Summary

- Oral antihistamines control most symptoms but not nasal congestion.
- Prophylactic sprays are effective therapy for nasal symptoms.
- Terfenadine and astemizole have potentially life-threatening cardiac side effects and interactions.
- Treatment may be started in advance of the season.

Seasonal allergic rhinitis (commonly known as hay fever) is caused by specific allergens that are present during defined parts of the year. Grass is the commonest allergen implicated and the symptoms associated with this condition include sneezing, rhinorrhea, watery eyes, nasal congestion, itching in the throat, eyes and ears and oedema around the eyes.

Hay fever is strictly seasonal as distinct from perennial allergic rhinitis which is a chronic disease caused by exposure to nonseasonal allergens such as dust mite or domestic pets. The symptoms of perennial rhinitis are similar to those of hay fever but nasal congestion is predominant while conjunctival itching is less frequent. Individuals may experience perennial rhinitis with seasonal exacerbations.

Allergic rhinitis can induce serious symptoms if left untreated. Total nasal obstruction may cause sleep apnoea, eustachian tube dysfunction, predisposition to sinus infections as well as interfering with daytime breathing.

TREATMENT

- Therapeutic objectives are symptom control allowing all usual activities with little or no adverse effects.
- Avoidance of allergens will reduce symptoms but can be restrictive on lifestyle and difficult to achieve.
- Pharmacotherapy is usually necessary to adequately control symptoms for most patients.
- Treatment in advance of the first symptoms presenting is an important aspect of management.

ANTIHISTAMINES

Antihistamines are the most frequently used oral medicines for the treatment of hay fever. Most are available without prescription and are a reasonable first line choice for many patients. They are effective in relieving ocular symptoms, rhinorrhea, sneezing and nasal irritation but have little effect on nasal congestion. Antihistamines are often more helpful than topical preparations in patients with troublesome symptoms at multiple sites e.g. itching of palate, pharynx or eyes. The clinical usefulness of these drugs may be limited by their adverse effects and drug interactions.

There are two main groups of antihistamines: First generation and Second generation.

First Generation Antihistamines. ("Sedative")
Sedation is the most important side effect of these drugs and may affect the patients ability to study, drive and operate machinery. They have a valuable role and in some situations these effects can prove to be an
advantage. The anti-cholinergic effects of some drugs can be of help in drying nasal secretions but they should not be used in patients with benign prostatic hypertrophy or narrow angle glaucoma.2

There are ways to maximise the antihistamine effects while decreasing sedation:

- by administering the agent at night.
- by reducing the dosage - antihistamine effects can often be obtained with less than the recommended dose without other side effects.
- by selecting a different agent - some classes of drug are more sedating than others but the patients response is an individual one and is unpredictable.
- initiating therapy by slowly titrating the dose which allows tolerance to develop to side effects.7

Early studies suggested that tolerance to therapeutic effects may develop, but recent studies have related this to reduced compliance.5,10

Of the older antihistamines, azatadine is the least sedating. Chlorpheniramine has intermediate sedative effects and has fairly prominent anticholinergic effects that can be useful in drying nasal secretions.9

Some physicians administer a single dose of a first generation antihistamine at bedtime and a morning dose of second generation antihistamine. No data exists regarding the efficacy or safety of these combinations.10

**Second Generation Antihistamines. ("Non Sedative")**

Terfenadine was the first to be marketed. Others include astemizole, loratadine and cetirizine.

They are less likely to cross the blood-brain barrier minimizing their sedative effect and cholinergic action.

Astemizole has a slow onset of action and a long half-life so dosing should ideally be started some days ahead of expected onset of symptoms. It should be taken at least an hour before food and it can cause weight gain in some individuals. The other agents have a rapid onset of clinical effect and are not affected by the presence of food in the stomach.2,9

Rare but hazardous arrhythmias have been associated with astemizole and terfenadine at high doses. They should be avoided in patients with cardiovascular disease or those with impaired liver function.

No cardiac side effects have been reported with cetirizine and loratadine at high doses.10 Cetirizine is excreted unchanged by the kidneys and may be safer for patients with liver dysfunction than the others which are more dependent on hepatic metabolism for elimination.10

Some of the second generation antihistamines have clinically significant interactions.2,11,12

Astemizole and terfenadine are metabolised in the liver and metabolism is inhibited by:

- Macrolide antibiotics including erythromycin and clarithromycin.
- Imidazole antifungals including ketoconazole and itraconazole leading to raised plasma levels and increased risk of arrhythmias. They should not be given to patients taking these antimicrobials.9,10 Grapefruit juice may have a similar effect if taken with terfenadine.

Astemizole and terfenadine should also be avoided in patients taking anti-arrhythmic drugs, drugs with arrhythmogenic potential such as tricyclic antidepressants, phenothiazines and other anti-psychotics and also diuretics (which can upset electrolyte balance and increase possibility of arrhythmias).

The half-life of loratadine is prolonged in elderly patients and drug levels may be increased when administered with macrolide antibiotics or imidazole antifungal agents. However, dug interactions have not been reported to date with loratadine or cetirizine.10
Terfenadine has recently been withdrawn from the US market following the introduction of fexofenadine—a metabolite of terfenadine providing the beneficial effects without the cardiotoxic risk.18

DECONGESTANTS

Decongestants have a limited role in hay fever and should be reserved for those periods of severe nasal congestion.5,13 Topical nasal decongestants should not be used for longer than three to five days because of the possibility of rebound congestion and should never be used in infants less than six months old.2

For hay fever sufferers in whom nasal congestion is a problem throughout the season a combination oral antihistamine-decongestant product may be effective (eg. clemastine/phenylpropanolamine).9

CORTICOSTEROIDS

Nasal drops and sprays reduce inflammation and swelling of the nasal mucosa and in normal dosage there is little evidence of systemic effects.14 It is best to start treatment a few weeks before the season begins.2,3

All the intranasal corticosteroids appear to have similar efficacy.14 Flunisolide and beclomethasone may be the agents of first choice. The once daily dosage regimen of budesonide and fluticasone may aid compliance and they have a better safety profile. However they are significantly more expensive.3,6,15

Adverse reactions are mild and transient and consist of nasal irritation and stinging, dryness, sneezing, sore throat, epistaxis and fungal overgrowth.3

• Oral steroids or depot injections should only be considered for certain groups of patients such as those doing state exams or those with severe continuous symptoms despite adequate standard therapies.2,4,5,6,13

CROMOGLYcate AND RELATED THERAPy

Sodium cromoglycate should be initiated before the pollen season begins.2 It is effective in relieving mild to moderate symptoms but less so in treating more severe attacks and its frequency of application is a disadvantage. It is safer but less effective than topical steroids.2,16

Cromoglycate 2% and nedocromil sodium 2% eye drops can help control some of the eye symptoms of hay fever not always controlled by antihistamines.5

OTHERS

• Intranasal ipratropium bromide is useful where rhinorrhoea is the predominant symptom. It does not relieve itching, sneezing or nasal blockage.5,17

• Azelastine is a topical nasal antihistamine with a rapid onset of action.6 It may provide an effective and safe alternative to oral medications but cost is a consideration.19,20

HAY FEVER AND PREGNANCY

Topical agents should be used in preference to systemic antihistamines if drug treatment is needed. Topical corticosteroids can be used but high doses of systemic corticosteroids should be avoided. Sodium
Cromoglycate is safe to use. Chlorpheniramine and promethazine are the agents of choice if topical treatment is ineffective.\textsuperscript{2,8}

**CHOICE OF THERAPY**

The choice of therapy is tailored to the predominant symptoms. Combination therapy may be required. The severity of symptoms and the adverse effects of each agent should be considered when individual treatment plans are being established.

Many patients will have tried oral antihistamines with or without a decongestant. They are a reasonable first choice and may be better than nasal sprays in patients with troublesome symptoms at multiple sites. Where nasal symptoms are prominent or uncontrolled, prophylactic sprays should be used. Where nasal congestion has occurred a topical or systemic decongestant may be necessary initially. For patients with persistent eye irritation eye drops such as sodium cromoglycate may be used.

**Cost of 28 days treatment for adult doses of some therapies used in treatment of Hay Fever.**

*Drug costs are based on data from GMS.*

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cost (GBP)</th>
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<tbody>
<tr>
<td><strong>FIRST GENERATION</strong></td>
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<tr>
<td>Azatadine (Optimine) 1mg BD</td>
<td>£0.84</td>
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<tr>
<td>Chlorpheniramine (Piriton) 4mg TID</td>
<td>£2.52</td>
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<td>Clemastine (Tavegil) 1mg BD</td>
<td>£5.37</td>
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<td>Mequitazine (Primalan) 5mg BD</td>
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<td>Phenindamine (Thephorin) 25mg TID</td>
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<td>Pheniramine (Daneral SA) 75mg OD</td>
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<td><strong>SECOND GENERATION</strong></td>
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<tr>
<td>Astemizole (Hismanal) 10mg OD</td>
<td>£5.60</td>
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<tr>
<td>Cetirizine (Zirtek) 10mg OD</td>
<td>£8.12</td>
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<tr>
<td>Loratadine (Claritin) 10mg OD</td>
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<tr>
<td>Terfenadine (Triludan) 50mg BD</td>
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<tr>
<td><strong>TOPICAL NASAL PREPARATIONS</strong></td>
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<tr>
<td>Beclomethasone (Beconase) 2 doses BD</td>
<td>£10.57</td>
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<td>Budesonide (Rhincon) 2 doses OD</td>
<td>£11.62</td>
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<td>Fluticasone (Flixonase) 2 doses OD</td>
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<td>Flunisolide (Syntaris) 2 doses BD</td>
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<tr>
<td>Sodium Cromoglycate 4% (Rynacrom) 1 dose BD</td>
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<td>Azelastine (Rhinest) 1 dose BD</td>
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<tr>
<td>Ipratropium (Rinatec) 1 dose QOS</td>
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<tr>
<td>Betamethasone drops (Betnesol) 2 drops BD</td>
<td>£1.68</td>
</tr>
</tbody>
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**REFERENCES**

1. Drugs 1996; 10:4-13
6. Drugs 1993;45:518-527
8. Pharm J 1994; 253:57-60
13. SAMJ 1996; 86:1315-1328
17. The Practitioner 1996;240:48-53
18. Pharm J 1997; 258:90