Allergic Rhinitis

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Abstract
Allergic rhinitis, sometimes referred to as “hay fever”, is an extremely common condition. It can significantly impair quality of life and may impact on work or school performance and attendance. Many patients seek the advice of a pharmacist regarding the prevention and management of allergic rhinitis. There are many preventative measures and therapeutic approaches that can be recommended in order to provide affected individuals with rapid and sustained symptomatic relief.

Introduction
Allergic rhinitis (AR) is a global health problem and patients from all countries, ethnic and socioeconomic groups and ages suffer from AR. Allergic rhinitis affects social life, sleep, school and work performance and its economic impact is substantial.1-4

In over 60% of cases the first line of help for allergic patients is the pharmacy.5 Given the varied population of patients affected, treatment needs to be individually tailored and should be selected based both on the efficacy and safety of the agent so as to provide the greatest symptomatic relief and with the least potential for harm.6

Prevalence
The actual prevalence of AR is difficult to determine and it is thought that the prevalence of AR has increased in recent decades. AR is estimated to affect 20% of the population.4

Aetiology
AR is defined as a symptomatic disorder of the nose, induced by immunoglobulin-E (IgE) -mediated inflammation after allergen exposure.4 In some people, these allergens may also cause reactions in the lungs (asthma) and eyes (allergic conjunctivitis).

The allergic reaction is characterised by activation of two types of inflammatory cells: mast cells and basophils. These cells produce inflammatory mediators, including histamine and leukotrienes, that cause fluid to build up in the nasal tissues (congestion), itching, sneezing, and rhinorrhoea.4,7 Over several hours, these substances activate other inflammatory cells that can cause persistent symptoms.7

Diagnosis
Pharmacists may play an important role in the identification of AR.

History: Taking a comprehensive patient history is vital. AR can begin at any age, although most people first develop symptoms in childhood or young adulthood.7

• Family history: The risk is much higher in people with asthma and/or eczema (atopic) and in people who have a family history of asthma or rhinitis.7

• Social history: In order to assess possible allergen exposure, a full history of housing conditions, pets and occupation is needed.2

• Drugs: A detailed drug history is important as topical decongestants, alpha-blockers, aspirin and non-steroidal anti-inflammatory drugs may cause rhinitis.2

Symptoms: There are four key symptoms that occur for two or more consecutive days for more than 1 hour most days1-4,6:

• Sneezing
• Nasal congestion
• Nasal itching
• Rhinorrhoea (runny nose)

Although the term “rhinitis” refers only to the nasal symptoms, many patients also experience other symptoms.1,7 These include:

• Itchy, red eyes, feeling of grittiness in the eyes, swelling and blueness of the skin below the eyes (called allergic shiners)
• Sore throat, hoarse voice, congestion or popping of the ears, itching of the throat or ears
• Sleep problems such as mouth breathing, frequent awakening, daytime fatigue, difficulty performing at work or school

When an allergen is present year-round, the predominant symptoms include post-nasal drip, persistent nasal congestion, and poor-quality sleep.7 Patients with AR typically feel “under par”.5

Note: The following symptoms are usually not associated with rhinitis5,3:
Unilateral nasal stuffiness
Mucopurulent rhinorrhoea
Mucoid postnasal drip
Pain
Recurrent epistaxis

Pharmacists must be aware of the diagnosis of the allergic versus infective conditions of the nose to ensure that “cold and flu” medicines are not repeatedly recommended to allergic patients. Unlike AR, colds are generally associated with sore throats, low grade fever and headache. Allergy should be suspected in patients who complain of a cold lasting more than 10 days.

AR is often associated with rhinosinusitis as nasal inflammation associated with AR can obstruct the sinuses, thereby predisposing sinuses to bacterial infection. Symptoms of bacterial sinusitis may include nasal congestion, purulent rhinorrhoea or postnasal drip, pain, and cough. Such patients should be referred to their doctor.

Classification
Traditionally, AR has been subdivided into:
• Seasonal allergic rhinitis (SAR) occurs at a particular time of the year
• Perennial allergic rhinitis (PAR) occurs year round

The allergens that most commonly cause SAR include pollen from trees, grasses, and weeds, as well as spores from fungi and moulds. The allergens that most commonly cause PAR are dust mites, cockroaches, animal dander, and fungi or moulds. PAR tends to be more difficult to treat.

The International Allergic Rhinitis and its Impact on Asthma (ARIA) task team in collaboration with the World Health Organization reclassified AR based on (see Figure 1):
• frequency of symptoms – intermittent or persistent
• severity of symptoms – mild or moderate/severe

Identifying the allergen
• Recall factors that precede symptoms
• Noting the time at which symptoms begin
• Identifying potential allergens in a person’s home, work, and school environments

Skin-prick testing remains the least expensive method of testing and will effectively diagnose the relevant allergies in over 80% of AR patients. A testing panel should include house dust mites, Bermuda grass, rye grass and cat, dog, cockroach and fungal spores in all regions of South Africa.

Management

Allergen avoidance
Although the general consensus is that allergen avoidance should lead to an improvement in symptoms, there is little evidence to support the use of a single physical or chemical method. (Table II)

Table 1: When to refer patients
• Wheezing and shortness of breath
• Tightness of chest
• Painful ear
• Painful sinuses
• Purulent conjunctivitis
• Failed medication

Table II: Measures for allergen avoidance for certain indoor allergens

<table>
<thead>
<tr>
<th>House dust mites</th>
<th>Pets</th>
</tr>
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<tbody>
<tr>
<td>• Encase bedding in permeable covers</td>
<td>• Remove cat/dog from home</td>
</tr>
<tr>
<td>• Wash bedding on a hot cycle</td>
<td>• Keep out of main living areas or bedroom</td>
</tr>
<tr>
<td>• Replace carpet with hard flooring</td>
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</table>

Figure 1: Classification of AR

Intermittent
Symptoms
• < 4 days per week
• or < 4 consecutive weeks

Mild
All of the following
• normal sleep
• no impairment of daily activities, sport, leisure
• no impairment of work and school
• symptoms present but not troublesome

Persistent
Symptoms
• > 4 days/week
• and > 4 consecutive weeks

Moderate – Severe
One or more items
• sleep disturbance
• impairment of daily activities, sport, leisure
• impairment of school or work
• troublesome symptoms
Pharmacotherapy

1. Oral antihistamines
   • First generation antihistamines include: chlorpheniramine (Allergex®), promethazine (Phenergan®) and hydroxyzine (Atarax®).
   • Second generation antihistamines include: loratadine (Claritin®), cetirizine (Zyrtec®), fexofenadine (Telfast®), desloratadine (Desaway®) and levocetirizine (Xyzal®).

   *Mode of action:* Antihistamines block histamine at the H1-receptor level. Some of the newer-generation antihistamines have been shown to have a range of additional anti-inflammatory properties; however the mechanism of action for these effects remains unclear.

   *Efficacy:* They are effective predominantly for symptoms mediated by histamine including itching, sneezing, rhinorrhoea and eye symptoms. They have the advantage of improving allergic symptoms at sites other than the nose such as the conjunctiva, skin and lower airways. They have been shown to significantly improve quality of life.

   *Pharmacokinetics:* Onset of action is within one hour for most agents and peak serum levels are attained in two to three hours.

   *Safety:*
   • First generation antihistamines display poor selectivity for the H1 receptor and block muscarinic receptors, causing substantial anticholinergic effects such as dry mouth, constipation, urinary retention and tachycardia. They also cause sedation which may interfere with work or academic performance. Due to their unfavourable risk-benefit ratio, they should not be recommended when second generation agents are available.
   • Second generation antihistamines induce no or little sedation (with fexofenadine the least sedating). They also lack anticholinergic effects. Regular therapy is more effective than “as needed” use in persistent rhinitis.

2. Topical antihistamines include:
   • Nasal Sprays: azelastine (Rhinolast®) and levocabastine (Sinumax Allergy Nasal Spray®)
   • Eye Drops: olopatadine (Patanol® eye drops)

   *Efficacy:* Intranasal antihistamines are effective only at the site of administration for itching, rhinorrhoea, sneezing and nasal congestion.

   *Pharmacokinetics:* Topical antihistamines have a fast onset of action (within 15 minutes) making them useful as rescue therapy.

   *Safety:* Local irritation and taste disturbance with azelastine can be bothersome to some patients and can be minimised by keeping the head tilted forward while spraying, to prevent the medicine from draining down the throat.

3. Topical intranasal corticosteroids

   Topical intranasal corticosteroids (INS) include: beclometasone dipropionate (Becloate Aquanase®) available over-the-counter and fluticasone propionate (Flixonase®), mometasone furoate (Nasonex®), triamcinolone acetonide (Nasacor T®) and budesonide (Rhinocort®) available on prescription.

   *Mechanism of action:* INS suppress inflammation at multiple points in the inflammatory cascade. High drug concentrations can be achieved at the receptor sites in the nasal mucosa with a minimal risk of systemic adverse events.

   *Efficacy:* INS are presently the most effective single maintenance therapy for AR and cause few side effects at recommended doses. INS reduce all symptoms of AR including ocular symptoms. If nasal congestion is present or if symptoms are frequent, an INS is the most appropriate first-line treatment as it is more effective than any other treatment, including antihistamines.

   *Comparative studies among different INS preparations have not demonstrated significant differences in efficacy.* However, there are differences in safety between molecules, those with the lowest bioavailability being the best tolerated.

   INS can be divided into:
   • First generation: beclometasone (unknown bioavailability)
   • Second generation: budesonide (10–34%) and mometasone furoate (undetectable)
   • Third generation: fluticasone propionate (< 2%) and mometasone furoate (undetectable)

   **Tips to optimise INS therapy**

   • If mucous crusting is present, clean the nose with saline nasal sprays or irrigation before the INS is applied.
   • Once daily preparations are more convenient and can help optimise compliance. These include: triamcinolone acetonide, budesonide, fluticasone propionate, mometasone furoate.
   • Once daily preparations may be more effective if administered in the evening, as nasal inflammation is greater at night.
   • Patients are sometimes alarmed by the term “steroid”, associating it with potent oral corticosteroids and their possible side effects and these concerns should be discussed.
   • Unlike decongestants, regular use is essential for full benefit. The importance of regular therapy needs to be explained to the patient in order to enhance compliance.

   Starting treatment two weeks prior to a known allergen season improves efficacy.
Pharmacokinetics: Onset of action is 6–8 hours after the first dose, clinical improvement may not be apparent for a few days and maximal effect may not be apparent until after two weeks of regular therapy.2,3

Safety: Local irritation of the nasal mucosa including, drying, burning, and epistaxis is reported by 2–10% of patients.10 These problems can be minimised by reducing the dose of the nasal steroid, applying a moisturising nasal gel or spray to the septum before using the spray, or switching to a water-based (rather than an alcohol-based) spray.7

Evidence shows that long-term use of INS is not associated with the side effects of long-term oral glucocorticosteroid therapy.4 The potential for systemic absorption with effects on growth in children has been a concern and has been evaluated in many studies. The rate of growth was slightly reduced in children treated regularly with intranasal beclomethasone over one year.4,10 However, no growth retardation has been observed in one year follow up studies of children treated with fluticasone propionate or mometasone furoate.4,10

Once symptoms are adequately controlled, the dose can be reduced at one week intervals to the lowest effective dose.10 Patients with severe symptoms will require daily use on a chronic basis.10

4. Systemic glucocorticosteroids
Systemic glucocorticosteroids including: dexamethasone, hydrocortisone or prednisolone are rarely indicated in AR, except for:

• Severe nasal obstruction
• Short-term rescue medication for uncontrolled symptoms on conventional pharmacotherapy

Systemic corticosteroids should be used briefly and in combination with an INS. There is a lack of comparative studies on the preferred dose, the route of administration and the dose-response relationship.4

5. Anti-leukotrienes or leukotriene receptor antagonists (LRAs)
Anti-leukotrienes or leukotriene receptor antagonists (LRAs) include: montelukast (Singulair®) and zafirlukast (Accolate®).

Mode of action: LRAs blocks leukotriene receptors in the airways producing anti-inflammatory effects on vascular permeability, eosinophils and mucous production.5

Efficacy: The therapeutic benefits of LRAs are generally equivalent to those of the antihistamines when used as monotherapy, but they appear to be less effective than INS.2,4,11 The addition of an antihistamine to montelukast appears to have added benefits and may be equivalent to INS.11 LRAs may be useful in patients with asthma and persistent rhinitis.2

Pharmacokinetics: Clinical effect is rapid in onset (within 48 hours). A trial of 14 days should be initiated and should be reviewed before chronic management is indicated.5

6. Decongestants
• Intranasal decongestants including: xylometazoline (Otrivin® Adult Drops/Adult Metered Dose Spray) and oxymetazoline (Vicks® Sinex Decongestant Nasal Spray®)
• Oral decongestants including: phenylephedrine, phenylpropanolamine and pseudoephedrine (Sudafed Sinus®)

Mode of action: They are sympathomimetics and act by constricting dilated mucosal blood vessels.

Efficacy: The sprays are effective for nasal obstruction/congestion in both allergic and non-allergic rhinitis.2,4 However, they do not improve nasal itching, sneezing or rhinorrhoea.4 Oral decongestants are weakly effective in reducing nasal congestion.2 They do not cause a rebound effect on withdrawal but are less effective than topical preparations for nasal congestion.2 They are not generally recommended for AR.2

Safety: Nasal decongestant sprays should not be used for more than two to three consecutive days because they may cause rhinitis medicamentosa, which presents as rebound nasal congestion.7

Systemic side effects include irritability, dizziness, headache, tremor and insomnia as well as tachycardia and hypertension.2,4 They should therefore not be recommended for patients with:

• Diabetes mellitus
• Coronary heart disease (angina)
• Hypertension
• Hyperthyroidism

7. Chromones including:
• Nasal spray: Sodium cromoglycate (Vivadrin®)
• Eye drops: Sodium cromoglycate (Vivadrin®) and Lodoxamide (Alomide®)

Mode of action: Chromones inhibit the degranulation of sensitised mast cells, inhibiting the release of inflammatory and allergic mediators.2

Efficacy: Chromones are modestly effective in nasal symptoms but are more effective for ocular symptoms.4 Cromoglycate can be effective as a prophylactic and should be started at least a week before the allergy season is likely to begin and is then used continuously.6 The nasal spray may be useful as an “add on” when watery rhinorrhoea persists despite intranasal steroid and antihistamines.2

Safety: Chromones have a particularly good safety profile.4

Other therapies
Saline: Nasal irrigation with saline is associated with an improvement in a variety of rhinitis conditions and is particularly useful for treating drainage down the back of the throat, sneez-
The treatment helps by rinsing out allergens and irritants from the nose. These preparations also have the advantage of being safe for daily use and can be used in infants, children and adults.

**Allergen immunotherapy**

Involves the repeated administration of gradually increasing quantities of an allergen extract in order to reduce symptoms on subsequent exposure to that allergen. It induces clinical and immunological tolerance, has long term efficacy, may prevent the progression of allergic disease and improves quality of life.

Guidelines recommend immunotherapy in patients with IgE-mediated disease in whom allergen avoidance is either undesirable or not feasible and who fail to respond to optimal treatment. Prior to undergoing immunotherapy patients need to have skin prick tests or blood RAST tests done to confirm their specific allergy.

Immunotherapy is available as subcutaneous injections or sublingual therapy. Both routes are highly effective for patients with house dust mite allergies or grass pollen allergies.

Immunotherapy injections carry a small risk of a severe allergic reaction (6 per 10,000 injections). Sublingual immunotherapy is an alternative to the subcutaneous route and has a good safety profile (no anaphylactic reactions reported) and is conveniently taken at home.

**Conclusion**

AR is common and patients frequently seek the advice of a pharmacist regarding the management of this troublesome condition. Pharmacists can make an important contribution towards the identification, education and management of patients presenting with allergic rhinitis.

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**Table III: Effect of therapies on rhinitis symptoms**

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Sneezing</th>
<th>Rhinorrhoea</th>
<th>Nasal obstruction</th>
<th>Nasal itch</th>
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**References**