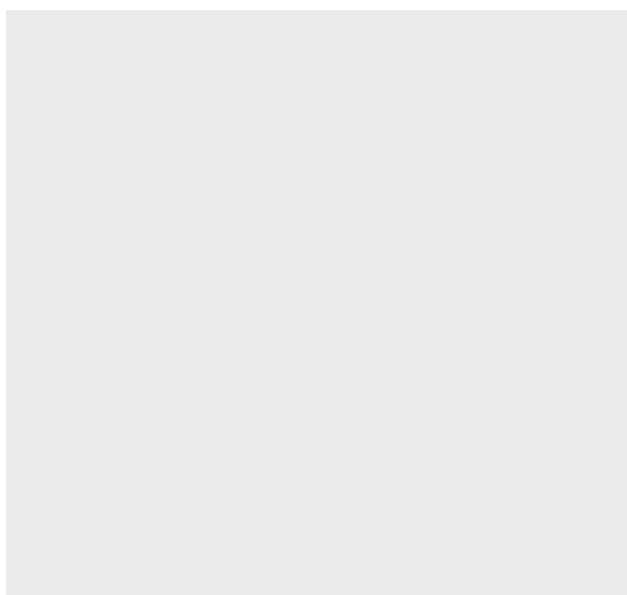


HOW TO TREAT HAY FEVER AND ASSOCIATED ALLERGIC CONDITIONS IN THE PHARMACY

By Alan Nathan, BPharm, FRPharmS

In this special feature the author provides an overview of hay fever and related allergic conditions and their treatment



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Grass pollen: the most frequent cause of hay fever in the United Kingdom

From a medical viewpoint hay fever is considered a relatively minor condition because it is not life threatening, sufferers are not completely incapacitated by it and it does not require permanent medication to keep it under control.

However, for sufferers, it is an extremely unpleasant condition that undermines their quality of life and ability to function to their full capacity. For example, at this time of year, for many school and university students hay fever can badly affect their preparation for, and performance in, examinations. Fortunately it is a condition that, for the large majority of sufferers, can be successfully self-treated. This can be achieved with the help of a pharmacist because nearly all effective medicines for hay fever are available without a prescription.

TERMINOLOGY

Hay fever is the common term for seasonal allergic rhinitis, an allergic hypersensitivity reaction in the nasal mucosa, and also in the conjunctiva of the eye (seasonal allergic conjunctivitis), caused by exposure to pollen or other allergens.

A reaction to episodic exposure to allergens that do not occur seasonally is termed acute allergic rhinitis. Perennial allergic rhinitis results when allergen exposure is chronic. Another form of perennial rhinitis is vasomotor rhinitis, where the cause is not allergens but physical or chemical irritants such as pungent odours, including perfumes, fumes, cold air or dry atmospheres. Treatment for this condition is often difficult and normally requires medical referral.

EPIDEMIOLOGY

Hay fever is estimated to affect between 10 and 15 per cent of the population in the United Kingdom, and the incidence appears to be rising, although this may be at least partly because more people recognise the condition and seek treatment. Up to 10 per cent of children and between 20 and 30 per

cent of adolescents are thought to suffer from hay fever. Incidence peaks in the early teens and then diminishes. About two-thirds of adult sufferers are under 30 years old. There is no gender difference in the incidence. Heredity may play a role: if neither parent suffers from hay fever, a child has only a one in 10 chance of developing the condition, but if one parent has the allergy the child runs a one in three or four risk, rising to one in two if both parents have hay fever.

CAUSES

The most frequent cause of hay fever is grass pollen, with about 90 per cent of UK sufferers sensitive to it. The pollen season lasts from May to July, and the highest levels occur in grassland areas of South Wales, the Midlands, East Anglia and central Southern England. Lowest pollen counts occur in coastal areas, particularly in Scotland and on western coasts, and in upland moorlands. Birch tree pollen affects about 25 per cent of hay fever sufferers; other trees that cause problems include alder, hazel and horse chestnut. The main season for tree pollens is from February to April, although for birch it is from April to July. Pollens from weeds

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such as plantains, mugwort and docks also cause hay fever.

In the UK, pollen counts peak in June and in rural areas daily peaks occur between 7am and 11am, and between 4pm and 7pm but at a lower level. In cities the peaks are in the late afternoon and early evening. Many types of fungal spores can also cause hay fever, their season extending through the late summer into autumn. Many fungi that produce allergenic spores can live inside as well as outdoors. Because of this, and their long pollen-producing periods, they are responsible for perennial rhinitis.

There is evidence to suggest that air pollution worsens hay fever and research has shown that the incidence of hay fever is higher in cities than in rural areas, although pollen counts are lower there. It has also been found that the incidence of hay fever is higher among people living along busy roads, suggesting that vehicle exhaust fumes may play a part. It is known that diesel particles increase sensitivity to allergens and that high concentrations of nitrogen and sulphur dioxides can irritate the upper respiratory tract. However, some photochemical pollutants that can affect breathing, including ozone, are more abundant in rural areas.

The main cause of perennial allergic rhinitis is the house dust mite, which lives on shed human skin scales and colonises beds and bedding, upholstered furniture and carpets. Other allergens and irritants in house dust include the fur of cats, dogs and other pets, and residues of their urine and saliva, as well as cockroaches and fungal spores. Vacuuming and dusting disturbs and agitates dust, exacerbating the problem. Sufferers may find that their symptoms worsen in late summer and early autumn when warm and humid atmospheric conditions produce the optimum environment for reproduction of the dust mite. Symptoms also tend to be worse at night and in the early morning, when exposure to allergens is at its greatest. They often improve during the day when the sufferer is out of the house.

AETIOLOGY

Hay fever is the result of a type I allergic reaction, in which initial exposure of a sensitive individual to an antigen results in the production of antigen-specific immunoglobulin E (IgE). IgE attaches to mast cells and basophils in the nasal mucosa and conjunctiva of the eye, which become sensitive to further antigenic material. On further exposure the antigen binds to IgE causing degranulation of the mast cells and release of chemical mediators, including histamine, leukotrienes and prostaglandins. These produce the inflammatory responses of vasodilation, mucosal oedema, mucous secretion and stimulation of itch receptors. Sensitivity increases with repeated exposure to allergen. Prolongation of exposure to allergen also leads to a late-phase sustained response, resulting in submucosal swelling and blockage causing nasal congestion.

Referral symptoms

A patient reporting the following symptoms associated with hay fever or perennial rhinitis should be referred for medical assessment or treatment:

- 1 Wheezing or shortness of breath, which could indicate asthma
- 1 Earache or facial pain, since these may indicate sinusitis or otitis media requiring antibiotic treatment
- 1 Purulent, rather than clear, discharge from the eyes, indicating the possibility of infection

SYMPTOMS

Allergic rhinitis

Rhinorrhoea (nasal discharge) Discharge is clear and watery, and frequent blowing and wiping can cause soreness around the nose, sometimes leading to infections.

Sneezing Sneezing begins within 60 seconds of inhalation of allergen and can result in long bouts of repeated sneezing, which is disruptive to normal activities and distressing.

Nasal pruritus (itching) Itching can be continual or intermittent and is extremely unpleasant and irritating. To relieve it the typical sufferer will rub the tip of the nose with the heel of the hand in an upward

direction in a motion known as the “allergic salute”. Children tend to wrinkle their nose constantly to relieve the itching, an action known as “bunny nose” or “rabbit nose”. Some sufferers also experience an itching sensation in the roof of the mouth.

Nasal congestion Congestion usually develops after some days of exposure to allergen, when the blood vessels in the nose become dilated. Congestion can be uni- or bilateral and may shift from one nostril to the other every few hours. Mouth-breathing might result, which can lead to a dry mouth, bad breath, disrupted sleep and anosmia (loss of sense of smell). Nasal congestion can also give rise to secondary infections such as sinusitis. The eustachian tubes can become blocked with mucus, and infected, and otitis media may result. Nasal congestion can cause frontal or sinus headaches.

Dark or bluish swelling In some cases a dark or bluish swelling, like a black eye, caused by impaired nasal venous outflow develops around the eyes.

Allergic conjunctivitis

Discharge Ophthalmic discharge is clear and watery.

Redness Redness is caused by dilation of the conjunctival blood vessels.

Ophthalmic itching Ophthalmic itching is sometimes so severe that the sufferer resorts to scratching the eyelids to relieve it.

Differential diagnosis

The main condition with which allergic rhinitis might be confused is the common cold, from which it can be distinguished by the following differences:

Allergic rhinitis

- 1 Nasal discharge usually remains clear, and if it does become infected takes much longer to do so
- 1 Sneezing is frequent
- 1 Nasal itching present
- 1 Ocular symptoms present
- 1 Symptoms continue for as long as the sufferer is exposed to the allergen, often several weeks
- 1 Symptoms usually begin quite suddenly
- 1 Symptoms occur at the same time each year, in spring or summer when the pollen that causes the allergic reaction in the sufferer is being produced (Symptoms of perennial rhinitis occur whenever the sufferer is in contact with the allergen.)
- 1 Only affects isolated individuals

Common cold

- 1 The initially clear nasal discharge usually thickens and becomes purulent within a few days
- 1 Sneezing is normally less frequent and paroxysmal
- 1 Nasal itching does not normally occur
- 1 Usually no ocular symptoms
- 1 Symptoms last for about four to seven days
- 1 Onset of symptoms is more gradual
- 1 Can occur at any time of year, but more usually in the winter months
- 1 Highly contagious, therefore other family members or acquaintances may well be suffering at the same time and the infection will be quite common within the community

Photophobia An abnormal intolerance and avoidance of light.

Skin folds Skin folds or pleats are parallel to the lower lid margin and extend from under the eye to the top of the cheekbone.

TREATMENT

As a result of POM-to-P reclassifications in recent years a full range of effective medicines for hay fever and allergic rhinitis is now available from pharmacies without prescription. These include systemic sedating and non-sedating antihistamines, and topical antihistamine and anti-inflammatory drugs for use in the nose and eyes, although not all drugs available in these categories have yet been reclassified to P. The drugs available without prescription are reviewed below; their proprietary names are given in brackets.

Oral antihistamines Histamine is the principal chemical mediator responsible for the inflammatory response of hay fever (and other allergic reactions). All oral formulations for treatment of hay fever are antihistamines and act through competitive antagonism of histamine at the H₁ receptor. The older, sedative antihistamines are lipophilic and cross the blood-brain barrier readily. In the brain, in addition to binding to H₁ receptors, sedative antihistamines bind to and block muscarinic (cholinergic), and in some cases α -adrenergic and serotonergic, receptors. As a result they cause several generally undesirable side effects including sedation, dry mouth, blurred vision, urinary retention, constipation and gastrointestinal disturbances.

The newer, non-sedative antihistamines are less lipophilic and do not penetrate the brain to a significant extent. They are therefore much less likely to cause centrally mediated adverse side effects. However, a small proportion of people exhibit drowsiness and other CNS side effects in response to placebo, and impairment of function, if it occurs, is not always accompanied by subjective feelings of drowsiness. Patients should therefore be warned that these antihistamines may affect driving and other skilled tasks, and that excess alcohol should be avoided.

Antihistamines are generally effective in controlling symptoms of hay fever and other allergic conditions including sneezing, nasal itching and rhinorrhoea. They are also effective, to a lesser extent, against allergic conjunctivitis but have little or no effect on nasal congestion. The maximum effect of antihistamines is not achieved until several hours after peak serum levels have been reached. In addition, they cannot reverse the consequences of H₁-receptor activation and are effective only if they are able to block histamine release before it occurs. Therefore, for maximum effectiveness, antihistamines should be taken when symptoms are expected rather than after they have started.

Non-sedative antihistamines Non-sedative antihistamines available OTC include

acrivastine (Benadryl Allergy Relief capsules), cetirizine (Zirtek Allergy tablets, Piriteze tablets, Benadryl One A Day tablets) and loratadine (Claritin Allergy tablets and syrup).

They are generally preferable to the older antihistamines because of the much lower incidence of side effects. All drugs in this group are equally effective. Acrivastine has a rapid onset of action and a short half-life, requiring more frequent dosing (four times daily) than cetirizine or loratadine, but it may be useful to give rapid relief. Peak plasma levels of cetirizine and loratadine are reached in about an hour, and they have a long elimination half-life, therefore are long acting, requiring only once daily dosing.

Although the incidence of sedation is extremely low for all three drugs, loratadine has a much lower incidence of sedation than acrivastine or cetirizine, and has been recommended as the antihistamine of choice for people in occupations in which any degree of sedation is undesirable.

Sedative antihistamines Sedative antihistamines available include chlorphenamine (Calimal tablets, Piriton Allergy tablets and syrup, Pollenase Antihistamine tablets), clemastine (Tavegil elixir and tablets), diphenhydramine (Histergan syrup and tablets), azatadine (Optimine syrup) and promethazine (Phenergan elixir and tablets).

There is no evidence of a difference in effectiveness between the older antihistamines, although individual response to specific drugs varies widely. Choice is often based on personal preference and factors such as degree of sedation caused and duration of action, which do differ between compounds.

Azatadine exhibits significantly less sedating and other CNS effects than other older antihistamines and is fairly long acting, requiring only twice daily dosing. Promethazine is highly sedative but has a long half-life, and a single dose may provide relief of symptoms for up to 24 hours. The dose is preferably taken at night, on the assumption that the sedative effect should have largely worn off by the following morning. Clemastine has an intermediate sedative effect and a duration of action of up to 12 hours. Chlorphenamine is about as sedating as clemastine, with a faster onset but shorter duration of action. Diphenhydramine has pronounced sedative properties.

The use of sedating antihistamines may be limited in some circumstances because of side effects and interactions with other drugs. Side effects include sedation and anticholinergic effects such as dry mouth, urinary retention, constipation and blurring of vision. The elderly are more susceptible to these. Antihistamines should therefore not be recommended to patients with glaucoma or prostate problems, and should be avoided in elderly patients generally. (Allergic rhinitis is unusual in the elderly, and an elderly person reporting symptoms should be referred.) The sedative effects of antidepressants, anxiolytics and hypnotics are

likely to be enhanced by sedative antihistamines, as are the antimuscarinic actions or side effects of drugs such as trihexyphenidyl (benzhexol), orphenadrine, tricyclic antidepressants and phenothiazines.

Combination products There are some combinations of antihistamines with sympathomimetic decongestants marketed for treating nasal congestion associated with hay fever.

Antihistamines on their own are effective for treating the typical symptoms of allergic rhinitis, known as the early phase. Sedative antihistamines reduce rhinorrhoea through their anticholinergic action but do little to relieve nasal congestion. Co-administration of a sympathomimetic decongestant may be helpful. Combination products marketed for hay fever include Haymine tablets (chlorphenamine with ephedrine) and Benadryl Plus capsules (acrivastine with pseudoephedrine).

Nasal preparations Nasal products contain either anti-inflammatory or antihistamine constituents.

Anti-inflammatory preparations Anti-inflammatory nasal preparations available include beclometasone and sodium cromoglicate. (Budesonide and flunisolide are classified as P, but there are currently no OTC products available.)

Beclometasone is a corticosteroid which down-regulates the inflammatory response of type I allergic reactions by reducing the number of basophils and mast cells and blocking release of mediator substances. It inhibits both early and late responses to allergen exposure and is therefore effective in relieving nasal congestion. Intranasal corticosteroids are now regarded as the treatment of choice in patients with moderate to severe hay fever and superior to oral antihistamines.

The mode of action of sodium cromoglicate remains uncertain: it was thought to act by stabilising mast cell membranes and preventing their degranulation, but newer evidence indicates that other factors are involved. The drug is effective against both early and late type I responses.

Beclometasone and sodium cromoglicate are effective in relieving all nasal symptoms of hay fever, including congestion. Both take some days to achieve optimum effect, and treatment should ideally be started at least two weeks before symptoms are expected.

Beclometasone is available as an aqueous non-aerosol spray (Beconase Hayfever spray, Nasobec Hayfever spray). Absorption from the nasal mucosa is low and at recommended doses systemic effects are unlikely; any local reactions, such as stinging, burning or aftertaste, are mild and transient. Patients should be advised that if symptoms are already present when treatment is started it may be several days before an effect is noted and several weeks before full relief is obtained. Long-term use appears to be safe. Treatment may need to be maintained throughout the hay fever season and repeated each year. The recom-

mended adult dosage is two sprays twice a day. Beclometasone is not licensed for use without prescription in children under 18 years, or in pregnant or lactating women. It should be avoided if there is infection in the nose or eye. There are otherwise no significant contraindications or interactions.

Sodium cromoglicate is available as an aqueous nasal spray containing 4 per cent sodium cromoglicate (Rynacrom) and also as an aqueous spray containing 2 per cent sodium cromoglicate with 0.025 per cent xylometazoline (Rynacrom Compound, Rynacrom Allergy Nasal Spray). Because sodium cromoglicate is a prophylactic agent, treatment should be initiated before the pollen season starts and continued throughout. It is less effective at controlling nasal symptoms than corticosteroids and has the disadvantage of requiring at least four times daily dosing. However, it is safe and is suitable for children from five years old. There are no specific cautions or contraindications associated with its use, and it does not interact with other drugs.

Antihistamine preparations Antihistamines available for topical nasal treatment are azelastine and levocabastine.

Azelastine (Rhinolast Allergy spray) is a non-sedative antihistamine. It is a potent long-acting anti-allergic compound with marked H₁ antagonist properties. It is marketed in the UK without prescription for intranasal use only (azelastine eye-drops are POM), and at the doses administered has only local activity. Twice daily use is recommended. Azelastine is not licensed for OTC sale for use in children, and caution is recommended for use in pregnant and breast-feeding women.

Levocabastine (Livostin Direct nasal spray) is a long-acting, potent antihistamine with a rapid onset of action that is licensed for use without prescription in both the nose and eyes. Clinical trials have shown it to be equally or more effective in treating the symptoms of seasonal allergic rhinitis than sodium cromoglicate. There have been rare reports of sedation when levocabastine nasal spray and eye-drops are used together, and the manufacturer recommends that use of both, together with an oral antihistamine, should be under medical supervision. The recommended dose of levocabastine nasal spray is two sprays twice daily, although this can be increased if necessary to three or four times a day. Levocabastine nasal spray is not recommended for use in children under 12 years, or for pregnant women.

Eye preparations Eye preparations for use in allergic conjunctivitis include sodium cromoglicate, levocabastine and combinations of an antihistamine with a sympathomimetic.

Sodium cromoglicate Most eye symptoms in hay fever sufferers will be controlled by oral antihistamines, but if symptoms are persistent or particularly troublesome, sodium cromoglicate 2 per cent eye-drops are usually effective. Several proprietary brands are

Avoidance measures

On the principle that prevention is better than cure, measures can be taken to reduce exposure of sensitive individuals to allergens.

Hay fever

- 1 Stay indoors and keep all windows closed, this reduces pollen exposure by up to a factor of 10,000
- 1 Avoid going out particularly in the early evening and mid-morning
- 1 Wear close-fitting sunglasses when going out, and a mask if symptoms are really severe
- 1 In the car, keep windows closed, especially on motorways, if possible use an air-conditioning system

Perennial allergic rhinitis

- 1 Use acaricide and fungicide preparations regularly on furniture and carpets to control dust mites and other allergens
- 1 Use non-allergenic foam filled pillows on beds
- 1 Cover pillows, mattresses, etc. with plastic sheeting, which should be vacuumed weekly
- 1 Wash bedding at least weekly at 60C to kill mites
- 1 Remove as much upholstered furniture and soft furnishings as possible from rooms where the sufferer lives and sleeps
- 1 Dust, using sprays to dampen down dust, and vacuum rooms thoroughly twice a week, while the sufferer is out of the house

available. Sodium cromoglicate is especially useful if hay fever symptoms occur only in the eyes, where it rapidly exerts an action. It is used four times daily, and can be used in children.

Levocabastine (Livostin Direct eye-drops) Comparative studies have shown levocabastine to be more effective in allergic conjunctivitis than sodium cromoglicate. It requires only twice daily application. It is not licensed for use in children under 12 years and is not recommended for use during pregnancy.

Antihistamine/decongestant combination (Otrivine-Antistin eye-drops) Otrivine-Antistin contains an antihistamine, antazoline sulphate 0.5 per cent, and xylometazoline 0.05 per cent; the latter is used for its vasoconstrictor action as a conjunctival decongestant. This preparation can be used for the short-term treatment of hay fever symptoms; prolonged use can raise intra-ocular pressure and precipitate glaucoma. The drops are used twice or three times daily and are suitable for use in children from five years of age.

Sodium cromoglicate, levocabastine and Otrivine-Antistin eye-drops contain benzalkonium chloride as a preservative. This is absorbed into soft contact lenses and released on to the cornea during wear, causing inflammation and irritation. Contact lenses should therefore be removed while using these products.

COMPLEMENTARY THERAPY TREATMENTS

Some herbal and homoeopathic treatments are marketed or recommended for hay fever and allergies, although there is little or no clinical trial evidence of their effectiveness.

Homoeopathic remedies include euphrasia, allium cepa, gelsemium, pulsatilla, sabadilla and silica. Some manufacturers produce combination remedies containing several ingredients, although this would seem to contradict the homoeopathic principle of a specific remedy for a specific symptom or condition.

The main ingredients of herbal hay fever remedies are echinacea and garlic. A recent randomised, double blind clinical trial found tablets containing extract of butterbur (*Petasites hybridus*) to be as effective as cetirizine for the symptoms of hay fever. There does not appear to be any licensed medicinal product containing this herb currently available in the UK, and concerns were expressed recently about the safety of butterbur in the crude herbal form. Until both the efficacy and safety of this herb has been confirmed pharmacists should avoid recommending it.

FURTHER READING

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