An update on hay fever treatments

About 10 per cent of the UK population suffers from seasonal allergic rhinitis and numbers have more than doubled in the past three decades. For many people the pharmacy is likely to be the first port of call. Sarah Marshall gives an update on treatment options.

Rhinitis refers to inflammation of the mucous membrane of the nose. It can be allergic or non-allergic in origin. Non-allergic causes include viral infections, changing hormone levels, triggers such as cold weather or spicy foods, and drugs (eg, angiotensin-converting enzyme inhibitors).

Allergic rhinitis involves the production of allergen specific IgE (after exposure to an allergen), which binds to mast cells. Subsequent exposure causes degranulation of these cells, resulting in the release of chemical mediators, such as histamine, and the production of leukotrienes and prostaglandins, leading to itching, runny nose, sneezing and nasal congestion. Infiltration of inflammatory cells follows, worsening nasal congestion.

Traditionally allergic rhinitis has been categorised as seasonal or perennial but, more recently, it has been classified as intermittent or persistent, and as mild or moderate/severe. Symptoms that occur occasionally, lasting less than four weeks or less than four days per week, are described as intermittent allergic rhinitis. Persistent allergic rhinitis describes symptoms for more than four days and more than four days per week. It is caused by allergens that are present all year round, such as dust mite, feathers and animal dander.

Seasonal allergic rhinitis, commonly known as hay fever, can fall into either of these categories. It is caused by contact with allergens that only occur at certain times of the year, such as tree pollen (spring), grass pollen (end of spring, beginning of summer), weed pollen (early spring to end of autumn) and fungal spores (autumn). The timing of symptoms may indicate likely allergens but some people are sensitive to many types of pollen and suffer persistent symptoms. About 90 per cent of people with hay fever are allergic to grass pollen and about 25 per cent are allergic to birch pollen.

The average age of onset of symptoms is 10 years with incidence peaking between 13 and 19 years. It has been suggested that the increase in the incidence of hay fever (and other allergies) is due to a decrease in the number of childhood infections.

The classic symptoms of hay fever are itching in the nose and mouth, rhinorrhea with a watery or yellow discharge, sneezing and nasal congestion. Eyes can become itchy and watery (allergic conjunctivitis). Symptoms coincide with and last for the duration of exposure to the culprit allergen and this pattern enables hay fever to be differentiated from other common types of rhinitis, such as sinusitis and viral rhinitis. Rhinitis in young children is likely to be viral — hay fever only develops after the age of two years because, in general, at least two seasons of exposure are required to sensitise a child.1 R rhinitis occurring for the first time in an elderly person is likely to be non-allergic.

Perennial allergic rhinitis symptoms are more akin to a mild cold of long duration, with predominant nasal congestion. Questions to help differentiate hay fever include:

- What are the predominant symptoms? (Generally, there is no fever, cough or malaise.)
- What is the appearance of any nasal discharge? (Green or grey discharge suggests sinusitis and initially watery and subsequently thick discharge indicates viral rhinitis.)
- Do you have any history or family history of allergies, eczema or asthma?
- When do you tend to get the symptoms?
- Have you noticed any triggers?
- What is your occupation? (Some triggers may be occupational, for example, bakers can be allergic to flour.)
- Do you take any medicines?

If the cause of the symptoms is unclear, patients may be referred for allergy testing. Blood tests for specific IgE antibodies can be carried out by GPs.

Sarah Marshall, PhD, MRPharmS, is a freelance pharmaceutical writer from Aberdeenshire.
Panel 1: Advice for avoiding pollen and spores
- Keep windows closed
- Wear wrap-around sunglasses
- Avoid walking in large grassy spaces
- Avoid going out when the pollen count is high and during peak pollen times (e.g., for grass pollen this is early morning, late afternoon and evening)
- Change clothing, shower and wash hair on returning home
- Allergy UK endorses several machines to filter allergens, including pollen and spores, from the air but removal does not necessarily equate to symptom improvement. Those considering trying an air purifier should ensure that it is powerful enough for size of the room in which it is to be used.
- Change any car pollen filters regularly

Panel 2: Relative efficacy of treatments for hay fever

<table>
<thead>
<tr>
<th>Product</th>
<th>Sneezing</th>
<th>Itch</th>
<th>Congestion</th>
<th>Runny nose</th>
<th>Eye symptoms</th>
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<tbody>
<tr>
<td>Oral antihistamine</td>
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<td>Intranasal antihistamine</td>
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<td>Oral decongestant</td>
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<td>Intranasal decongestant</td>
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<tr>
<td>Intranasal mast cell stabiliser</td>
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Key: – no benefit; * minimal benefit; ** modest benefit; *** substantial benefit

Antihistamines
For people with mild or intermittent symptoms, an antihistamine should be the first-line treatment. These drugs relieve sneezing, itching, rhinorrhea and eye irritation but are less effective for nasal congestion. A through both sedating and non-sedating antihistamines have been shown to improve symptoms. The second generation antihistamines are recommended as first-line because they have fewer side effects and interactions. Cetirizine, loratidine (or fexofenadine on prescription — see below) are recommended for people who prefer oral therapy and those with allergic conjunctivitis. Intranasal azelastine is the first choice for others (see later). A cetirizine has a rapid onset of action but a short half-life and so needs to be taken three times daily. It is not suitable for the elderly (no studies have been carried out in this age group) or children under 12 years.

Sedating antihistamines generally have a shorter duration of action than non-sedating antihistamines. Some have to be taken up to four times daily. People using these first generation antihistamines should be reminded that they can affect the performance of skilled tasks, such as driving, and performance in examinations, but it should be noted that second generation drugs also occasionally cause drowsiness.

Sedating antihistamines have many potential interactions, cautions and side effects (see Panel 3). Although some are licensed for use in children from one year, the British National Formulary for Children recommends that sedating antihistamines are not given to children under the age of two years.

Ocular symptoms due to hay fever can often be treated effectively with oral antihistamines. However, an eye drop containing antazoline combined with xylocaine is available. Because of the possibility of systemic absorption this product has the potential for similar interactions, cautions and side effects as other sedative antihistamines and oral decongestants. It should not be used for more than seven days because there is concern about rebound allergic conjunctivitis. Eye drops containing benzalkonium chloride should not be used while wearing soft contact lenses.

The British National Formulary notes that topical antihistamines are considered more effective than sodium cromoglicate but less effective than topical corticosteroids.

Corticosteroids
Intranasal corticosteroids are considered the treatment of choice for moderate to severe symptoms. They have been shown to be more effective in reducing nasal symptoms than azelastine and, possibly, oral antihistamines.

Intranasal corticosteroids are particularly suitable for nasal congestion but their onset of action is slow, taking about two weeks before the full benefit is felt. It is important to explain this to people because they may think that the treatment does not work. Sufferers may benefit from an oral antihistamine during this time. Beclomethasone, fluticasone and triamcinolone are available over the counter as nasal sprays. Fluticasone and triamcinolone are used once daily whereas beclomethasone requires twice daily dosing. Intranasal corticosteroids (including those on prescription) appear equally effective.

but skin-prick tests are only available through specialist clinics. Although their value is debated, finger-prick testing kits are now being marketed to the public; these allow IgE levels to single allergens (e.g., house dust mite) to be tested.

Multiple allergen testing kits are being used by some pharmacists who are providing allergy screening services. Training for this was developed by Allergy UK, the Centre for Postgraduate Pharmacy Education and the National Pharmacy Association. So far, some 116 pharmacists in England and Wales have been accredited.

Treatment options
Mild or severe hay fever symptoms can cause considerable suffering, affecting work or school, as well as leisure activities. Secondary symptoms can include fatigue, headache, sleep disturbance and impaired cognitive function. Hay fever can also exacerbate other conditions, such as otitis media and sinusitis, and is a risk factor for asthma.

The first step in symptom relief is to reduce exposure to the allergens (see Panel 1). Complete avoidance, however, may not be feasible and there are several pharmacotherapeutic approaches. The treatment chosen will depend on factors, such as patient preference and age, and predominant symptoms, and their severity. Different agents relieve symptoms to varying degrees and Panel 2 compares some of these.
Panel 3: Summary of the features of OTC medicines for hay fever

Non-sedating antihistamines (acrivastine, cetirizine, loratidine)
- Onset of action within three hours
- Drowsiness is least likely with loratidine
- Good safety profile
- Interactions with ketoconazole and antimuscarinics
- Caution recommended in renal impairment, hepatic disease, acute porphyria and epilepsy

Sedating antihistamines (chlorphenamine, clemastine, cyproheptadine, diphenhydramine, promethazine)
- Drowsiness least likely with chlorphenamine and clemastine
- Antimuscarinic effects include dry mouth, blurred vision, gastrointestinal disturbances and urinary retention
- BNFC says not for use in children under two years old
- Interactions with drugs with sedative or antimuscarinic effects (eg, alcohol, antidepressants)
- Caution advised in prostatic hypertrophy, urinary retention, glaucoma, hepatic disease and epilepsy

Ocular antihistamines (antazoline)
- Antazoline is available combined with xylometazoline

Intranasal corticosteroids
- For OTC use in people aged over 18 years
- Side effects include nose and throat irritation and dryness, nose bleeds, headache and changes in smell and taste
- May have additive effect with other corticosteroids
- Caution in glaucoma

Phenylephrine, xylometazoline and oxymetazoline are available in nasal sprays or drops. They should not be used continuously for more than seven days because they can cause rebound congestion. Topical nasal decongestants can be useful for clearing the nasal passages to allow penetration of a nasal corticosteroid or sodium cromoglicate.

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Nasal decongestants (oral and topical) should not be used continuously for more than seven days because they can cause rebound congestion. The BNFC comments that oral nasal decongestants are of doubtful value but they do not cause rebound congestion.

Combination products (eg, an oral antihistamine plus an intranasal corticosteroid) may be used in an attempt to control all the symptoms. However, there is little evidence for the value of this practice.

Ideally, treatment should be started at least a week before the pollen season begins and continue until it ends. The difficulty is knowing when this is. If the culprit pollen is known, a pollen calendar (such as the one available at www.pollenuk.org) can be used as a guide. However, timings and pollen peaks will differ depending on location and the weather. In addition, the pollen count can be used to decide when to start treatment. This is the number of pollen grains per m3 of air, averaged over 24 hours. The pollen forecast is usually given as low (<30 grains per m3), moderate (30–49 grains per m3), high (50–149

OTC corticosteroid nasal sprays are only for licensed use in people aged over 18 years. Some people tend to direct the spray towards the midline of the nose. It may be possible to reduce the incidence of local irritation by correcting this technique by directing the spray away from the septum. Intranasal corticosteroids can have an additive effect when used with other corticosteroids (eg, intranasal and systemic) and careful monitoring is advised.

Intranasal mast cell stabilisers
- Sodium cromoglicate is available as a nasal spray or eye drops. It is thought to work primarily by stabilising mast cell membranes, preventing release of histamine and other inflammatory mediators. It has few side effects and is particularly suitable for children. However, it requires four times a day dosing, or more, which may affect compliance.

Sodium cromoglicate is an option for pregnant or breastfeeding women (as is nasal douching with saline). Although antihistamines and intranasal corticosteroids are recommended by experts, manufacturers advise their avoidance in pregnancy and breastfeeding or use only on the advice of a doctor.

Lodoxamide eye drops may be sold for the treatment of allergic conjunctivitis in adults and children over the age of four years.

Decongestants
- Sympathomimetics, such as phenylephrine and pseudoephedrine, cause vasoconstriction in the nasal mucosa, reducing swelling, widening the nasal passages and improving drainage.

Intranasal corticosteroids are considered the treatment of choice for moderate to severe symptoms.
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grains per m$^3$) or very high (>150 grains per m$^3$). Most hay fever sufferers will begin to experience symptoms when the pollen count is moderate.

People given treatment should be advised to return in two weeks if they experience no improvement, or earlier if ocular symptoms are unresolved or if symptoms are moderate or severe.

Cigarette smoke can exacerbate hay fever symptoms so sufferers and close relatives of sufferers should be advised to stop smoking.

People in whom treatment has failed or who have the following symptoms should be referred:

- Wheeze, shortness of breath or chest tightness
- Earache
- Eye, ear or sinus infection
- Unilateral nasal discharge (may suggest a foreign body in nose, especially in children)
- Drug-induced rhinitis
- Nasal obstruction (ie, permanent congestion — may indicate a structural problem, such as polyps)

Treatments on prescription

Prescription-only antihistamines and intranasal corticosteroids generally offer no advantages over those available OTC.$^{2,3}$ Despite the wide variety of prescription-only products (eg, eye drops for allergic conjunctivitis include emedastine, epinastine, ketotifen and olaparadine and nedocromil sodium) there appears to be little guidance regarding choice. However, on prescription, intranasal corticosteroids can be used by younger age groups and for longer periods.

Clinical Knowledge Summaries recommends budesonide, fluticasone or mometasone for children because they are least likely to affect growth.

If some drugs such as azelastine and budesonide, meet certain specifications they can be sold to the public for hay fever but pharmacy-only forms of a product do not always exist so a prescription is required for supply. Intranasal azelastine acts in 15 minutes and is suitable for children over five years.

Although efficacy has been demonstrated, the product do not always exist so a prescription is required. It is concluded that there is no evidence of effectiveness of the homeopathic remedy G alpisma glaua and the herbal treatment butterbur (Petasites hybrida) but this requires further verification.$^{2,4}$

Ingestion of honey does not improve symptoms and there is no clinical evidence to support using the food supplement bee pollen.$^{2,5}$ It is not known whether acupuncture is of value.$^{2,6}$ N asal filters (small filters inserted in the nostrils) may be beneficial.$^{2,7}$

Subcutaneous injections of grasses and rye or tree pollen extract (birch, alder and hazel) are available (Pollinex). The course is given annually for three years. Because of the risk of anaphylaxis, patients must be treated where facilities for cardiopulmonary resuscitation are immediately available and are monitored closely for one hour after each dose. Treatment is contraindicated in various conditions such as asthma and chronic obstructive pulmonary disease.

Immunotherapy in the form of sublingual tablets of grass pollen extract (Graxal) is also available. The tablets are taken once daily, starting four months before the pollen season and continuing for up to three years. It is recommended that the first dose is taken under medical supervision. A review by the D rug and T herapeutics B ulletin concluded that there is no convincing evidence of worthwhile benefit for this treatment (PJ, 16 February 2008, p170) but recent guidelines advocate its use.$^{2,8}$

Alternative approaches

There are numerous complementary and alternative treatments for hay fever. Although some people find them helpful, in general, there is conflicting clinical trial evidence as to their effectiveness and insufficient evidence to recommend them.$^{2,9}$ There is some evidence for effectiveness of the homeopathic remedy G alpisma glaua and the herbal treatment butterbur (Petasites hybrida) but this requires further verification.$^{2,4}$

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References

1. ARIA. Allergic rhinitis and its impact on asthma. European Journal of Allergy and Clinical Immunology 2008;63(Suppl 86):1–160.
2. Centre for Postgraduate Pharmacy Education. Allergy manifestations and management. CPPE 2008.