Allergic rhinitis – an overview and treatment

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Abstract

Allergic rhinitis is a common disease that affects adults and children. Symptoms include an itchy, runny, stuffy nose and sneezing. Very commonly, patients also develop itchy, runny eyes that may become swollen due to intense eye rubbing. Diagnosis of allergic rhinitis is based on the presence of these typical symptoms on exposure to inhaled proteins from common allergenic sources that include pollens, house dust mite and animal danders - supported by the results of skin prick tests and/or the presence of specific antibodies (IgE antibodies) to these allergens in blood tests.

Standard treatments for allergic rhinitis include taking modern non-sedating anti histamine tablets and regular use of nasal corticosteroid sprays. These medications may be highly effective in reducing symptoms – but they do not eliminate the allergy or modify the disease long-term. In the small proportion of patients with severe allergic rhinitis who do not response adequately to these medications, allergen-specific immunotherapy may be highly effective. This treatment involves receiving a standardised extract of the allergen to which you are sensitive in the form of injections into the skin or liquid, or tablet formulations of the allergen placed under the tongue. Immunotherapy is generally given for a minimum of three years and has the advantage of longterm clinical effectiveness for years after the treatment is discontinued.

What is allergic rhinitis?

Allergic rhinitis (AR), also called hay fever, is a frequent disease worldwide and affects up to1 in 4 people in UK and Europe. Allergic rhinitis happens when the immune system overreacts to an airborne substance (an allergen such as grass pollen) that would otherwise be harmless. Allergic rhinitis symptoms generally include an itchy, runny or stuffy nose and sneezing. Some patients may present also ocular symptoms (~70%), including watery, red, itchy and puffy eyes. When symptoms affect the nose and eyes, this condition is called allergic rhinoconjunctivitis. Allergic rhinitis sufferers may also report cough, postnasal drip, fatigue and need for continuous rubbing or their nose and eyes.



Although many cases are mild, allergic rhinitis may often cause troublesome symptoms that affect quality of life, work and school productivity, sleep quality, social interactions and the ability to perform outdoor activities such as sports and leisure.

Common triggers of allergic rhinitis are pollen (a fine powder produced by wind-pollinated plants including grasses, trees and weeds), house dust mite faeces (microscopic arachnids found in household dust), moulds (spores released by moulds in damp environments), animal dander (proteins found in animal saliva, urine, fur and skin flakes), cockroach and some occupational agents (such as laboratory animals, latex, etc). Bright flowers, whose pollination is facilitated by insects, do not cause allergic rhinitis, as their pollen is too heavy to be suspended or carried by air.

People who suffer from AR may present symptoms during specific seasons of the year (seasonal AR) or during the whole year (perennial AR). When symptoms are present during the early months of the year (March - May), these may be associated with tree pollen (e.g. birch, alder, cedar) while, during late spring and summer (May – July), grass pollen may be the most common symptoms eliciting allergen. Later in the year, weeds pollen (July – September) and moulds (August – October) are common allergen triggers.

Some AR sufferers present with symptoms throughout the year. In these cases, symptoms may be caused by continuous exposure to indoor allergens such as house dust mite, cockroaches or animal dander, including cats, dogs and horses (Figures 1 and 2). AR sufferers may be allergic to a single, a few or many allergens. <u>A pollen calendar for</u> <u>different regions in the United Kingdom can be found here</u>.

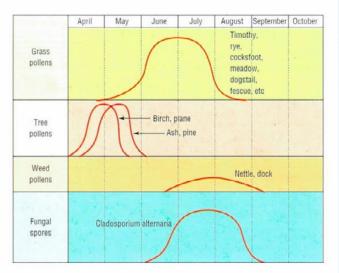


Figure 1. Pollen calendar in the United Kingdom

Figure 2. Common allergen sources (a. Rye grass, b. House dust mite, c. Cat dander)



Up to 40% of subjects with allergic rhinitis have or will develop allergic asthma. This has been identified by numerous clinical and epidemiological studies. Patients with asthma should be treated with the right treatment, depending on the severity of the disease. This includes corticosteroid inhalers, in an effective dose to control their symptoms, with minimal risk of side effects and use of inhaled bronchodilators. Modern asthma inhalers also include a corticosteroid and a long-acting bronchodilator in the same inhaler. These "combination" inhalers are highly effective. A small proportion of patients with asthma may also benefit from allergen immunotherapy, under the supervision of a specialist and provided their asthma is wellcontrolled on their inhalers.

What is the mechanism of allergic rhinitis?

Predisposing factors include the genetic background of the individual, method of childbirth, early-life exposure to allergens and microbes, some micronutrient intake, geographical conditions of the place where the individual was born or lives, access to vaccines and antibiotics in early life and ambient factors (e.g. air pollution or tobacco smoke).

During the initial exposure to an allergen, the immune system of susceptible individuals mistakenly identifies a harmless allergen as a harmful substance. Subsequently, a complex network of cells interacts to produce a defence mechanism that mainly depends on an antibody called Immunoglobulin E. This antibody, produced by the plasma cells, circulates in blood, and is present in many organs, such as the nose, the lungs, the eyes and the digestive system. On subsequent re-exposure to the allergen to which the patient is sensitised, immunoglobulin E provokes the activation of cells called mast cells, that release histamine and other inflammatory mediators like leukotrienes, and prostaglandins that cause dilatation of blood vessels and an increase the permeability of blood vessels of the nasal mucosa, that leads to swelling, increased mucus production, sneezing and itching.

How is allergic rhinitis diagnosed?

The diagnosis of allergic rhinitis is based on the patient's symptoms and their association with the exposure to particular allergen sources. To identify the culprit allergen(s), the patient may need to be referred to an NHS allergy service where a specialist-trained doctor or nurse will ask questions about general health, assess the patient's symptoms and perform a physical examination, which should include the inspection of the nostrils (rhinoscopy), the conjunctiva (surface of the membranes that cover the eyes) listen to the chest with a stethoscope and examination of the skin. The allergist may perform a skin prick test. This is generally performed on the patient's forearm. For this test, the allergist selects a limited number of allergens (generally 10 to 12) based on the patient's symptoms. The allergens are placed on the patient's forearm skin in the form of liquid drops, and then a tiny amount of the allergen is introduced into the superficial layer of the skin using a sterile lancet that has a short fine tip (less than 1mm). The test is very well tolerated and does not cause discomfort. The results of these tests are assessed after 15 minutes and any positive results are evaluated by measuring any wheal produced in response to the allergen exposure, and then these are compared with a negative and a positive control (Figure 3). Afterwards, the results are interpreted in the light of the patient's symptoms.

Figure 3. Skin prick tests for allergy diagnosis

(a. Skin prick test solutions, b. Sterile lancet, c. Patient sensitised to grass pollen and house dust mite - photo shows positive [histamine] and negative [saline solution] controls-)



A few patients may require blood tests to determine the presence of specific IgE antibodies against allergens.

Having allergic rhinitis also means that you may be more prone to react to non-allergic triggers that include cold air, temperature changes, tobacco, pollutants, perfumes, bleach, emotional factors and more. Other conditions that may mimic allergic rhinitis include drug-induced rhinitis (aspirin and other painkillers - but not paracetamol). Certain medications for blood pressure may cause rhinitis (such as propranolol, bisoprolol), sinus infections, while structural problems of the nose such as a deviated nasal septum and nasal polyps may mimic rhinitis.

What is the treatment of allergic rhinitis?

Current treatment includes the avoidance of exposure to the provoking allergen where possible. Over the counter or prescription medications are widely available to reduce the symptoms. Non-sedating antihistamines are medicines that block the histamine receptor. These include cetirizine, loratadine, desloratadine, levocetirizine, fexofenadine. The antihistamines are effective in reducing sneezing and runny nose. In patients with more severe symptoms, intranasal corticosteroids (anti-inflammatory medications) are very effective These reduce nasal congestion as well as the itching and sneezing and runny nose (examples of these include beclomethasone, fluticasone, mometasone, etc). Antihistamines are also available as nasal sprays. Azelastine is a good example. Nasal saline douches (Neilmed® sinus rinse and Sterimar®) may also be helpful in clearing the nasal passages.

Recently, combination nasal sprays that include a corticosteroid and an antihistamine in the same spray device have become available. These are highly effective but should only be used when previously mentioned medications have not provided adequate relief (Figure 4).

When used properly, these interventions are highly effective. Whereas antihistamines are recommended to be used as needed, the corticosteroid sprays need to be taken regularly and ideally starting 1-2 weeks before the anticipated pollen season and taken throughout the season, whether or not the Hay fever symptoms are present at the time. Similarly, patients with perennial symptoms may need to take the corticosteroid spray all year round. The commonest cause of treatment failure is poor adherence to the treatment or failure to take the nasal spray correctly. The correct use of nasal sprays should be explained to the patient and their technique checked. Please see the guideline produced by the British Society of Allergy and Clinical Immunology (BSACI) (Figure 5, page 4) and follow this link to a video produced by BMJ Learn explaining the correct technique to use the nasal sprays.

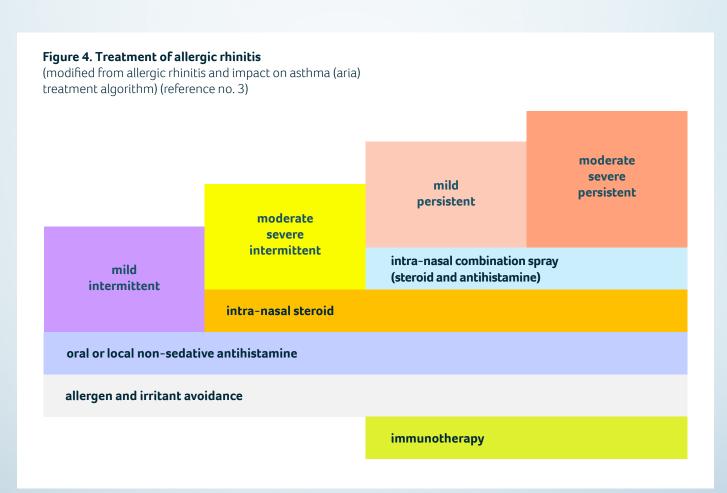
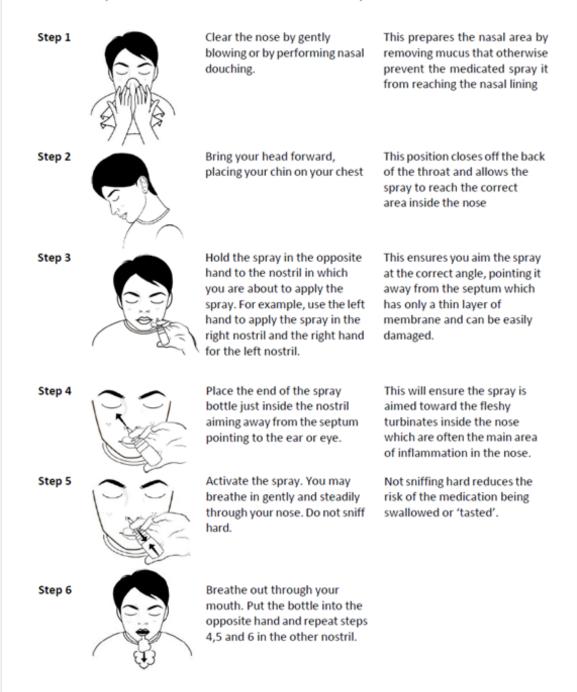


Figure 5. How to use a nasal spray

(adapted from the British Society of Allergy and Clinical Immunology leaflet (reference no. 4))

Before use

- Shake the bottle before use, and remove cap
- You will need to prime the nasal spray if it is new, or if you have not used it for 2 weeks or more (see manufacturer instructions for how to do this).



- If you need to administer two sprays into each nostril, repeat steps 3 to 6 again.
- Once you have finished, wipe the nozzle so that it is clean, and put the cap back on
- It may take a few weeks before you notice any improvement in your symptoms. Please always use your nasal spray as prescribed by your doctor or pharmacist.

Several national and international guidelines have been developed, based on robust scientific evidence to recommend the best treatment for allergic rhinitis. Those patients with moderate to severe symptoms who have an insufficient response to the above medications, have troublesome adverse effects with the medications, or when avoidance of the triggering allergens is not feasible, may benefit from allergen immunotherapy. These interventions are also known as "allergy shots" or "desensitisation injections". Subcutaneous allergen immunotherapy (SCIT) consists of the introduction of small amounts of the offending allergen through injections under the patient's skin (usually in the upper arm deltoid area). These injections are administered initially weekly with increasing doses of the standardised allergen. After several weeks of "updosing," these injections are given monthly generally for three years. This has been the standard of practice for allergen immunotherapy for over 100 years! Allergen immunotherapy should only be given by specialist nurses under medical supervision in an NHS clinic. This is because there is a very small risk of developing severe allergic reactions, such that patients must be observed in the clinic for 60 minutes after the injections.

Recently sublingual allergen immunotherapy (SLIT) has become available as an effective and safe alternative to sub cutaneous immunotherapy. SLIT involves the administration of standardised allergens under the tongue, delivered as tablets or liquid drops. SLIT has proven to be highly effective and safe. The first dose is given in the allergy clinic and thereafter may be self-administered in the patient's home. SLIT needs to be taken daily for three years and close adherence to treatment is necessary for full benefits.

There are precise indications and contraindications to prescribe allergen immunotherapy. Patient appropriate

selection is crucial to increase the likelihood of an effective outcome of allergen immunotherapy for allergic rhinitis. This also reduces the risk of potential side effects. In the UK, allergen formulations of grass pollen, Tree pollens and house dust mite are licensed to be prescribed as SCIT or SLIT for allergic rhinitis. Allergen immunotherapy is allergen specific. Thus, patients who are allergic to a single or a few closely related allergens (e.g. a distinct grass species) are more likely to respond better than those allergic to multiple different allergen species.

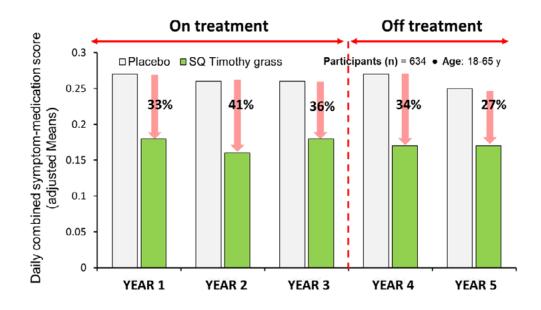
Allergen immunotherapy is the only intervention that induces long-term tolerance to the offending allergen and induces persistence of benefits for several years following discontinuation. International guidelines and robust clinical trials recommend administering SCIT or SLIT for at least three years to observe these long-lasting effects. Four large clinical trials of SLIT including hundreds of participants for grass or tree pollen and three studies of SCIT for grass and tree pollen have shown the persistence of the benefit of allergen immunotherapy for at least two years after the discontinuation of a complete course of three years of immunotherapy. (Figure 6).

It is likely that this is also true for house dust mite allergen immunotherapy although more studies are needed on long-term benefits of immunotherapy in patients with mite allergy.

Although the use of SLIT for house dust mite allergy in children is not currently approved for use in the UK, a recent robust clinical trial in children 5-11 years old with perennial allergic rhinitis (n=1460) showed that those treated with a house dust mite SLIT tablet had a significant reduction in symptoms and rhinitis medications compared to those who received placebo - so watch this space!

Figure 6. Long term benefits of allergen immunotherapy.

Benefits persist at least two years after immunotherapy discontinuation. (Adapted from reference no. 5)



Conclusions and future perspectives

Allergic rhinitis is a common immunological disease, and its prevalence worldwide is increasing. Early diagnosis and early treatment are fundamental. Conventional treatment including non-sedating oral antihistamines, intranasal corticosteroids, intranasal antihistamines and avoidance measures are generally effective but do not cure the underlaying cause of the disease. Some patients with moderate to severe forms of the disease or those that do not tolerate the medications, should be considered to receive allergen specific immunotherapy. The response to immunotherapy will depend on the patient's characteristics and the adherence to treatment. Further research is required to determine the long-term effects of immunotherapy for house dust mite and its role in allergy prevention.

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