to treat or not to treat. *Can Respir J* 1999; **6** (Suppl. A):46A–50A.
- 216 Hurst JR, Donaldson GC, Wilkinson TM, Perera WR, Wedzicha JA. Epidemiological relationships between the common cold and exacerbation frequency in COPD. *Eur Respir J* 2005; **26**:846–52.
- 217 Johnston SL, Pattemore PK, Sanderson G *et al*. Community study of role of viral infections in exacerbations of asthma in 9–11 year old children. *BMJ* 1995; **310**:1225–9.
- 218 Ramadan HH. Pediatric sinusitis: update. *J Otolaryngol* 2005; **34** (Suppl. 1):S14–7.
- 219 Fokkens W, Lund V, Bachert C *et al*. EAACI position paper on rhinosinusitis and nasal polyps executive summary. *Allergy* 2005; **60**:583–601.
- 220 Leone C, Teodoro C, Pelucchi A *et al*. Bronchial responsiveness and airway inflammation in patients with nonallergic rhinitis with eosinophilia syndrome. *J Allergy Clin Immunol* 1997; **100**:775–80.
- 221 Garay R. Mechanisms of vasomotor rhinitis. *Allergy* 2004; **59** (Suppl. 76):4–9.
- 222 Yewell J, Haydon R, Archer S, Manaligod JM. Complications of intranasal prescription narcotic abuse. *Ann Otol Rhinol Laryngol* 2002; **111**:174–7.
- 223 Hamano N, Terada N, Maesako K, Numata T, Konno A. Effect of sex hormones on eosinophilic inflammation in nasal mucosa. *Allergy Asthma Proc* 1998; **19**:263–9.
- 224 Philpott CM, El-Alami M, Murty GE. The effect of the steroid sex hormones on the nasal airway during the normal menstrual cycle. *Clin Otolaryngol Allied Sci* 2004; **29**:138–42.
- 225 Scadding GK. Non-allergic rhinitis: diagnosis and management. *Curr Opin Allergy Clin Immunol* 2001; **1**:15–20.
- 226 Bachert C. Persistent rhinitis – allergic or nonallergic? *Allergy* 2004; **59** (Suppl. 76):11–5.
- 227 Ferguson JL, McCaffrey TV, Kern EB, Martin WJ. Effect of *Klebsiella ozaenae* on ciliary activity in vitro: implications in the pathogenesis of atrophic rhinitis. *Otolaryngol Head Neck Surg* 1990; **102**:207–11.
- 228 Moore EJ, Kern EB. Atrophic rhinitis: a review of 242 cases. *Am J Rhinol* 2001; **15**:355–61.
- 229 Krzeski A, Kapiszewska-Dzedzej D, Gorski NP, Jakubczyk I. Cystic fibrosis in rhinologic practice. *Am J Rhinol* 2002; **16**:155–60.

- 230 Cottin V, Cordier JF. Churg–Strauss syndrome. *Rev Pneumol Clin* 2003; 59:17–24.
- 231 Rasmussen N. Management of the ear, nose, and throat manifestations of Wegener granulomatosis: an otorhinolaryngologist's perspective. *Curr Opin Rheumatol* 2001; 13: 3–11.
- 232 van Rijswijk JB, Boeke EL, Keizer JM, Mulder PG, Blom HM, Fokkens WJ. Intranasal capsaicin reduces nasal hyperreactivity in idiopathic rhinitis: a double-blind randomized application regimen study. *Allergy* 2003; 58:754–61.
- 233 van Rijswijk JB, Gerth van WR. Capsaicin treatment of idiopathic rhinitis: the new panacea? *Curr Allergy Asthma Rep* 2006; 6:132–7.
- 234 Blom HM, van Rijswijk JB, Garrelts IM, Mulder PG, Timmermans T, Gerth van WR. Intranasal capsaicin is efficacious in non-allergic, non-infectious perennial rhinitis. A placebo-controlled study. *Clin Exp Allergy* 1997; 27:796–801.
- 235 Van Cauwenberge PB, Bachert C, Passalacqua G *et al.* Consensus statement on the treatment of allergic rhinitis. European academy of allergology and clinical immunology. *Allergy* 2000; 55:116–34.

## Appendix A

**Table A1.** Recommendations on the use of single measures on HDM avoidance (letters in column 2 and 3 denote grade of recommendation)

Measures used individually	In favour	Against
Encase mattress and pillows in plastic or special allergen proof fabric	D	A*
Hot wash bedding at 55 °C and damp wipe mite proof covers every 1–2 weeks	D	None
Remove carpets and replace with hard wood floor	D	None
Use of acaricides on carpets and soft furnishing	D	None
Minimise objects that accumulate dust	D	None
Remove soft toys from the bed as they harbour high levels of Der p 1	D	None
Remove upholstered furniture and replace with leather, plastic or vinyl furniture	D	None
Do not dry clothes on radiators and remove infrequently worn clothing from the bedroom	D	None

\*May be useful if used as part of a range of measures to reduce HDM exposure.  
HDM, house dust mite.

**Table A2.** Recommendations on the use of pollen avoidance measures

Intervention	Grade of recommendation
Nasal filters (see <a href="http://www.nasalaiguard.co.uk">www.nasalaiguard.co.uk</a> ) [47]	B
Minimizing early morning activity when the greatest pollen is emitted – after the dew dries after sunrise to late morning	D
Avoiding going out after thunderstorms or on windy days when dust and pollen are blown about	D
Wearing wraparound sunglasses	D
Not mowing the grass, and staying inside when it is being mown. If mowing is unavoidable, wear a mask	D
Planning holidays to avoid the pollen season	D
Keeping windows closed both at home and particularly when in the car. In particular keeping windows closed at night to prevent pollens or moulds from drifting into the home. Instead, if needed, use air conditioning, which cleans, cools and dries the air	D
If the patient is sensitized to a particular plant or tree – consider removal	D
Shower and wash hair once home	D
Bathing eyes and douche nose frequently	D
Staying indoors when the pollen count or humidity is reported to be high	D
Bringing in washing before pollen levels increase in the evening	D

**Table A3.** Recommendations on cat allergen avoidance measures

Measure	In favour*	Against
Remove cat, followed by thorough cleaning of house, steam cleaning walls, shampooing carpets	D	None
Keeping cat out of bedroom and other commonly used rooms	D	None
Washing cat weekly	D	None
Removing carpets and replacing with hardwood floors and cleaning regularly	D	None
Air filtration units in rooms where the patient spends the majority of their time	D	None
Increase ventilation with fans, air-conditioning or by opening windows	D	None

\*Letters denote grade of recommendation.

**Table A4.** Grades of recommendation for various interventions

Intervention	Seasonal allergic rhinitis (SAR)		Perennial allergic rhinitis (PAR)	
	Adults	Children	Adults	Children
Oral anti-H1	A	A	A	A
Intranasal anti-H1	A	A	A	A
Intranasal CS	A	A	A	A
Intranasal chromone	A	A	A	A
Subcutaneous SIT	A	A	A	A
Sublingual/nasal SIT	A	A	A	A
Anti-leukotriene	A	A	-	-
Allergen avoidance	A	D	D	D

CS, corticosteroid; SIT, specific immunotherapy.