

**Review Article****ALLERGIC RHINITIS: IMPACT, DIAGNOSIS, SYMPTOMS AND TREATMENT**Simran Kaur¹, Saptarshi Das²

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ABSTRACT

Allergic rhinitis is a common disorder that is robustly associated to asthma and conjunctivitis. It is usually a long-standing condition that often goes undetected in the primary-care setting. The classic symptoms of the disorder are nasal congestion, nasal itch, rhinorrhea and sneezing. Allergic rhinitis (AR) is one of the most common diseases affecting adults. It is the most common chronic disease in children in the world today and most common chronic disease. Allergic rhinitis results from an immunological abnormality in which atopic individuals produce immunoglobulin E (IgE) to allergens (e.g. pollen, house dust mites, animal dander and moulds). IgE activates mast cells, which respond by releasing inflammatory mediators. Histamine stimulates the early symptoms, predominately mucus production, nasal itching and sneezing. Leukotrienes and cytokines attract and activate eosinophils to cause allergic inflammation. A thorough history, physical examination and allergen skin testing are important for establishing the diagnosis of allergic rhinitis. Second-generation oral antihistamines and intranasal corticosteroids are the basis of treatment. Allergen immunotherapy is an effective immune-modulating treatment that should be recommended if pharmacologic therapy for allergic rhinitis is not effective or is not tolerated. This article provides an overview of the pathophysiology, diagnosis, and appropriate management of this disorder.

Keywords: RHINITIS**Introduction**

Rhinitis is broadly defined as inflammation of the nasal mucosa. It is a common disorder that affects up to 40% of the population. Allergic rhinitis (AR) is a major health problem with high and ever-increasing prevalence. Allergic rhinitis was considered to be a disorder localized to the nose and nasal passages, but current evidence indicates that it may represent a component of systemic airway disease involving the entire respiratory tract. There are a number of physiological, functional and immunological relationships between the upper (nose, nasal cavity, paranasal sinuses, pharynx and larynx) and lower (trachea, bronchial tubes, bronchioles and lungs) respiratory tracts [1-5].

PATHOPHYSIOLOGY

In allergic rhinitis, numerous inflammatory cells, including mast cells, CD4-positive T cells, B cells, macrophages, and eosinophils, infiltrate the nasal lining upon exposure to an inciting allergen (most commonly airborne dust mite fecal particles, cockroach residues, animal dander, moulds, and pollens). The T cells infiltrating the nasal mucosa are predominantly T helper (Th) in nature and release cytokines (e.g., interleukin [IL-3, IL-4, IL-5, and IL-13] that promote immunoglobulin E (IgE) production by plasma cells. IgE production, in turn, triggers the release of mediators, such as histamine and leukotrienes, that are responsible for arteriolar dilation, increased vascular permeability, itching, rhinorrhea (runny nose), mucous secretion, and smooth muscle contraction [1, 2,6-8]. The mediators and cytokines released during the early phase of an immune response to an inciting allergen, trigger a further cellular

inflammatory response over the next 4 to 8 hours (late-phase inflammatory response)

which results in recurrent symptoms (usually nasal congestion) [6,7-9].

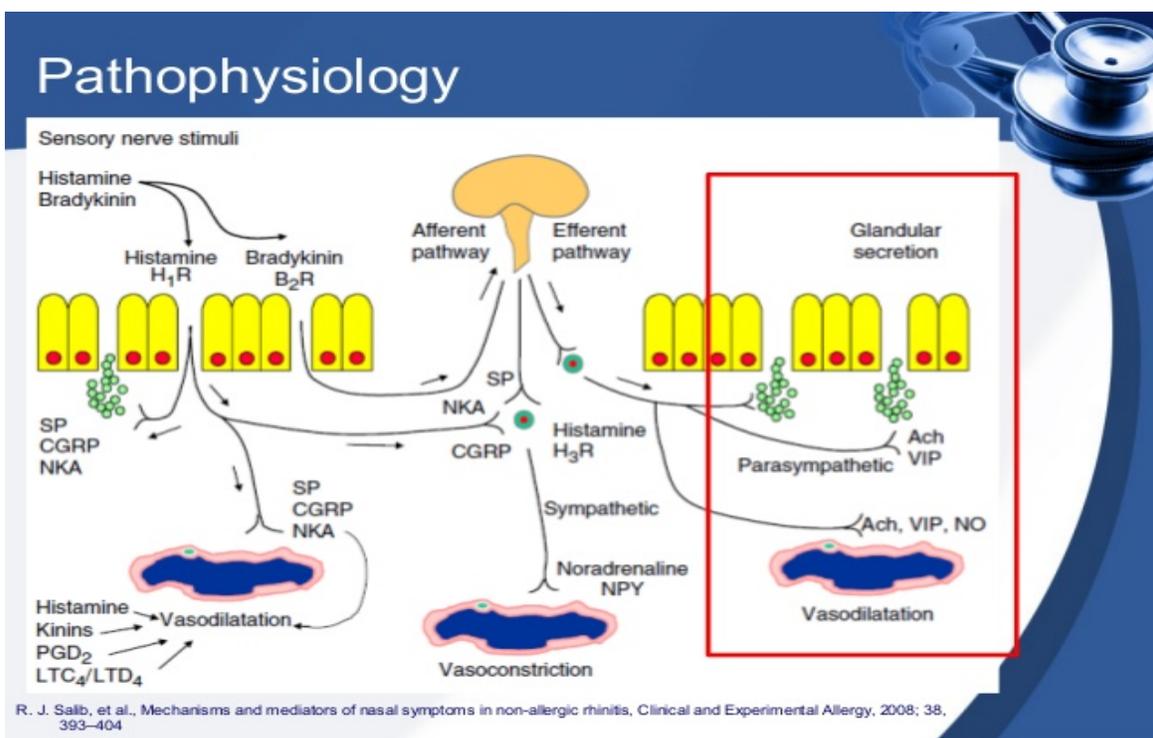


Figure 1: Pathophysiology of no allergic Rhinitis

CLASSIFICATION

Rhinitis is classified into one of the following categories according to etiology: IgE-mediated (allergic), autonomic, infectious and idiopathic (unknown). Although the focus of this article is allergic rhinitis, a brief description of the other forms of rhinitis is provided [3-5, 8-10].

Table 1: Classification of Allergic Rhinitis

Type	Description	Allergen (Example)
Seasonal	Response to seasonal aeroallergens	Pollen
Perennial	Response to year-round allergens	Mold, dust mites, animals
Episodic	Response to exposure that is abnormal for the individual	A friend's pet
Type	Description	Symptom (Example)
Intermittent	Response lasting <4 days/wk or <4 wk/y	NA
Persistent	Response lasting >4 days/wk or >4 wk/y	NA
Mild	Symptoms that do not interfere with quality of life	NA
Moderate-to-severe	Symptoms that interfere with quality of life	Sleep disturbance, work performance

NA: not applicable.
Source: References 6, 8.

Table 2: Etiological classification of rhinitis [1]

	Description
IgE-mediated (allergic)	<ul style="list-style-type: none"> • IgE-mediated inflammation of the nasal mucosa, resulting in eosinophilic and Th2-cell infiltration of the nasal lining • Further classified as intermittent or persistent
Autonomic	<ul style="list-style-type: none"> • Drug-induced (rhinitis medicamentosa) • Hypothyroidism • Hormonal • Non-allergic rhinitis with eosinophilia syndrome (NARES)
Infectious	<ul style="list-style-type: none"> • Precipitated by viral (most common), bacterial, or fungal infection
Idiopathic	<ul style="list-style-type: none"> • Etiology cannot be determined

Table 3: Characteristics of Allergic Rhinitis

Characteristics of Allergic Rhinitis*		
<i>Characteristic</i>	<i>Seasonal</i>	<i>Perennial</i>
Obstruction	Variable	Always, predominant
Secretion	Watery, common	Seromucous, postnasal drip, variable
Sneezing	Always	Variable
Smell disturbance	Variable	Common
Eye symptoms	Common	Rare
Asthma	Variable	Common
Chronic sinusitis	Occasional	Frequent

IMPACT OF ALLERGIC RHINITIS [1-3, 5-7, 10-12]

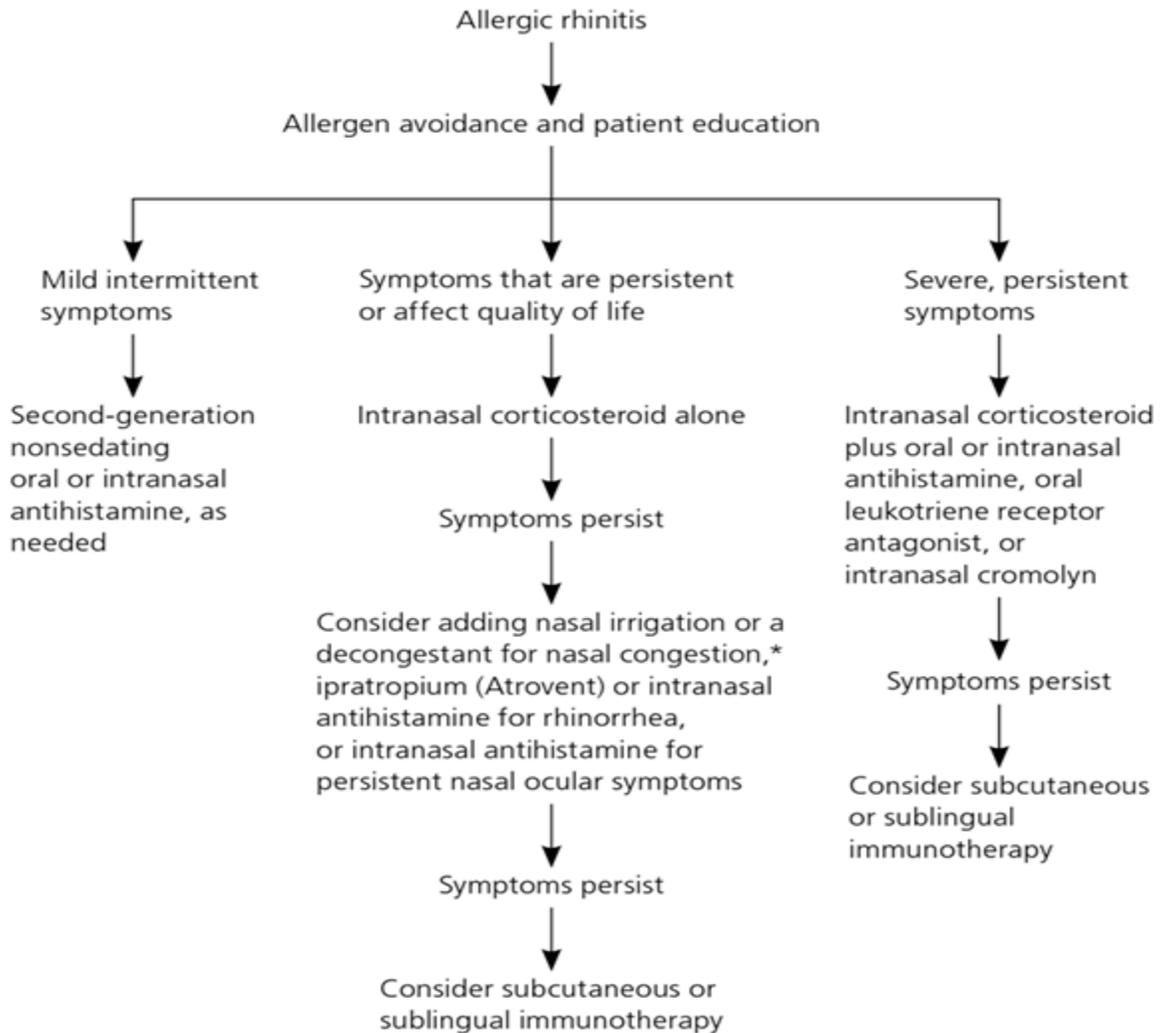
- One of the most common allergic diseases in the U.S.
- Affects over 40 million Americans
- Fifth most common chronic illness
- Most prevalent chronic condition in patients under 18 years of age
- Both physical and mental health status adversely affected
- 3.8 million lost work and school days annually
- Direct costs approximately \$4.5 billion/year

IMPACT ON ASTHMA

The Allergic Rhinitis and its Impact on Asthma (ARIA) classification system was introduced in 2001 and is based on duration and severity of symptoms and their impact on QoL (Bousquet et al 2001). The duration of AR is split into intermittent and persistent patterns. Intermittent AR is defined by symptoms that occur for 4 or less days per week or for not more than 4 consecutive weeks, whereas persistent AR (PER) lasts for more than 4 days per week and for more than 4 consecutive weeks. Symptoms of intermittent AR or PER may be mild or moderate-to-severe based on its

impact on QoL and symptom severity. Mild rhinitis characteristically does not affect daily, leisure, or sport activities, normal work or school attendance, or disturb sleep, and causes no bothersome symptoms. Moderate-to-severe rhinitis is characterized by impairment of at least one of these parameters. Compared with

patients with intermittent AR, PER patients had more severe symptoms, a higher rate of self awareness, previous diagnosis of AR, differed in their use of medication, and had a clearly distinct allergen sensitization pattern [1-3, 6-9, 11-14].



*—Use of nasal decongestants for longer than three days is not recommended because of possible rebound congestion.

Figure 2: symptoms and treatment of allergic rhinitis

CAUSES AND DEVELOPMENT [2-4, 14-18]

1. Pollens, grasses, or ragweed (in certain seasons and areas)
2. Dust and household mites
3. Changes in temperature or humidity
4. Spicy foods
5. Smoking or prolonged exposure to second-hand smoke.

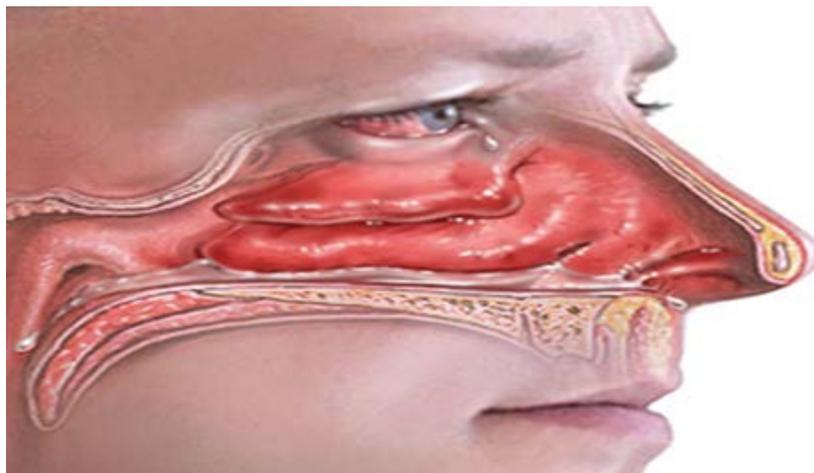


Figure 3: Nasal cavity: allergic rhinitis

SIGNS AND SYMPTOMS [25-18]

- | | |
|---|--|
| <ol style="list-style-type: none"> 1. Sneezing 2. a runny nose 3. a stuffy nose 4. an itchy nose 5. coughing 6. a sore or scratchy throat 7. itchy eyes 8. watery eyes 16. | <ol style="list-style-type: none"> 9. dark circles under the eyes 10. frequent headaches 11. eczema-type symptoms, such as having extremely dry, itchy skin that often blisters 12. hives 13. excessive fatigue 14. Fatigue and irritability 15. Headache |
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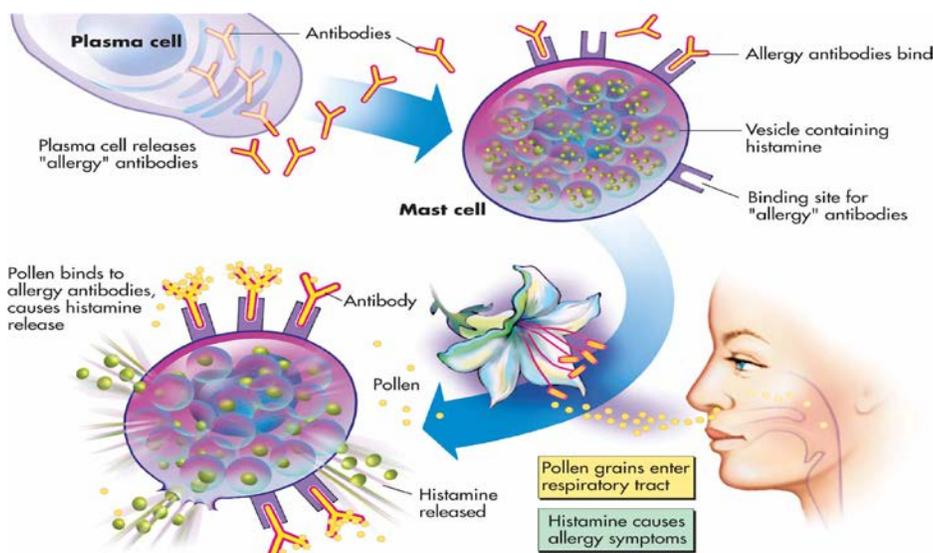


Figure 4: Causes and mechanism of allergic rhinitis

Risk factors for allergic rhinitis [2, 14-18]

- | | |
|---|--|
| <ul style="list-style-type: none"> • cigarette smoke • chemicals • cold temperatures • humidity | <ul style="list-style-type: none"> • wind • air pollution • hairspray • perfumes • colognes |
|---|--|

- wood smoke
- fumes

DIAGNOSIS

The most common diagnostic tests [13-15, 17-20] for allergic rhinitis are the percutaneous skin test and the allergen-specific immunoglobulin E (IgE) antibody test. Less common diagnostic tools include nasal provocation testing, nasal cytology, nasolaryngoscopy, and intra-dermal skin testing. Skin testing involves introducing controlled amounts of allergen and control substances into the skin.

Laboratory tests used in the diagnosis of allergic rhinitis include the following:

- 1 Allergy skin tests (immediate hypersensitivity testing):** An in vivo method of determining immediate (IgE-mediated) hypersensitivity to specific allergens.
- 2 Fluorescence enzyme immunoassay (FEIA):** Indirectly measures the quantity of immunoglobulin E (IgE) serving as an antibody to a particular antigen.
- 3 Total serum IgE:** Neither sensitive nor specific for allergic rhinitis, but the results can be helpful in some cases when combined with other factors.
- 4 Total blood eosinophil count:** Neither sensitive nor specific for the diagnosis, but, as with total serum IgE, can sometimes be helpful when combined with other factors.

ALLERGY TESTING

If the exact cause of allergic rhinitis is uncertain, doctor may refer to the patient to a hospital allergy clinic for allergy testing.

The two main allergy tests are:

- 1-skin prick test:** where the allergen is placed on your arm and the surface of the skin is pricked with a needle to introduce the allergen to your immune system; if you're allergic to the substance, a small itchy spot (welt) will appear.
- 2-blood test:** to check for the immunoglobulin E (IgE) antibody in your blood; your immune system produces this antibody in response to a suspected allergen.

FURTHER TESTS

In some cases further hospital tests may be needed to check for complications, such as nasal polyps or sinusitis.

For example, you may need:

- 1- A nasal endoscopy:** where a thin tube with a light source and video camera at one end (endoscope) is inserted up your nose so your doctor can see inside your nose
- 2- A nasal inspiratory flow test:** where a small device is placed over your mouth and nose to measure the air flow when you inhale through your nose
- 3- A computerized tomography (CT) scan:** a scan that uses X-rays and a computer to create detailed images of the inside of the body

Table 4: Advantages and disadvantages of diagnosis of Allergen-specific IgE by in-vitro than simple skin test

Advantages	Disadvantages (compared to skin testing)
Safe No experience / expertise / reagents required by the medical practitioner for the performance of the test Suitable for patients with Skin disease Dermatographism Recent antihistamine Rx Infancy / cord blood sampling Severe anaphylaxis in whom there is a concern that skin testing may provoke an anaphylactic reaction (foods, latex, stinging insects, antibiotics)	Expensive Less sensitive than Skin Tests RAST tests to "mixes" of allergen may give falsely negative results Delay before results are available Information is more abstract -i.e. less immediately relevant to the patient Stability of allergen a problem for some allergens (particularly food allergens)

Diagnostic of Allergy Testing



Figure 5: Diagnosis tools for Allergy testing

ALLERGY SKIN TESTING [1-3, 19-21]

Skin testing remains the central test to confirm allergic sensitivity when it can be performed-

- Skin testing is fast (15-30 minutes), safe, sensitive and involves minimally invasive procedures which can be cost effective
- When performed correctly, skin testing is reproducible

- Skin testing has demonstrated good correlation with results of nasal challenge and bronchial challenges

- Results of skin test should always be used as an adjunct to the clinical history and physical examination when making the diagnosis of allergic disease.

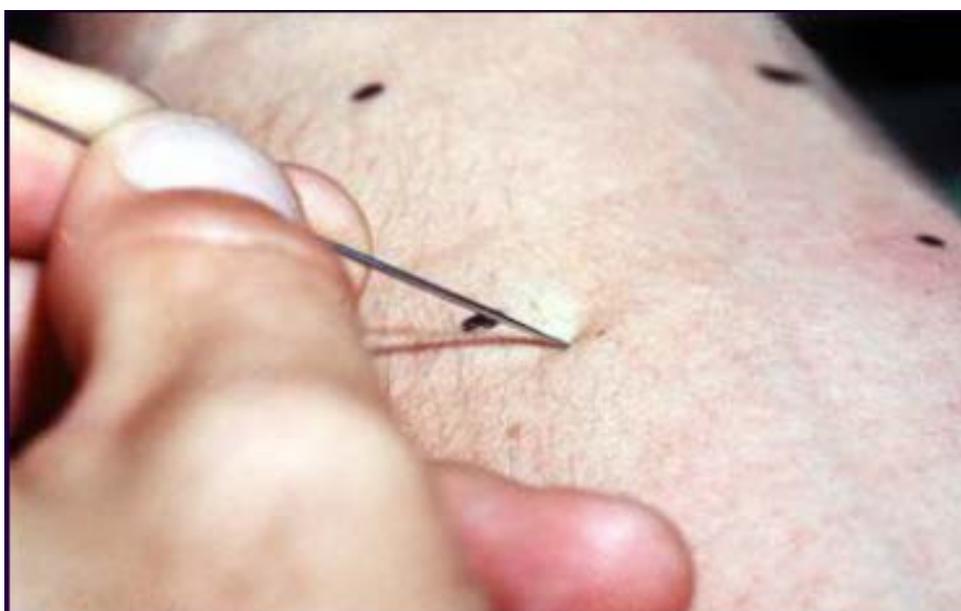


Figure 6: Skin testing remains the central test to confirm allergic sensitivity



Figure 7: Measurement and confirmation of Skin testing

TREATMENT

In most cases treatment [20-25] aims to relieve symptoms such as sneezing and a blocked or runny nose. If you have mild allergic rhinitis, you can often treat the symptoms yourself. You should visit your GP if your symptoms are more severe and affecting your quality of life, or if self-help measures haven't been effective.

Self-help

It's possible to treat the symptoms of mild allergic rhinitis with over-the-counter medications, such as long-acting, non-sedating antihistamines. If possible, try to reduce exposure to the allergen that triggers the condition. See preventing allergic rhinitis for more information and advice about this.

Cleaning your nasal passages

Regularly cleaning your nasal passages with a salt water solution – known as nasal douching or irrigation – can also help by keeping your nose free of irritants. You can do this either by using a homemade solution or a solution made with sachets of ingredients bought from a pharmacy. Small syringes or pots that often look like small horns or teapots are also available to help flush the solution around the inside of your nose.

To make the solution at home, mix half a teaspoon of salt and half a teaspoon of bicarbonate of soda (baking powder) into a pint

(568ml) of boiled water that's been left to cool to around body temperature and do not attempt to rinse your nose while the water is still hot.

To rinse your nose:

- 1- Stand over a sink, cup the palm of one hand and pour a small amount of the solution into it
- 2- Sniff the water into one nostril at a time
- 3- Repeat this until your nose feels comfortable – you may not need to use all of the solution

While you do this, some solution may pass into your throat through the back of your nose. The solution is harmless if swallowed, but try to spit out as much of it as possible. Nasal irrigation can be carried out as often as necessary, but a fresh solution should be made each time.

Medication

Medication [3-6. 25-27] won't cure your allergy, but it can be used to treat the common symptoms. If your symptoms are caused by seasonal allergens, such as pollen, you should be able to stop taking your medication after the risk of exposure has passed. Visit your GP if your symptoms don't respond to medication after two weeks.

Antihistamines

Antihistamines relieve symptoms of allergic rhinitis by blocking the action of a chemical called histamine, which the body releases when

it thinks it's under attack from an allergen. You can buy antihistamine tablets over the counter from your pharmacist without a prescription, but antihistamine nasal sprays are only available with a prescription. Antihistamines can sometimes cause drowsiness. If you're taking them for the first time, see how you react to them before driving or operating heavy machinery. In particular, antihistamines can cause drowsiness if you drink alcohol while taking them.

Corticosteroids

If you have frequent or persistent symptoms and you have a nasal blockage or nasal polyps, your GP may recommend a nasal spray or drops containing corticosteroids.

Corticosteroids help reduce inflammation and swelling. They take longer to work than antihistamines, but their effects last longer. Side effects from inhaled corticosteroids are rare, but can include nasal dryness, irritation and nosebleeds. If you have a particularly severe bout of symptoms and need rapid relief, your GP may prescribe a short course of corticosteroid tablets lasting 5 to 10 days.

Add-on treatments

If allergic rhinitis doesn't respond to treatment, your GP may choose to add to your original treatment.

SUGGESTIONS

Increasing the dose of your corticosteroid nasal spray using a short-term course of a decongestant nasal spray to take with your other medication combining antihistamine

tablets with corticosteroid nasal sprays, and possibly decongestants using a nasal spray that contains a medicine called ipratropium, which will help reduce excessive nasal discharge using a leukotriene receptor antagonist medication, that blocks the effects of chemicals called leukotrienes, which are released during an allergic reaction

If you don't respond to the add-on treatments, you may be referred to a specialist for further assessment and treatment.

Immunotherapy

Immunotherapy, also known as hyposensitisation or desensitisation, is another type of treatment used for some allergies. It's only suitable for people with certain types of allergies, such as hay fever, and is usually only considered if your symptoms are severe. Immunotherapy involves gradually introducing more and more of the allergen into your body to make your immune system less sensitive to it. The allergen is often injected under the skin of your upper arm. Injections are given at weekly intervals, with a slightly increased dose each time. Immunotherapy can also be carried out using tablets that contain an allergen, such as grass pollen, which are placed under your tongue. When a dose is reached that's effective in reducing your allergic reaction (the maintenance dose), you'll need to continue with the injections or tablets for up to three years. Immunotherapy should only be carried out under the close supervision of a specially trained doctor as there's a risk it may cause a serious allergic reaction.

Table 5: Diagnosis and treatment of allergic rhinitis

Diagnosis/Testing	Treatment	Prevention/Education/ Risk Factors	Other Therapies	Outcomes
<ul style="list-style-type: none"> • Diagnosis of AR • Differentiating nonallergic nasal conditions from AR • When should a patient be referred to an allergy specialist? • Differentiating perennial or seasonal AR • Identifying and treating comorbidities • When is it acceptable to test for allergic component(s), and what type of test should be performed? • Accuracy of self-diagnosis • Accuracy of clinician diagnosis based on clinical assessment • Children age 2 and older with a diagnosis of allergies, since age 2 is the earliest age to consider allergy testing • Role and appropriate use of imaging • Role of nasal endoscopy • Accurate use of instruments to measure symptoms/objective testing for baseline • When is it necessary to perform specific allergy testing and/or IgE test? 	<ul style="list-style-type: none"> • First-line therapy upon diagnosis • When does combining 2 different classes of allergy pharmacology benefit the patient? • Pharmacology and the different medication classes that offer additive vs negative effects • Self-directed therapy or over-the-counter medications vs physician-directed or prescription medications • Use and safety of nasal, oral, topical steroids • When is it acceptable to add a second or third medication? • Treatment of allergic conjunctivitis • Role of surgical management • Managing chronic inflammation of lung, sinus, skin, and ears • Role of immunotherapy • Efficacy of different antihistamines • Measuring response to therapy and identifying further need for therapy • Role of environmental controls 	<ul style="list-style-type: none"> • Methods for preventing the development of AR • Role of patient education • When is it appropriate to manage symptoms over the phone (or internet)? • Role of dietary modifications • Value of pollen counts in determining symptom severity and self-guidance • Role of stress management in the creation of, or exacerbation of, AR symptoms • Identification of risk factors for the development of AR 	<ul style="list-style-type: none"> • Role of acupuncture • Role of herbal medicines • Role of homeopathy • Role of nasal rinses • Role of capsaicin • Role of antibiotics 	<ul style="list-style-type: none"> • Initial evaluation of the patient • Improvement in accuracy of diagnosis; avoidance of unnecessary testing • Reduction in care variation and unnecessary radiation exposure from sinonasa imaging • Expenditure reduction for ineffective environmental measure: • Increased treatment optimization and reduced complications from comorbidities • Optimization of proven effective therapy • Avoidance of sedating antihistamine and promotion of direct therapy • Improved awareness of the different classes of medication for effective treatment of AR • Reduction in the use of a less effective first-line agent • Improved symptom control and reduction in care variation • Increased awareness and appropriate use of immunotherapy and reduction in care variation • Improved nasal breathing and quality of life • Increased awareness of acupuncture as a treatment option • Increased awareness of herbal therapy as a treatment option

PREVENTION

The best way to prevent allergic rhinitis [3-6, 20-25] is to avoid the allergen that causes it.

But this isn't always easy. Allergens, such as dust mites, aren't always easy to spot and can breed in even the cleanest house. It can also be difficult to avoid coming into contact with pets, particularly if they belong to friends and family. Below is some advice to help you avoid the most common allergens.

House dust mites

Dust mites are one of the biggest causes of allergies. They're microscopic insects that breed in household dust.

Help limit the number of mites in your house, you should:

- 1) Consider buying an air-permeable occlusive mattress and bedding covers – this type of bedding acts as a barrier to dust mites and their droppings
 - 2) Choose wood or hard vinyl floor coverings instead of carpet
 - 3) Fit roller blinds that can be easily wiped clean
 - 4) Regularly clean cushions, soft toys, curtains and upholstered furniture, either by washing or vacuuming them
 - 5) Use synthetic pillows and acrylic duvets instead of woollen blankets or feather bedding
 - 6) Use a vacuum cleaner fitted with a high efficiency particulate air (HEPA) filter – it can remove more dust than ordinary vacuum cleaners
 - 7) Use a clean damp cloth to wipe surfaces – dry dusting can spread allergens further
- Concentrate your efforts on controlling dust mites in the areas of your home where you spend most time, such as the bedroom and living room.

Pets

It isn't pet fur that causes an allergic reaction, but exposure to flakes of their dead skin, saliva and dried urine.

If we can't permanently remove a pet from the house, you may find the following tips useful:

1- Keep pets outside as much as possible or limit them to one room, preferably one without carpet

2- Don't allow pets in bedrooms

3- Wash pets at least once a fortnight

4- Groom dogs regularly outside

5- Regularly wash bedding and soft furnishings your pet has been on

If you're visiting a friend or relative with a pet, ask them not to dust or vacuum on the day you're visiting because it will disturb allergens into the air.

Taking an antihistamine medicine one hour before you enter a house with a pet can help reduce your symptoms.

Pollen

Different plants and trees pollinate at different times of the year, so when you get allergic rhinitis will depend on what sort of pollen(s) you're allergic to.

Most people are affected during the spring and summer months because this is when most trees and plants pollinate.

To avoid exposure to pollen, you may find the following tips useful:

1. Check weather reports for the pollen count and stay indoors when it's high
2. Avoid line-drying clothes and bedding when the pollen count is high
3. Wear wraparound sunglasses to protect your eyes from pollen
4. Keep doors and windows shut during mid-morning and early evening, when there's most pollen in the air
5. Shower, wash your hair and change your clothes after being outside
6. Avoid grassy areas, such as parks and fields, when possible
7. If you have a lawn, consider asking someone else to cut the grass for you

Mould spores

Moulds can grow on any decaying matter, both in and outside the house. The moulds themselves aren't allergens, but the spores they release are.

Spores are released when there's a sudden rise in temperature in a moist environment, such as

when central heating is turned on in a damp house or wet clothes are dried next to a fireplace.

Help prevent mould spores, we should:

- 1- keep your home dry and well ventilated
- 2- when showering or cooking, open windows but keep internal doors closed to prevent damp air spreading through the house, and use extractor fans
- 3- Avoid drying clothes indoors, storing clothes in damp cupboards and packing clothes too tightly in wardrobes deal with any damp and condensation in your home.

REFERENCE

1. <http://www.nhs.uk/Conditions/Rhinitis---allergic/Pages/Prevention.aspx>
2. <http://www.nhs.uk/Conditions/Rhinitis---allergic/Pages/Treatment.aspx>
3. <http://www.aafp.org/afp/2006/0501/p1583.html#sec-3>
4. <http://www.nhs.uk/Conditions/Rhinitis---allergic/Pages/Diagnosis.aspx>
5. <http://emedicine.medscape.com/article/134825-overview>
6. <https://aacijournal.biomedcentral.com/articles/10.1186/1710-1492-7-S1-S3>
7. <https://www.allergy.org.au/health-professionals/papers/tests-in-the-diagnosis-of-allergic-diseases>
8. www.aafp.org/afp/2010/0615/p1440.html
9. <file:///C:/Users/user/Downloads/Allergic%20Rhinitis/Allergic%20Rhinitis%20%20Causes,%20Symptoms,%20and%20Diagnosis.htm>
10. file:///C:/Users/user/Downloads/Allergic Rhinitis/Allergic rhinitis diagnosis and management_GPonline.htm
11. Schoenwetter WF, Dupclay L Jr, Appajosyula S, Botteman MF, Pashos CL. Economic impact and quality-of-life burden of allergic rhinitis. *Curr Med Res Opin* 2004; 20:305-17. IV
12. Settipane RA. Rhinitis: a dose of epidemiological reality. *Allergy Asthma Proc* 2003; 24:147-54. IV
13. Druce H. Allergic and nonallergic rhinitis. In: Middleton E, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, editors. *Allergy principles and practice*. 5th ed. St Louis: Mosby-Year Book; 1998. p. 1005-16. IV
14. Settipane RJ, Hagy GW, Settipane GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Proc* 1994;15:21-5. III
15. Varjonen E, Kalimo K, Lammintausta K, Terho P. Prevalence of atopic disorders among adolescents in Turku, Finland. *Allergy* 1992; 47:243-8. III
16. Smith JM. A five-year prospective survey of rural children with asthma and hay fever. *J Allergy* 1971; 47:23-30. III
17. Settipane RA, Charnock DR. Epidemiology of rhinitis: allergic and nonallergic. *Clin Allergy Immunol* 2007; 19:23-34. IV
18. Min YG. The pathophysiology, diagnosis and treatment of allergic rhinitis. *Allergy Asthma Immunol Res*. 2010; 2(2):65-76.
19. Bernstein L, Li J, Bernstein D, Hamilton R, Spector S, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy* 2008; 100:S1-148. IV
20. Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic Rhinitis. *Lancet* 2011;378:2112-22
21. Sur DK, Scandale S. Treatment of allergic rhinitis. *Am Fam Physician*. 2010; 81:1440-6.
22. Nelson HS, Rachelefsky GS, Bernick J. *The Allergy Report*. Milwaukee, Wis.: American Academy of Allergy, Asthma & Immunology; 2000.
23. Sutton BJ and Gould HJ. The human IgE network. *Nature* 1993;366:421-8
24. Homburger HA. Methods in laboratory immunology. In *Allergy: Principles and Practice*, edited by Middleton E. Jr, 1998 Edition. Mosby-Year Book Inc. Missouri
25. Schwartz LB, et al. Tryptase as an indicator of mast cell activation in systemic anaphylaxis and mastocytosis. *N Engl J Med* 1987; 316:1622-6) Kim H, Kaplan A: Treatment and management of allergic rhinitis [feature]. *Clinical Focus*. 2008, 1-4. Google Scholar.
26. Dykewicz MS, Fineman S, Skoner DP, Nicklas R, Lee R, Blessing-Moore J, et al. Diagnosis and management of rhinitis: complete

guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. American Academy of Allergy, Asthma, and Immunology. Ann Allergy Asthma Immunol. 1998; 81(pt 2):478–518.

27. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001; 108:S147-334. IV.