BSACI guidelines for the management of allergic and non–allergic rhinitis


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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

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, rhinorrhea, 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.
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

<table>
<thead>
<tr>
<th>Agents</th>
<th>High MW</th>
<th>Low MW</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal proteins</td>
<td>Mouse, rat, guinea pig, crabs, etc.</td>
<td>Urinary and epithelial proteins</td>
<td>Laboratory research, animal breeding [207–209], crab processing industry [210]</td>
</tr>
<tr>
<td>Vegetable proteins</td>
<td>Wheat and other cereal flours and grains, latex [51]</td>
<td></td>
<td>Baking [211], milling, food processing, hospital workers</td>
</tr>
<tr>
<td>Enzymes</td>
<td>Protease, amylase, cellulase, lipase</td>
<td></td>
<td>Food processing, detergent manufacture, pharmaceuticals</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>Antibiotics, morphine, cimetidine</td>
<td>Diasocyanates, colophony fumes, (trimellitic) acid anhydrides (TMA) [212], cyanoacrylates, epoxy resins, alkyd/polyunsaturated polyester resins [213]</td>
<td>Pharmaceutical manufacture and dispensing</td>
</tr>
</tbody>
</table>

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

- **Intermittent symptoms**
  - < 4 days/week
  - or < 4 weeks at a time

- **Persistent symptoms**
  - ≥ 4 days/week
  - and ≥ 4 weeks at a time

- **Mild**
  - Normal sleep
  - Normal daily activities
  - Normal work and school
  - No troublesome symptoms

- **Moderate–severe**
  - One or more items
  - Abnormal sleep
  - Impairment of daily activities, sport, leisure
  - Problems caused at school or work
  - Troublesome symptoms

**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.

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Drugs. A detailed drug history is vital as drugs such as topical sympathomimetics, α-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, α-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
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 pledges 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
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-
analyis 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 interven-
tions [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 ineffec-
tive [48]. However, it is likely that cat removal will
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].

![BSACI guidelines for allergic and non-allergic rhinitis](https://www.researchgate.net/profile/BSACI/publication/27)

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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.

**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,
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 antiarrhythmics, antibiotics and β-blockers.

H1-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 not controlled 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].

Adverse events

- 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 ritonivir may increase systemic bioavailability of intranasal corticosteroids [92, 93].

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

<table>
<thead>
<tr>
<th>Age</th>
<th>Non-sedating antihistamine</th>
<th>Sedating antihistamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;6 months</td>
<td>Alimemazine (trimeprazine)</td>
<td></td>
</tr>
<tr>
<td>&gt;1 year</td>
<td>Desloratadine</td>
<td>Hydroxyzine hydrochloride</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clemastine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chlorphenamine</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>Cetirizine hydrochloride (SAR only)</td>
<td>Cyproheptadine hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Loratadine</td>
<td>Promethazine hydrochloride</td>
</tr>
<tr>
<td></td>
<td>Levocetirizine hydrochloride</td>
<td>Ketotifen</td>
</tr>
<tr>
<td>&gt;6 years</td>
<td>Fexofenadine hydrochloride (SAR only)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cetirizine hydrochloride</td>
<td></td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>Acrivastine</td>
<td></td>
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<tr>
<td></td>
<td>Mizolastine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fexofenadine hydrochloride</td>
<td></td>
</tr>
</tbody>
</table>

SAR, seasonal allergic rhinitis

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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 corticostoid. 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]. However, 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®, 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 \(\alpha\)-agonist ephedrine (as nasal drops) and \(\alpha\)-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 \(= I +\)). Recent reviews include the ‘ARIA Update’...
‘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 under-powered 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 updosing 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 hyperreactivity 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 rhinorrhea 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
inappropriate treatment, non-adherence is not indicative of negligence. It is antici-
pated to an automatic defence for negligence and conversely non-AR. Adherence to these guidelines does not consti-
tute an automatic defence for negligence and conversely non-adherence is not indicative of negligence. It is antici-
pated that these guidelines will be reviewed yearly.

Acknowledgements

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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 mea-
ures – particularly HDM.
- Aetiological factors that can be altered to reduce the incidence of rhinitis.
- Prospective study examining whether early identifica-
tion 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.

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 antihista-
mine requirement [55].
• Leukotriene receptor antagonists may have a role if there is concomitant asthma [103].
• To treat underlying allergic disease, allergen immu-
notherapy is widely used in Europe but has yet to gain general acceptance in the United Kingdom [136, 137]. Efficacy has been demonstrated with both subcuta-
neous [137, 199] and SLIT [200–203] but is contra-
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Appendix A

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

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

*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

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal filters (see <a href="http://www.nasalairguard.co.uk">www.nasalairguard.co.uk</a>) [47]</td>
<td>B</td>
</tr>
<tr>
<td>Minimizing early morning activity when the greatest pollen is emitted – after the dew dries after sunrise to late morning</td>
<td>D</td>
</tr>
<tr>
<td>Avoiding going out after thunderstorms or on windy days when dust and pollen are blown about</td>
<td>D</td>
</tr>
<tr>
<td>Wearing wraparound sunglasses</td>
<td>D</td>
</tr>
<tr>
<td>Not mowing the grass, and staying inside when it is being mown. If mowing is unavoidable, wear a mask</td>
<td>D</td>
</tr>
<tr>
<td>Planning holidays to avoid the pollen season</td>
<td>D</td>
</tr>
<tr>
<td>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</td>
<td>D</td>
</tr>
<tr>
<td>If the patient is sensitized to a particular plant or tree – consider removal</td>
<td>D</td>
</tr>
<tr>
<td>Shower and wash hair once home</td>
<td>D</td>
</tr>
<tr>
<td>Bathing eyes and douche nose frequently</td>
<td>D</td>
</tr>
<tr>
<td>Staying indoors when the pollen count or humidity is reported to be high</td>
<td>D</td>
</tr>
<tr>
<td>Bringing in washing before pollen levels increase in the evening</td>
<td>D</td>
</tr>
</tbody>
</table>
### Table A3. Recommendations on cat allergen avoidance measures

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

*Letters denote grade of recommendation.*

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

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Seasonal allergic rhinitis (SAR)</th>
<th>Perennial allergic rhinitis (PAR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
<td>Children</td>
</tr>
<tr>
<td>Oral anti-H1</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Intranasal anti-H1</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Intranasal CS</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Intranasal chromone</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Subcutaneous SIT</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Sublingual/nasal SIT</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Anti-leukotriene</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Allergen avoidance</td>
<td>A</td>
<td>D</td>
</tr>
</tbody>
</table>

CS, corticosteroid; SIT, specific immunotherapy.