



The Association of  
Otolaryngologists of India

# Indian Guidelines on Allergic Rhinitis

**Formulated by The Association of Otolaryngologists of India**





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Dear Colleagues,

Allergic rhinitis affects more than 25% of the Indian population, and these numbers are increasing every year. Allergic rhinitis reduces quality of life as well as school and work performance. Still considered a trivial disease, it remains under diagnosed and under treated. Allergic Rhinitis continues to be treated with sedating anti-histamines with no attempt to diagnose the causative allergens.

Integrated care pathways are needed to enable comprehensive care within the national health systems. The Association of Otolaryngologists of India conducted a series of meetings with experts in allergy management to come up with the Indian Guidelines for Management of Allergic Rhinitis with the aim of providing improved care for patients suffering from allergic rhinitis.

We have taken real world evidence into account in the creation of these practice-oriented Guidelines. An algorithm to simplify management protocols has been proposed by the consensus group. An attempt has also been made to address the relevant merits of using oral anti-histamines, intra-nasal anti-histamines, intra-nasal corticosteroids and LTRAs, either alone or in combination. The significance of Skin Prick test and immunotherapy has also been highlighted.

These Guidelines provide specific recommendations for choice of treatment and the rationale for choosing management that is most suited for an individual patient.

**Dr. Samir Bhargava**

National President AOI - 2020,2021

Chief Coordinator - Indian Guidelines on Allergic Rhinitis



# Indian guidelines on diagnosis and management of Allergic Rhinitis

## ∞ A consensus approach ∞

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## Introduction

Allergic rhinitis (AR), the most common type of chronic rhinitis, is a symptomatic inflammatory disorder of the nasal mucosa<sup>1,2</sup>. The inflammation is induced by allergen triggers, and mediated by immunological response. AR can also be influenced by non-allergenic triggers. There are four major clinical manifestations of AR – sneezing, rhinorrhoea, nasal itching, and nasal congestion<sup>1</sup>. AR has an estimated worldwide prevalence of 10% to 25% and is one of the most common diseases in childhood with a prevalence reaching up to 40% in some regions.<sup>3,4</sup> It was previously considered that AR is a localized disorder of the nose and the nasal passages. However, current clinical knowledge indicates that AR may manifest as a component of systemic airway disease involving the entire respiratory tract. Studies have indicated that trigger of the upper airways by an allergen leads to a local inflammatory response as well as other inflammatory processes in the lower airways, supported by the fact that rhinitis frequently coexists with asthma<sup>2</sup>. In India, around 20–30% of the people suffer from AR and 15% progress to develop asthma.<sup>1</sup> Also, symptoms of AR may cause other clinical manifestations such as sleep disturbance, fatigue, depressed mood, and decline in cognitive function, thus impairing quality of life and functional productivity.<sup>5</sup>

Thus, AR should be considered as a systemic disease and should not be overlooked as a local disease.

## Phenotypes of rhinitis

Allergic rhinitis is one of the common phenotypes of rhinitis. On the basis of aetiology, other phenotypes of rhinitis are classified into - autonomic, infectious, other, and idiopathic<sup>2,6</sup> (Table 1).

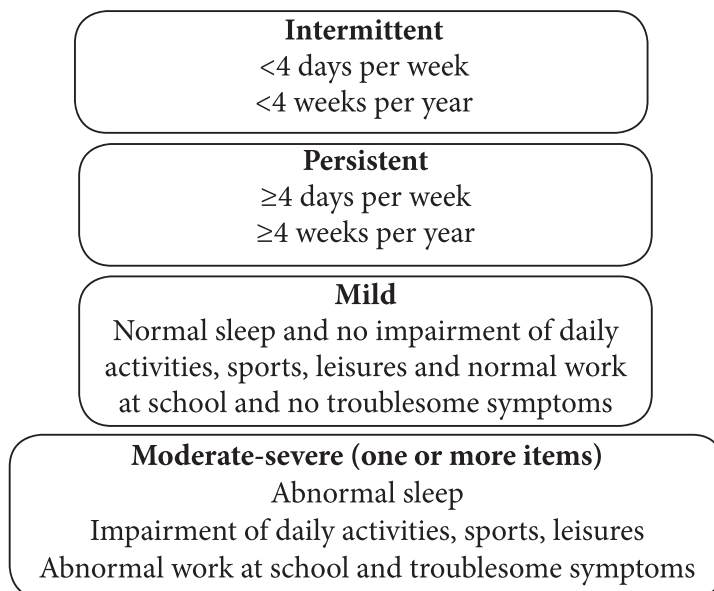
**Table 1: Phenotypes of rhinitis (based on aetiological factors)**

Aetiology	Component
<b>Allergic (IgE-mediated)</b>	<ul style="list-style-type: none"><li>• IgE-mediated inflammation of the nasal mucosa, resulting in eosinophilic and Th2-cell infiltration of the nasal lining<sup>2</sup></li><li>• Intermittent or persistent<sup>2</sup></li></ul>
<b>Non-allergic, non-infective rhinitis</b>	<ul style="list-style-type: none"><li>• Drug-induced (rhinitis medicamentosa)<sup>2,6</sup></li><li>• Hypothyroidism<sup>2</sup></li><li>• Hormonal (rhinitis of pregnancy)<sup>2,6</sup></li><li>• Rhinitis of elderly<sup>2,6</sup></li><li>• Occupational rhinitis<sup>2</sup></li><li>• Non-allergic rhinitis with eosinophilia syndrome (NARES)<sup>2,6</sup></li><li>• Gustatory rhinitis<sup>6</sup></li><li>• Vasomotor rhinitis<sup>6</sup></li><li>• Nasal mastocytosis<sup>6</sup></li><li>• Atrophic rhinitis<sup>6</sup></li></ul>
<b>Infectious</b>	<ul style="list-style-type: none"><li>• Viral (most common), bacterial, or fungal infection<sup>2</sup></li></ul>
<b>Idiopathic</b>	<ul style="list-style-type: none"><li>• Not determined<sup>2</sup></li></ul>

## Classification of AR

Allergic rhinitis, traditionally, has been classified as seasonal i.e. occurring during a specific season, or perennial, i.e. occurring throughout the year. However, this classification system fails to include all patients affected with AR<sup>2</sup>. In some cases, symptoms of perennial AR may not necessarily persist throughout the year. AR due to pollen may be seasonal in cooler climates, but perennial in warmer climates<sup>2,7</sup>. In addition, seasonal exacerbations may be observed in patients with perennial AR when they are exposed to pollens. Moreover, people with multiple allergies may present with perennial AR<sup>2,7</sup>. In 2001, a new classification system was proposed by ARIA, Allergic Rhinitis and its Impact on Asthma, based on frequency and severity of the symptoms<sup>7</sup> (Figure 1)

- Frequency/Symptom duration-based: Intermittent or persistent
- Severity-based: Mild, moderate, or severe



**Figure 1: Classification of AR based on duration and severity of symptoms**

Although AR is a global health problem and one of the most common clinical presentations, the actual prevalence of AR may be underestimated. There also exists significant geographical variation in prevalence of AR, however regional estimates for AR prevalence in India are lacking.<sup>1</sup> In addition, many people with AR are underdiagnosed or misdiagnosed or do not seek treatment for their clinical condition. Misdiagnosis or untreated AR/inadequately treated AR contribute to exacerbation of AR symptoms, increased risk of comorbid conditions like asthma, rhinosinusitis, etc. and overall poor quality of life of affected people.<sup>8</sup>

### Need for AR practice guideline

There exists a lack of high quality clinical evidence on AR diagnostic approach and treatment decisions. Although, clinical trials have generated huge amount of clinical evidence on various therapeutic options in the management of AR, they have often failed to compare active treatments and use endpoints that are regulatory driven. Moreover, a common knowledge

of AR and measures to control is lacking between clinicians and/or patients. Also, currently available guidelines on diagnostic workup and therapeutic pathways seldom refer to real-life scenarios, leading to significant clinical gaps in everyday practice. Thus, it is important to address the practical challenges with respect to diagnosis and treatment aspects of AR.

### Methodology

The objective of the present guideline is to attempt to fill in the clinical gaps to ensure systematic and step-wise diagnostic work-up with clinically relevant treatment decisions, which are in compliance with other existing guidelines. An extensive literature search was carried out through PUBMED database and Google search engine to obtain clinical evidences for diagnostic and treatment recommendations in the management of AR. An experts' committee critically reviewed available evidences, correlated them with their respective clinical practice and discussed clinical relevance of the available evidence in order to draw consensus recommendations. In case of lack of evidence, a practice-based consensus was reached among the experts.

Level of scientific evidence	
1++	High-quality meta-analyses, high-quality systematic reviews of clinical trials with very little risk of bias.
1+	Well-conducted meta-analyses, systematic review of clinical trials or well-conducted clinical trials with low risk of bias.
1-	Meta-analyses systematic reviews of clinical trials or clinical trials with high risk of bias.
2++	High-quality systematic reviews of cohort or case and control studies cohort of case and control studies with very low risk of bias and probability of establishing a causal relationship.
2+	Well-conducted cohort or case and control studies with low risk of bias and moderate probability a causal relationship.
2-	Cohort or case and control studies with high risk of bias and significant risk that the relationship is not causal.
3	Non-analytical studies, such as case reports and case series.
4	Expert opinion.

Grades of recommendations	
A	At least one meta analysis, systematic review or clinical trial classified as 1++ and directly applicable to the target population of the guideline, or a volume of scientific evidence comprising studies classified as 1+ and which are highly consistent with each other.
B	A body of scientific evidence comprising studies classified as 2++, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 1++ or 1+.
C	A body of scientific evidence comprising studies classified as 2+, directly applicable to the target population of the guideline and highly consistent with each other, or scientific evidence extrapolated from studies classified as 2++.
D	Level 3 or 4 scientific evidence, or scientific evidence extrapolated from studies classified as 2+.

### A) Preliminary investigations

A thorough history examination along with physical and clinical examinations forms the basis of establishing a diagnosis of AR.

- a) **History examination** – A detailed history evaluation is an essential preliminary investigation as a part of diagnosing AR. History examination includes personal history such as symptom severity and frequency, seasonality, triggering factors, family history, social environment, presence of comorbid conditions, medication or drug use, response to previous medications if any, etc.<sup>2,9</sup> (Table 2)

**Table 2: List of the components of a complete history examination<sup>2,9</sup>**

Sr. No.	History	Component
1	Symptoms	<ul style="list-style-type: none"><li>• Nasal itch, rhinorrhea, sneezing, eye involvement</li><li>• Presence of seasonal variation of symptoms</li><li>• Diurnal pattern of symptoms</li><li>• Symptom trigger when indoor or outdoor</li><li>• Any triggers</li></ul>
2	Personal	<ul style="list-style-type: none"><li>• Pregnancy (to rule out pregnancy-induced rhinitis)</li></ul>
3	Family	Allergy or asthma
4	Environmental	Potential allergens – Outdoor or Indoor <ul style="list-style-type: none"><li>• House dust mites, pollens, furred animals, flooring/upholstery, molds, etc.</li><li>• Tobacco exposure</li><li>• Humidity levels</li><li>• Pets</li></ul>
5	Occupational exposure	Industrial smoke, cotton, asbestos, chemicals, latex, etc.
6	Medication/drug use	<ul style="list-style-type: none"><li>• Beta-blockers, aspirin, Non-steroidal anti inflammatory drugs (NSAIDs), angiotensin-converting-enzyme inhibitor (ACE inhibitors)</li><li>• Hormone therapy</li><li>• Recreational drug use</li></ul>
7	Comorbidities	<ul style="list-style-type: none"><li>• Mouth breathing, snoring, sinus involvement, otitis media, nasal polyps, conjunctivitis, hyper-reactive airway diseases and skin allergies</li></ul>
8	Response to previous medications	<ul style="list-style-type: none"><li>• Antihistamines</li><li>• Intranasal corticosteroids</li></ul>

As a part of history examination, it is also important to know the impact of symptoms on the quality of life of patients by assessing reduced performance, school/work absenteeism, and lack of sleep. It helps in classifying the symptoms as mild, moderate or severe.

## b) Physical and clinical examination

In a patient with suspected AR, physical examination includes visual assessment for outward signs such as mouth breathing, frequent sniffing or throat clearing, allergic salute or nasal crease.<sup>5</sup> Clinical examination involves anterior rhinoscopy and nasal endoscopy for abnormal secretions, or structural abnormalities (Table 3 and 4). Other assessments include examination of ears, sinus, oropharynx, chest and skin.<sup>2</sup>

**Table 3: Clinical examinations in suspected AR**

Technique	Examination
Anterior rhinoscopy <sup>2</sup>	Hypertrophic, pale and boggy inferior and/or middle turbinates suggesting inflammation
	Presence or absence of clear, colored or purulent secretions
	Presence of deviated septum (it usually does not cause rhinitis)
	Presence or absence of nasal polyps <ul style="list-style-type: none"><li>• Small polyps confined to sinuses might be missed</li><li>• Larger polyps can be observed in the nasal vestibule in yellow/grey color (different from the inferior turbinate)</li></ul>
	Presence of nodules, crusting, granulations, and septal perforations <ul style="list-style-type: none"><li>• Yellow submucosal nodules with a cobblestone appearance suggest sarcoidosis</li><li>• Crusting and granulations suggest vasculitis</li><li>• Septal perforation may occur after septal surgery or due to chronic vasoconstriction (cocaine, alpha agonists), granulomatous polyangiitis, anti-phospholipid antibody syndrome and nose picking</li></ul>
	Throat examination-cobblestoned lymphoid hyperplasia, post-nasal drip
Nasal endoscopy <sup>2</sup>	<ul style="list-style-type: none"><li>• Examination of both anterior and posterior parts of the nasal cavity</li><li>• It is more specific than rhinoscopy</li></ul>

**Table 4: Components of physical and clinical examination**

Sr. No.	Assessment	Component
1	Physical <sup>2</sup>	Allergic salute and/or horizontal nasal crease across dorsum of nose and/or eye involvement
		Chronic mouth breathing
		Allergic shiners (dark circles under eyes)
		Frequent sniffing and/or throat clearing
2	Clinical <sup>2</sup>	Anterior rhinoscopy or nasal endoscopy <ul style="list-style-type: none"><li>• Mucosal swelling, bleeding</li><li>• Abnormal secretions - pale, thin</li><li>• Polyps or other structural abnormalities</li></ul>

		Sinuses <ul style="list-style-type: none"> <li>• Palpation of sinuses for signs of tenderness</li> <li>• Maxillary tooth sensitivity</li> </ul>
		Posterior oropharynx <ul style="list-style-type: none"> <li>• Postnasal drip</li> <li>• Lymphoid hyperplasia (“cobblestoning”)</li> <li>• Tonsillar hypertrophy</li> </ul>
		Chest and skin <ul style="list-style-type: none"> <li>• Atopic disease</li> <li>• Wheezing</li> </ul>

**c) Differentiating indicators between common cold and allergic rhinitis**

Common cold is an example of infectious rhinitis which could be acute or chronic. Symptoms of chronic infectious rhinosinusitis include mucopurulent nasal discharge, facial pain and pressure, olfactory disturbance, and postnasal drainage with cough.<sup>10</sup> Additionally, symptoms of AR are frequently mistaken for those of common cold. The main difference between common cold and AR is duration of symptoms. In addition, presence of fever, malaise, and sore throat are more indicative of common cold. If the symptoms last for more than 2 weeks, regardless of the time of the year, it should be an indication of a cause other than common cold infection. Also, AR may have a seasonal component or clear allergic aggravation, and is unlikely to have an accompanying sore throat as in common cold.<sup>10</sup>

**d) Identification of common signs and symptoms of allergic rhinitis**

The classic symptoms of rhinitis are sneezing, rhinorrhea (runny nose), nasal congestion, and itching. Rhinitis condition suggestive of allergy includes sneezing, itchy nose, itching palate, and eye involvement.<sup>11</sup>

An appropriate diagnosis of allergic rhinitis is based on examining the history of allergic symptoms and identifying features of sneezers and runners<sup>1</sup> (Table 5).

**Table 5: Features of sneezers/runners and blockers**

Symptoms	Sneezers and Runners <sup>1</sup>	Blockers <sup>1</sup>
Sneezing	Especially paroxysmal	Little or more
Rhinorrhea	Watery anterior or posterior	Thick mucus more posterior
Nasal itching	Yes	No
Nasal blockage	Variable	Often severe
Diurnal rhythm	Worse during day Improving at night	Constant day and night May be worse at night
Conjunctivitis	Often present	---



## I. Nasal symptoms of AR

- **Sneezing** – Paroxysmal repetitive sneezing (10 to 15 times in a row or even more), is a classic symptom of allergic rhinitis, caused by stimulation of irritant receptors supplied by trigeminal nerve endings, which initiates a central reflex.<sup>12</sup>
- **Rhinorrhea** – In AR, rhinorrhea can be anterior or posterior, generally manifesting as postnasal drip.<sup>5</sup>
- Bilateral clear secretion is a significant and common feature of AR, whereas, isolated, unilateral clear nasal discharge is uncommon.<sup>5,11</sup>
- Discolored secretions can also be associated with allergy e.g. eosinophils in secretions give a yellow coloration (allergy or infection), neutrophils give green secretions (infection).<sup>5,11</sup>
- **Nasal obstruction** – In AR, nasal obstruction may be partial or complete. Its severity often correlates with systemic manifestations.<sup>5,11</sup>
- AR usually causes bilateral nasal obstruction; however, it may also be due to nasal polyps or septal deviation.<sup>5</sup>
- Alternating nostril obstruction may occur due to rhinitis, exposing the nasal cycle i.e. changes in blood pooling in capacitance vessels from one side of the nose to the other, contributing to mucosal swelling. Other causes of obstruction include nasal polyps, foreign bodies, and rarely tumors.<sup>5,11</sup>
- **Itching** – Another important clinical feature of allergic rhinitis is nasal itching. People with AR are also reported to have itching of the eyes, soft palate and inner ear.<sup>13</sup>

## II. Extranasal symptoms

- **Ocular symptoms** – AR also involves intense itching, redness and swelling of the conjunctiva of the eye with lacrimation, eyelid swelling and (in severe cases) periorbital oedema, which can be aggravated by eye rubbing.<sup>11</sup>
- **Other extranasal symptoms** – dry mouth, fatigue, mouth breathing, and daytime somnolence.<sup>14</sup>

Extranasal symptoms of AR are frequently overlooked in patients with AR, especially in chronic AR. They may significantly affect the health-related quality of life of the patients with AR.<sup>14</sup> These symptoms have been suggested to correlate well with physical health and mental health in allergic rhinitis patients, indicating assessment and therapeutic consideration for extranasal symptoms in AR.<sup>14</sup>

### e) Aggravating factors and specific allergens contributing to AR

Common triggers of AR are domestic allergens as mites, domestic animals, insects or may be of plant origin; common outdoor allergens include pollens and molds; occupational triggers as latex; tobacco smoke; automobile exhaust which includes ozone, oxides of nitrogen and sulphur dioxide; aspirin and other non-steroidal anti-inflammatory drugs.<sup>1</sup> An evaluation of the patient's home and work/school environments is recommended to determine potential triggers of allergic rhinitis.<sup>2</sup>



### **Recommendations: Preliminary evaluation**

1. History examination should include personal history such as symptom severity and frequency, seasonality, triggering factors, family history, social environment, presence of comorbid conditions, medication or drug use, response to previous medications.
2. Physical assessment should include signs such as allergic salute, mouth breathing, throat clearing, and sniffing.
3. Clinical assessment should include anterior rhinoscopy or nasal endoscopy
4. Identification of primary symptoms of AR –
  - Sneezing (paroxysmal repetitive)
  - Rhinorrhea - Bilateral clear secretions; unilateral clear secretion is uncommon; discoloured secretions may indicate allergy or infection
  - Nasal obstruction – bilateral obstruction which can be partial or complete. Nasal polyps and septal deviation may also cause obstruction
  - Nasal itching and ocular symptoms (itching, redness and swelling)
5. Nasal crusting or bleeding is uncommon in AR. Its presence should indicate other conditions such as chronic rhinosinusitis, nose picking, atrophic rhinitis, etc. or frequent use of decongestants
6. Identification of extranasal nasal symptoms should be routinely performed for all patients with AR
  - The severity of extranasal symptoms implies chronicity of AR condition
  - It is important to assess their effect on physical and mental health of the patient
7. Duration of symptoms for more than 2 weeks should indicate allergic causality
8. Evaluation and determination of potential triggers is essential

### **B) Diagnosis and differential diagnosis**

#### **A) Diagnosis**

Diagnosis of allergic rhinitis is made essentially by history and clinical examination. Skin prick allergy test remains as one of the important tests in diagnosing AR (table 6). Laboratory investigations are usually unnecessary, their use is guided by the history, examination and results of skin prick tests.<sup>5</sup>

**Table 6: Common clinical investigations in AR**

Test	Features
<b>Skin-prick allergy test</b>	Helps in diagnosing causative allergen
<b>Cytology Nasal secretion</b>	Useful investigation in NARES
<b>Allergen-specific IgE testing</b>	It can be done in individuals in whom skin prick allergy test is contraindicated
<b>CBC, DC, Peripheral smear</b>	Only if specifically anything in history
NARES: Non-allergic rhinitis with eosinophilia syndrome; CBC: Complete blood count; DC: Differential count	

### a) Skin prick test

Skin prick testing is a strongly recommended procedure to confirm sensitization in IgE-mediated allergic reaction. It is minimally invasive, inexpensive, and rapid i.e. the results can be interpreted within 15-20 minutes. The test provides objective confirmation of sensitivity.<sup>15</sup> For allergens, the peak of the skin wheal to be reached around 10–20 min after the test, and a reading of the largest diameter of the skin wheals after 15 min is considered. It is recommended from infancy to old age.<sup>16</sup>

Skin prick test is contraindicated in -

- Pregnancy - Uterine contractions are a possibility when epinephrine is administered if a systemic reaction ever occurs<sup>15</sup>
- Patients with severe eczema, or those who are taking antihistamines, or other medications such as certain antidepressants, beta blockers or calcineurin inhibitors<sup>15</sup>
- People with chronic illnesses such as renal failure, or cancer which may decrease the skin test reactivity<sup>15</sup>

b) **Allergen-specific IgE testing** – It provides an in vitro measure of a patient's IgE levels against a specific allergen. It is performed typically by modified sandwich immunoassay.<sup>2</sup> It is carried out when skin testing is not possible (in case of eczema or use of antihistamines) or allergen reagent is not available or if there is expected risk of anaphylaxis in skin prick allergy test.<sup>11</sup> It has low sensitivity and is cost ineffective compared to skin prick test.<sup>2</sup> It generally correlates with the results of skin prick test, showing similar sensitivity, especially for house dust mites, but not for other inhaled allergens.<sup>11</sup>

c) **Total IgE and allergen-specific IgE testing** – Testing total IgE may lead to erroneous assumption of allergy as the cause of symptoms, if it is elevated, thus is of limited benefit. However, it may be used in cases like severe eczema, where total IgE may be grossly elevated and modest elevations in allergen-specific IgE may have a lower positive predictive value.<sup>11</sup>

While the above section summarizes the available tests, there is no recommendation as to when and which tests should be prescribed to which patient

### AR with asthma

Clinical tests to diagnose AR with asthma involves allergic testing using skin prick test or IgE estimation along with lung function tests<sup>5</sup>

### AR with comorbid conditions

Comorbidities in allergic rhinitis include conjunctivitis, chronic otitis media with effusion, eustachian tube dysfunction, sleep impairment, obstructive sleep apnea, rhinosinusitis, hyposmia and bronchial hyper-reactivity. A wide range of clinical tests are employed in order to diagnose AR with comorbid clinical conditions. These tests include pulmonary function tests, CT scan, endoscopy, sleep pattern test, thyroid function tests, etc.<sup>11</sup> There can also be association of other IgE-mediated disorder such as food allergy and drug allergy in these patients.

## B) Differential diagnosis

Crusting of secretions within the nose is an unusual symptom of AR.<sup>11</sup> If nose-crusting and nose bleeding are primary complaints, it may suggest other conditions like chronic rhinosinusitis, nose picking, Wegener granulomatosis, sarcoidosis, other vasculitides, ozena/atrophic rhinitis (wasting away of the bony ridges and mucous membranes inside the nose), or frequent use of nasal decongestants.<sup>5,11</sup> The conditions that comprise differential diagnosis in a patient with AR are given in table 7 with their features.<sup>11</sup>

**Table 7: Differential diagnosis of AR**

Type	Feature
NARES	<ul style="list-style-type: none"><li>• Skin tests negative; nasal smears show eosinophilia</li><li>• It may go on to develop nasal polyposis</li></ul>
Autonomic rhinitis (vasomotor)	<ul style="list-style-type: none"><li>• Physical/chemical triggers</li><li>• More common in middle age with clear rhinorrhea, especially in the morning.</li></ul>
Drug-induced rhinitis	<ul style="list-style-type: none"><li>• <math>\beta</math>-adrenergic blockers, angiotensin-converting enzyme inhibitors.</li><li>• Rhinitis medicamentosa with chronic nasal decongestant use</li></ul>
Hormonal	Pregnancy, oral contraceptives, thyroid disease
Cystic fibrosis	Children with polyps
Immunodeficiency	Chronic infective sinusitis secondary to antibody deficiency
Malignancy	Bloody, purulent discharge, pain, and nasal blockage – symptoms may be unilateral.
Structural abnormalities	Unilateral nasal obstruction secondary to nasal septal deviation
Local AR	Skin and serum IgE test negative but positive response to nasal allergen challenge
Idiopathic/noninfectious non-AR	Cause unclear; may respond to topical capsaicin

### Recommendations: Diagnosis and differential diagnosis

- For diagnosis of AR, laboratory investigations including blood count, cytology, is recommended.
- Skin prick test is strongly recommended as a routine procedure in all age groups in order to identify the specific allergen that the patient is sensitized with.
- Resuscitation therapy should be made accessible for emergency cases of skin prick test and should be written as adverse reaction of skin prick test (can become intradermal in some cases)
- IgE testing is recommended in unequivocal and unexpected skin test results.
- Differential diagnoses should be ruled out in order to direct appropriate treatment options for AR.

## C) Treatment

The main treatment goal for allergic rhinitis is symptom relief and prevention of disease progression and treatment complications.<sup>2,17</sup> The rationale for treatment choice depends on level of efficacy of the drugs and their affordable costs. Recommended drugs for the treatment of AR are oral/intranasal antihistamines, intranasal corticosteroids, leukotriene receptor antagonists, etc. along with decongestants and oral corticosteroids in particular group of patients.<sup>1,2</sup> Each available treatment option has variable effects of symptoms of AR.<sup>1</sup> (Table 8)

**Table 9: Treatment options and their effect on the symptoms of AR**

Drugs	Antihistamines			Corticosteroids	Chromones		Decongestants		Anticholinergics	Leukotriene antagonists
	oral	intranasal	intraocular		intranasal	intraocular	intranasal	oral		
Sneezing										
Rhinorrhoea										
Nasal Obstruction										
Nasal itching										
Eye Symptoms										

Green – Effective (light to dark shade suggests strength of response); Red – Not effective

## Pharmacotherapy

### 1. Antihistamines

Second generation drugs are the preferred first-line treatment for all patients with AR.<sup>2</sup> They are largely non-sedating and have a better safety profile with no clinically significant anti-cholinergic activity at therapeutic doses.<sup>5,18</sup> Overall, antihistamines (oral, intranasal, ocular) demonstrate clinical efficacy with least adverse effects and improve quality of life of patients with AR.<sup>5</sup> They effectively improve sneezing, itching and rhinorrhea when taken regularly at the time of maximal symptoms or before exposure to an allergen.<sup>2</sup> They have only a modest effect on nasal congestion.<sup>5,18</sup> Given their more lipid solubility than second generation antihistamines, first generation antihistamines cross the blood brain barrier and are associated with sedation, fatigue, and impaired mental status.<sup>18</sup> Antihistamines are the first-line of treatment in mild intermittent AR.<sup>5</sup>

Advantages of intranasal antihistamines over oral antihistamines<sup>5</sup>

- Target delivery of the drug with faster onset of action<sup>18</sup>
- Improvement of AR symptoms and decreased nasal obstruction<sup>5</sup>
- Convenient rescue therapy, for breakthrough symptoms<sup>5</sup>
- Effective in case of failed oral antihistamine therapy<sup>5</sup>

## 2. Corticosteroids

When the disease becomes persistent, intranasal corticosteroids are the mainstay of management of AR.<sup>2,18</sup> They can be used alone or in combination with oral antihistamines. They are effective in reducing inflammation of the nasal mucosa and improve mucosal pathology.<sup>2</sup> They demonstrate significant total AR symptom reduction with variable effects on associated eye symptoms.<sup>5</sup> Unlike other treatment options, they are effective in treating nasal congestion.<sup>5</sup> They also reduce lower airway symptoms in patients with concurrent asthma and allergic rhinitis.<sup>2</sup>

Intranasal steroids (INS) have low systemic absorption, and are extremely safe for prolonged local usage. Some of the intranasal corticosteroids like budesonide and beclomethasone have systemic side effects like glaucoma and local side effects like epistaxis.<sup>19</sup> Oral corticosteroids when used are only recommended for short-term (5-7 days) duration in severe cases, not responding to intranasal corticosteroids and oral antihistamines.<sup>2,20</sup> In chronic rhinosinusitis with nasal polyps where inflammation is more severe and accompanied with severe nasal obstruction, short bursts of oral steroids may be given under the care of the treating physician keeping the side effects in mind.<sup>5</sup>

When a patient is symptomatic despite treatment with oral antihistamines and INS, the first step is to check adherence and the use of the correct technique by the patient.<sup>21</sup> Clinical practice suggests that most patients who have found INS unhelpful have not persisted with treatment for an adequate period.<sup>22</sup> Patients should be advised that the onset of action of INS takes some time and that they should be used regularly for a minimum of two weeks before considering them unsuccessful.<sup>23</sup> Patients with seasonal AR should commence therapy two weeks before the pollen season as this improves efficacy.<sup>24,25</sup> To maximize the response to treatment, patients using INS should be given clear instructions on this aspect. They must also be advised to direct the nasal spray laterally (rather than medially towards the nasal septum) towards the lowest and anterior most part of inferior turbinate of that side and not to sniff for at least 10 minutes after spraying. All these measures will increase benefit. Tipping the head back and sniffing hard decreases treatment efficacy because the spray will run down the nasopharynx and patients should be advised not to do this. To maximize effect patients may well be advised to douche with saline prior to using their nasal spray. Saline douching clears mucus and mucus plugs if any, from the nasal cavity permitting local absorption of the INS, thereby increasing its effectiveness. The use of saline douching has demonstrable benefit in symptom reduction in children and adults with seasonal rhinitis as well as in chronic rhino-sinusitis.<sup>26,27</sup> When saline nasal douching is advised along with INS, it needs to be done followed by application of INS.

## 3. Anti-leukotrienes

Clinical studies have demonstrated that the therapeutic profile of leukotriene receptor

antagonist or anti-leukotrienes is similar to antihistamines. However, their clinical response is less consistent than that observed with antihistamines. In addition, they are less effective than topical nasal corticosteroids.<sup>5</sup> They are well tolerated with frequent adverse events such as occasional headache, gastrointestinal symptoms or rashes. They also reduce bronchospasm and attenuate the inflammatory response, thus may be useful in patients with concomitant asthma.<sup>18</sup> In case of inefficacy or tolerability issues of oral antihistamines and/or intranasal corticosteroids, LTRAs may be considered.<sup>2</sup>

In 2008, the US FDA issued an alert about an increased risk of psychiatric events such as sleep disturbances, suicidal behaviour, or psychotic reactions associated with montelukast use, especially in children and adolescents. There have been safety concerns regarding increased risk of sleep disturbances in infants and children and depression or anxiety symptoms and psychotic reactions in adolescents.<sup>28</sup> Montelukast is recommended to be used for not more than 6 weeks.<sup>29,30</sup>

#### 4. Decongestants

Oral and intranasal decongestants are useful for relieving nasal congestion in patients with allergic rhinitis.<sup>2,18</sup> Intranasal decongestants allow delivery of intranasal drugs beyond the inferior turbinates and relieve nasal congestion via vasoconstriction within minutes, faster and with greater impact than intranasal steroids.<sup>5</sup> In pregnant women, they act as uterine stimulants and may trigger pre-mature labour, hence are contraindicated during pregnancy.<sup>31,32</sup> They are also contraindicated in patients with uncontrolled hypertension and severe coronary artery disease.<sup>2</sup> They should be only used as a short-term therapy (5-10 days); their prolonged use carries the risk of rhinitis medicamentosa (rebound nasal congestion).<sup>2,18</sup>

#### 5. Anticholinergics

Clinical evidence suggests use of anticholinergic drugs in presence of rhinorrhea.<sup>5,18</sup> It decreases rhinorrhea, particularly if it is of neurogenic origin rather than inflammatory. It usually has no effect on other nasal symptoms. They may be used as add-on if watery rhinorrhea persists despite using topical steroids and antihistamines.<sup>5</sup>

#### Pharmacological management of allergic rhinitis

Class	Mechanism of action	Available drugs	Recommendations and clinical use	Common adverse events
Antihistamines	Block histamine H1 receptors <sup>18</sup>	First generation Chlorpheniramine Diphenhydramine Triprolidine	Limited usage in specific clinical categories like infants below 6 months and pregnant women	Sedation <sup>18</sup>



	<b>Second generation drugs*</b> Oral Bilastine Cetirizine Desloratadine Ebastine Fexofenadine Levocetirizine Loratadine	<ul style="list-style-type: none"> <li>First-line therapy for mild to moderate intermittent and mild persistent AR<sup>5</sup></li> <li>Addition to intranasal steroids for moderate/severe persistent AR uncontrolled on topical intranasal corticosteroids alone, particularly when eye symptoms are present<sup>5</sup></li> <li>Additional treatment for runners / severe ophthalmic symptoms</li> </ul>	Primarily non-sedative; may cause sedation in few susceptible patients only <sup>18</sup>
	<b>Local</b> Azelastine (intranasal) Olopatadine (intranasal/intraocular)		Bitter aftertaste, headache, nasal irritation, and epistaxis <sup>18</sup>

\*Second generation antihistamines are listed in alphabetical order

<b>Corticosteroids (Intranasal)</b>	<ul style="list-style-type: none"> <li>Decreases the influx of inflammatory cells<sup>18</sup></li> <li>Inhibits the release of cytokines<sup>18</sup></li> <li>Reduces inflammation of the nasal mucosa<sup>18</sup></li> </ul>	Fluticasone furoate/propionate Mometasone Budesonide Beclomethasone Triamcinolone acetonide	<ul style="list-style-type: none"> <li>First-line therapy for moderate-to-severe persistent symptoms<sup>5</sup></li> <li>First line of therapy if presenting with severe nasal obstruction, possibly combined with a short-term nasal decongestant<sup>5</sup></li> </ul>	Long term use of budesonide is associated with risk of glaucoma Long term use of beclomethasone and triamcinolone are associated
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				with localized epistaxis and crusting
<p>Budesonide is the only drug with FDA pregnancy B category<sup>18</sup></p> <p>Mometasone and Fluticasone furoate molecule can be used in children above 2 years<sup>18</sup></p> <p>Fluticasone is mostly preferred in furoate formulation than propionate given its higher receptor affinity, better absorption in tissues and longer duration of action<sup>33</sup></p>				
<b>Decongestants</b>	<ul style="list-style-type: none"> <li>• Acts on adrenergic receptors<sup>18</sup></li> <li>• Causes vasoconstriction in the nasal mucosa<sup>18</sup></li> <li>• Decreases inflammation<sup>18</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Phenylephrine (systemic)</li> <li>• Pseudoephedrine (systemic)</li> <li>• Oxymetazoline and xylometazoline (local)</li> </ul>	<ul style="list-style-type: none"> <li>• Decongestants may be considered for SHORT TERM use in patients without improvement in congestion with intranasal corticosteroids<sup>18</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Sneezing and nasal dryness, drowsiness<sup>18</sup></li> <li>• Pseudoephedrine is associated with cardiac issues, primarily palpitations in hypertensive patients</li> <li>• Prolonged usage of local decongestants causes Rhinitis Medicamentosa so usage should not be more than a few days at a time<sup>18</sup></li> </ul>



<b>Chromones</b>	<ul style="list-style-type: none"> <li>• Inhibit the degranulation of mast cells and release of histamine<sup>18</sup></li> </ul>	Sodium cromoglycate	<ul style="list-style-type: none"> <li>• Children and adults with mild symptoms only and sporadic problems in season or on limited allergen exposure<sup>5</sup></li> <li>• Useful for individuals unable to take other medications, for example pregnant females<sup>5</sup></li> <li>• Eye drops are useful in conjunctivitis as topical therapy<sup>5</sup></li> </ul>	Epistaxis, nasal irritation, sneezing <sup>18</sup>
<b>Anticholinergics (Intranasal)</b>	Block acetylcholine receptors <sup>18</sup>	Ipratropium	<ul style="list-style-type: none"> <li>• Patients with watery rhinorrhoea despite compliance with intranasal steroid or intranasal plus antihistamine<sup>5</sup></li> </ul>	Dryness of the nasal mucosa, epistaxis, and Headache <sup>18</sup>
<b>Antileukotrienes</b>	Block leukotriene D4 receptor <sup>18</sup>	Montelukast	<ul style="list-style-type: none"> <li>• LTRAs should be considered when oral antihistamines and/or intranasal corticosteroids are not well tolerated or are ineffective in controlling the symptoms of allergic rhinitis<sup>2</sup></li> <li>• It may be particularly useful in patients with coexistent asthma<sup>18</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Elevated levels of alanine transaminase, aspartate transaminase, and bilirubin<sup>18</sup></li> <li>• Prolonged usage of montelukast has been</li> </ul>

				reported to have neuro-psychiatric disturbance sespecially in children <sup>28</sup>
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## Specific populations

### a) Children

- The principles of treatment for children are the same as for adults, but special care is advised to avoid the side effects in this age group. Doses of medication have to be adjusted with special considerations<sup>1</sup>
- In children, symptoms of allergic rhinitis can impair cognitive functioning and school performance. Use of oral H1-antihistamines may further impair cognitive function<sup>1</sup>
- Nasal saline irrigation is effective in the treatment of AR in children<sup>5</sup>
- Disodium cromoglycate is safe and is commonly used to treat allergic rhinoconjunctivitis in children<sup>1</sup>
- Oral and intramuscular glucocorticosteroids should be avoided in the treatment of rhinitis in young children. Intranasal glucocorticosteroid is an effective treatment for allergic rhinitis. However, their possible effect on growth is of concern<sup>1</sup>
- Mometasone and fluticasone furoate are the only intranasal corticosteroids which are indicated for children more than 2 years of age<sup>18</sup>
- Topical concomitant use of decongestant for 3 days is effective in children with significant nasal blockage<sup>5</sup>

### b) Pregnancy

- Caution is advised for all medications to be used in pregnancy since most of the medicines cross the placenta<sup>5</sup>
- Chromones have not shown teratogenic effects in animals and are the safest drug recommended in the first 3 months of pregnancy (they require multiple daily administration)<sup>5</sup>
- Budesonide is a FDA category B drug and is a preferred intranasal corticosteroid during pregnancy<sup>5,18</sup>
- There is considerable clinical experience with chlorphenamine, loratadine and cetirizine in pregnancy and may be used additionally<sup>5</sup>
- Decongestants should be avoided<sup>1</sup>
- The initiation of immunotherapy and up-dosing is contraindicated<sup>1</sup>

- Antihistamines and nasal steroids should only be used when the clinical imperative outweighs the potential harm to the child<sup>5</sup>

### c) Treatment of AR with asthma

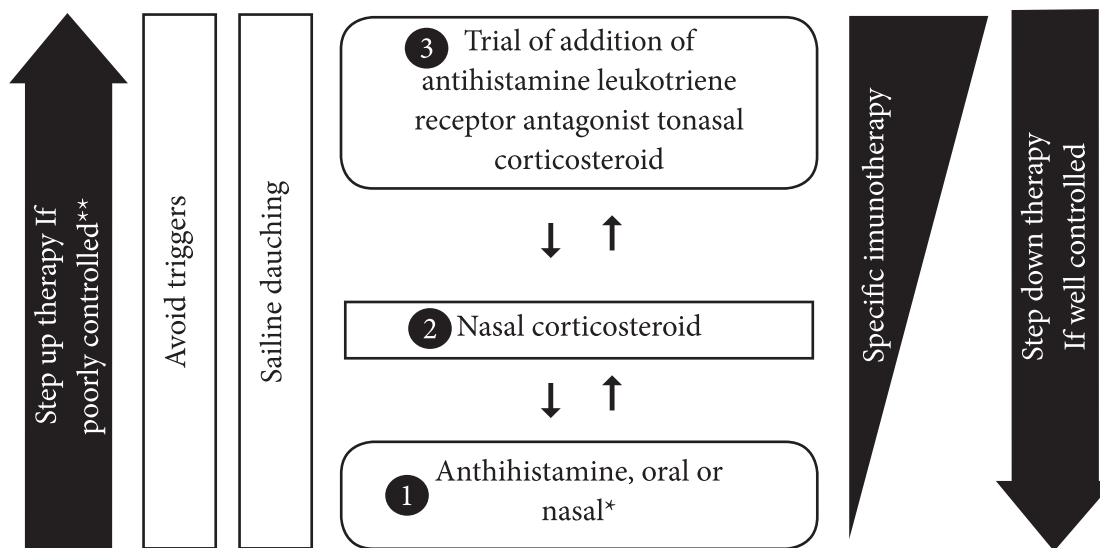
Optimal management of rhinitis may improve the symptoms of coexisting asthma especially if it is mild asthma coexisting asthma. Glucocorticoids and anti-leukotrienes are effective in the treatment of both AR and asthma. Inhaled corticosteroids are the drug of choice in the treatment of both allergic rhinitis and asthma. Oral administration of drugs, only in severe refractory cases, may affect both nasal and bronchial symptoms<sup>1</sup>.

### Combination therapy (Oral/Nasal)

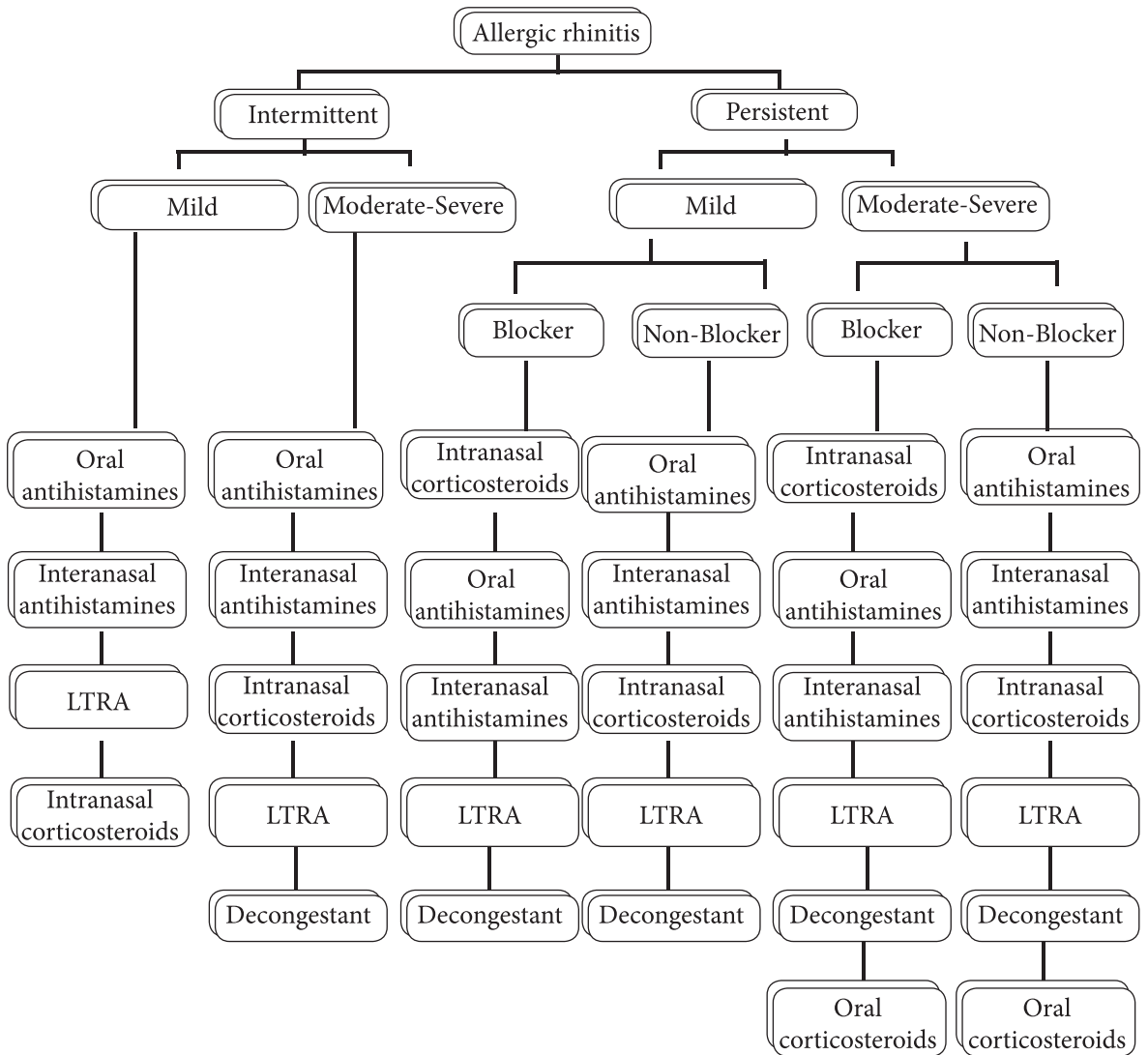
Combination therapy is indicated in patients with severe or persistent symptoms of AR. A wide range of combination therapies are available in the treatment of AR. These include combination of intranasal corticosteroid with oral antihistamines, intranasal corticosteroid and LTRA, intranasal anticholinergics and oral antihistamines, intranasal corticosteroids and intranasal decongestants, etc.<sup>34</sup> Clinical studies demonstrate that combination therapy is no more effective than an intranasal corticosteroid alone. However, combination of azelastine and fluticasone has shown superior efficacy results with faster relief with individual treatments in patients with more severe AR.<sup>18</sup>

### Recommended treatment approach for AR

\*Oral antihistamines may be better tolerated, while intranasal antihistamines have a more rapid onset of action. \*\*Reconsider diagnosis if not controlled within 1–2 weeks



## Step-wise pharmacological recommendations for AR



Recommendations are based on the order of drug preference

Caution:

- Oral corticosteroids, if used, should be administered for short course i.e. 5-7 days at full adequate dose
- Decongestants should be only used as a short-term therapy i.e. 5-10 days

Step-down treatment to be continued for 3 months

After tapering, continue with minimal dose of the drug as per the patient's needs

## Treatment recommendations

The panel provided the rationale for the recommendations and the consideration (in lines with the ARIA 2016) of all factors influencing the recommendations such as availability and certainty of clinical evidence, values and preferences, feasibility, acceptability by stakeholders, requirements for resources, feasibility, and effect on health outcomes.<sup>35</sup>

Treatment option	Recommendation		Assumed values and preferences	Explanations and other considerations
	A	B		
<b>Combination of OAH and INCS versus INCS alone</b>	In patients with SAR, either a combination of an INCS with an OAH or an INCS alone is recommended (conditional recommendation; low certainty of evidence)	In patients with PAR, we suggest an INCS alone rather than a combination of an INCS with an OAH is recommended (conditional recommendation; very low certainty of evidence)	<ul style="list-style-type: none"> <li>• The choice of treatment would depend mostly on patient preferences and local availability and cost of treatment.</li> <li>• In the majority of situations, potential net benefit would not justify spending additional resources.</li> </ul>	<ul style="list-style-type: none"> <li>• This is a conditional recommendation, and thus different choices will be appropriate for different patients. In settings in which the additional cost of an OAH is not large and/or patients' values and preferences differ from those assumed by guideline panel members, a combination therapy might be a reasonable choice, especially in patients whose symptoms are not well controlled with an INCS alone, those with pronounced ocular symptoms, or those commencing</li> </ul>

				<p>treatment because of likely faster onset of treatment effects.</p> <ul style="list-style-type: none"> <li>• This recommendation concerns regular use of newer and less sedative OAHs and INCSs in patients with SAR. For older OAHs with more sedative effects, the balance of desirable and undesirable effects may be different.</li> <li>• Currently available evidence suggests that there is no additional benefit from a combination therapy compared with INCS</li> </ul>
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				alone, and there might be additional undesirable effects. This recommendation is conditional because of sparse information and thus very low certainty of the estimated effects.
<b>Combination of INAH and INCS versus INCS alone</b>	In patients with SAR, either a combination of an INCS with an INAH or an INCS alone is recommended (conditional recommendation; moderate certainty of evidence)	In patients with PAR, either a combination of an INCS with an INAH or an INCS alone is recommended (conditional recommendation; very low certainty of evidence)	<ul style="list-style-type: none"> <li>• The choice of treatment will mostly depend on patient preferences and local availability and cost of treatment.</li> <li>• At initiation of treatment (approximately the first 2 weeks), a combination of an INCS with an INAH might act faster than an INCS alone and</li> </ul>	<ul style="list-style-type: none"> <li>• This is a conditional recommendation, and thus different choices will be appropriate for different patients.</li> <li>• In settings in which the additional cost of combination therapy is not large and/or patients value potential benefits more than any increased risk</li> </ul>

			thus might be preferred by some patients	of adverse effects, a combination therapy might be a reasonable choice.
<b>Combination of an INAH and an INCS versus INAH alone</b>	In patients with SAR, combination of an INCS with an INAH rather than an INAH alone is recommended (conditional recommendation; low certainty of evidence)	-----	<ul style="list-style-type: none"> <li>• This recommendation places higher value on additional reduction of symptoms and improved quality of life with a combination therapy compared with an INAH alone.</li> <li>• It places a lower value on avoiding additional cost (expenditure of resources).</li> </ul>	<ul style="list-style-type: none"> <li>• This is a conditional recommendation, and thus different choices will be appropriate for different patients.</li> <li>• In settings in which the additional cost of a combination therapy is large, an alternative choice (i.e., and INAH alone) might be equally reasonable.</li> <li>• One panel member thought that the recommendation should be conditional for either the intervention or comparison.</li> </ul>



<p><b>LTRA vs an OAH</b></p>	<p>In patients with SAR, either an LTRA or an oral antihistamine is recommended (conditional recommendation; moderate certainty of evidence)</p>	<p>In patients with PAR, an oral antihistamine rather than a LTRA is recommended (conditional recommendation; low certainty of evidence)</p>	<ul style="list-style-type: none"> <li>• The choice of an LTRA or oral antihistamine will mostly depend on patient preferences and local availability and cost of specific medications.</li> <li>• In many settings an OAH might still be more cost-effective, but this will largely depend on availability of generic LTRAs and the local cost of various newer-generation OAHs and LTRAs.</li> <li>• This recommendation places a higher value on possibly larger improvement of symptoms and quality of life with an OAH compared with an LTRA.</li> </ul>	<ul style="list-style-type: none"> <li>• Some patients with AR who have concomitant asthma, especially exercise-induced and/or aspirin-exacerbated respiratory disease, might benefit from an LTRA more than from an oral antihistamine</li> <li>• However, this recommendation applies to treatment of AR but not to treatment of asthma. Patients with asthma who have concomitant AR should receive an appropriate treatment according to the guidelines for the treatment of asthma.</li> <li>• This is a conditional recommendation, and</li> </ul>
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			<p>It places a lower value on possible increased risk of somnolence.</p>	<p>thus different choices will be appropriate for different patients based on their preferences for reduction of symptoms vs avoiding the risk of adverse effects. This might be more important for patients with PAR than those with SAR because they might use those medications for longer periods of time. Some patients with AR and concomitant asthma, especially exercise-induced and/or aspirin-exacerbated respiratory disease, might benefit from an LTRA more than from an OAH. However, this recommendation applies to treatment of AR but not to</p>
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				treatment of asthma. Patients with asthma who have concomitant AR should receive an appropriate treatment according to the guidelines for the treatment of asthma.
<b>INAH vs an INCS</b>	In patients with SAR, an INCS rather than an INAH is recommended (conditional recommendation; moderate certainty of evidence)	In patients with PAR, we suggest an INCS rather than an INAH (conditional recommendation; low certainty of evidence)	<ul style="list-style-type: none"> <li>• This recommendation places a higher value on likely small but greater reduction of symptoms and improvement of quality of life with an INCS compared with an INAH and a lower value on avoiding larger cost of treatment with an INCS in many jurisdictions.</li> <li>• This recommendation places a higher value on probably greater</li> </ul>	<ul style="list-style-type: none"> <li>• This is a conditional recommendation, and thus different choices will be appropriate for different patients.</li> <li>• Clinicians must help each patient to arrive at a decision consistent with her or his values and preferences, considering local availability and costs.</li> </ul>

			reduction of nasal symptoms with an INCS compared with an INAH, although the overall difference is likely small. It places a lower value on avoiding larger cost of treatment with an INCS in many jurisdictions.	
<b>INAH vs an OAH</b>	In patients with SAR, we suggest either an INAH or OAH (conditional recommendation; low certainty of evidence)	In patients with PAR, we suggest either an INAH or OAH (conditional recommendation; very low certainty of evidence)	<ul style="list-style-type: none"> <li>• The panel members acknowledged that the choice of treatment will depend mostly on patient preferences and local availability and cost of treatment.</li> </ul>	<ul style="list-style-type: none"> <li>• This is a conditional recommendation, and thus different choices will be appropriate for different patients. Clinicians must help each patient to arrive at a decision consistent with her or his preferences, considering local availability, coverage, and costs.</li> </ul>
INAH, Intranasal H1-antihistamine; INCS, intranasal corticosteroid; LTRA, leukotriene receptor antagonist; OAH, oral H1-antihistamine.				

## Recommendations: AR in children, pregnancy, and patients with asthma

### AR in children

- Mometasone and fluticasone furoate is recommended in children above 2 years of age
- Topical concomitant use of decongestant is effective for short term
- Oral and intramuscular glucocorticosteroids to be avoided in children
- Immunotherapy is recommended in subjects who have not adequately responded to maximal pharmacotherapy

### AR during pregnancy

- Chlorphenamine, loratadine and cetirizine are safe in pregnancy
- Intranasal corticosteroid budesonide is a category B drug
- Decongestants and initiation of immunotherapy are to be avoided
- Risk benefit ratio to be determined when using antihistamines and nasal steroids

### AR with asthma

- Intranasal corticosteroid is a preferred treatment option
- Anti-leukotrienes are also effective in AR with asthma

## Non-pharmacological treatment

Along with pharmacotherapy, the management of AR includes patient education on avoidance of allergens, adjunctive treatments, allergen-specific immunotherapy, and surgery.

### a) Allergen avoidance

The most effective primary prevention measure of AR is avoidance of relevant indoor and outdoor allergens. In case of seasonal AR, allergen avoidance is effective for e.g. a person with AR triggered by pollen is symptom-free outside pollen season.<sup>36</sup> Table 10 shows types of triggers and their common examples.

**Table 10: Types and examples of triggers**

Trigger type	Examples of triggers	Types of AR
Indoor	Mites – house dust mites, storage mites	Perennial
	Pets – cats, dogs	Perennial
	Pets – cats, dogs	Seasonal/Perennial
Outdoor	Pollens	Seasonal
	Occupational allergens –Flour, latex, laboratory animals, wood dust, chlorine, chloramine, enzymes, other airborne proteins	Perennial
	Animals – rodents, horses	Perennial
	Smoke, traffic pollution	Perennial

Sensitization to inhalant allergens is a strong risk factor for asthma and allergic rhinitis. Domestic allergen exposure in early life increases the risk of the subsequent development of sensitization and asthma.<sup>37</sup> Relocation of allergic patients to low allergenic environment was found to improve allergic symptoms.<sup>38</sup> Guidelines have differing opinions on the effectiveness of currently used measures, suggesting that single intervention measures carry no benefit. ARIA suggests using combination methods instead of single clinical or physical preventing method of avoidance.<sup>39</sup> Avoidance measures for house dust mite was found to be beneficial in highly motivated patients with multiple allergen avoidance measures.<sup>24</sup>

#### **Recommendations: Allergen avoidance**

- Allergen avoidance is strongly recommended for in the management of AR for pollens, house dust mites, pets, and environmental allergens
- The cornerstones of a clinically successful intervention strategy involve effective control measures and identification of patients who may benefit from early intervention in the natural history of disease. Moreover, effective control measures must ensure that low allergen environment is achieved and maintained over a prolonged period.

Allergen	Recommended avoidance measures
<b>House dust mites</b> <ul style="list-style-type: none"> <li>• Mite faecal particles were found to have major allergens Der p1, Der p 2 and Der p 7 of heavy particle size 15-40 mcg.</li> <li>• Maximum concentration of house dust mite remains in bed.</li> </ul>	<ul style="list-style-type: none"> <li>• Wash bedding and duvets regularly (every 1-2 weeks) at 55 -60°C to kill mites</li> <li>• Encase pillows and mattresses with mite impermeable encasings with size of 6 micrometer or less</li> <li>• Exposure of mattresses and rugs to detect strong sun light for more than 3 hours</li> <li>• Sufficient ventilation of dwellings to decrease humidity. Indoor relative humidity of below 50% is desirable</li> <li>• Replace carpets with hard flooring</li> <li>• Vacuum cleaning with High Efficiency Particulate Air (HEPA) filters may be of use</li> <li>• Keep away soft toys from bed room/ wash them at 55-60°C / freeze them in deep freezer</li> <li>• Replace fabric covered seating with leather or vinyl</li> <li>• Use wet mopping instead of dry dusting</li> </ul>

	<ul style="list-style-type: none"> <li>• Air purifiers are not useful in controlling house dust mite allergy</li> </ul>
<b>Pollens</b> <ul style="list-style-type: none"> <li>• Aerodynamic size of pollen is around 25-40 micrometers</li> <li>• Pollens get released from plants in the morning hours</li> <li>• In tropical country like India with varied flora, it becomes difficult to define a specific pollen season</li> </ul>	<ul style="list-style-type: none"> <li>• Keep windows closed at peak pollen time</li> <li>• Wear glasses with side covers to prevent pollen entering eye</li> <li>• Consider wearing mask</li> <li>• Install car pollen filter and pollen filter for air condition</li> </ul>
<b>Pets</b> <ul style="list-style-type: none"> <li>• Pet allergen particles are very light and range between 2-25 micrometers and hence they remain air borne for very long time and hence exposure level can be very high.</li> <li>• Unlike in mites, where dose response relationship is linear, response curve is bell shaped in cat allergen exposure<sup>40</sup>, and hence with high allergen exposure it could be protective effect.</li> </ul>	<ul style="list-style-type: none"> <li>• Pet removal is the only appropriate advice<sup>41</sup></li> <li>• Keep pets outdoor. If pet is not removed from home, exclude them from bed room</li> <li>• Vacuum carpets and mattresses regularly</li> <li>• Change clothes before going out if you had contact with any PET</li> <li>• Washing pets reduces level of allergen in the fur and dander samples for few days<sup>42</sup></li> </ul>
<b>Cockroach</b> <ul style="list-style-type: none"> <li>• It is observed that strategies that reduce cockroach allergen by environmental management are clinically beneficial to patients<sup>43</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Eradicate cockroaches with appropriate insecticidal bait</li> <li>• Seal cracks in floor and sealing</li> <li>• Enclose all food</li> <li>• Do not store waste in the home</li> <li>• Scrub floor with water and detergents</li> </ul>
<b>Moulds</b>	<ul style="list-style-type: none"> <li>• Use dehumidifiers, if relative humidity is consistently above 50%</li> <li>• Ensure that heating, ventilation or air conditioning systems are properly maintained</li> <li>• Use 5% ammonia solution to remove fungal contaminated surface</li> <li>• Replace carpets with hard flooring and replace wall papers with paint</li> <li>• Repair any indoor water damage immediately</li> </ul>

<b>Irritants</b>	<ul style="list-style-type: none"> <li>• Avoid exposure to vehicle exhaust pollution. PM10 / diesel exhaust can increase expression of allergenic pro inflammatory gene<sup>44</sup></li> <li>• Avoid excessive exposure to ambient indoor Volatile Organic Component (VOC) from new woods and many synthetic materials</li> <li>• Avoid Incense sticks and Perfumes and Room fresheners</li> <li>• Avoid smoking</li> </ul>
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### **Lifestyle and allergic disorders:**

Over the last 60 years, the extent of increase in the incidence of allergic disorders is overwhelming, which is only going to continue rising in future. This allergic disease burden is not only because of exposure to allergens but also the way we have chosen to live. Primary hygiene and excessive sanitisation, furnishing of home, time spent on-screen, and dietary modifications have led to secondary complications.<sup>45</sup> A few lifestyle recommendations that may help prevent any allergic disorders are given below -

- Increase time spent outdoors
- Take up outdoor activity or physical exercise
- Spend more time in the sun for vitamin D
- Include healthy dietary habits
- Yoga exercises

Yogic breathing techniques are also known to have non-pharmacological supportive role in the management of asthma and related disorders. However, it should be made clear to the patients and respective family that yoga only has an adjunctive role and cannot not replace pharmacotherapy.<sup>46</sup>

### **b) Adjunctive therapy**

In the management of AR, a simple and inexpensive non-pharmacological therapy commonly recommended is nasal irrigation using saline solution. There doesn't exist any clear differentiation on use of nasal saline irrigation with respect to types of AR – mild, moderate or severe. However, nasal irrigation can be applied in addition to pharmacologic treatment and/or immunotherapy in moderate to severe forms of AR. Clinical evidence is still warranted in using nasal irrigation alone as initial symptomatic therapy in mild AR. It can help reducing medicine consumption and associated medical costs.<sup>47</sup>

### **Nasal irrigation**

Spectrum of application – nasal spray or douching i.e. rinsing the nose with 250 ml of saline solution.<sup>47</sup>



The mechanical stimulus involved in the spray application of saltwater plays a role in the achieved effect by causing neuronal changes in the immunologic process. This could explain the greater effect of the spray application.<sup>47</sup>

Type of solution - Isotonic rinsing solution is generally preferred to the hypertonic solution because optimal mucociliary transport can only be ensured at a neutral pH.<sup>47</sup>

### **Clinical evidence on effectiveness of nasal irrigation treatment**

A meta-analysis of prospective, randomized, controlled trials was conducted to assess the effects of saline nasal irrigation on four parameters, nasal symptom score, medicine consumption, mucociliary clearance time, and quality of life. The results demonstrated decrease in nasal symptom score by 27.66%, improvement in mucociliary clearance time by 31.19%, decrease in medicine consumption by 2.99%, and improvement in quality of life by 27.88%.<sup>47</sup>

Also, it was observed that application of spray with a much smaller volume yielded more distinct improvements (23%-45%) than the use of nasal irrigation with larger volumes (200–400 mL, 3.2 and 45.5%).<sup>47</sup>

### **Role of nasal saline irrigation**

The mechanism of action is unknown. The proposed mechanisms for improvement of mucosal function is<sup>47</sup> –

- Direct physical cleansing by flushing out thick mucus, crusts, debris, allergens, air pollutants, etc.
- Removal of inflammatory mediators
- Better mucociliary clearance by improving ciliary beat frequency

#### **Recommendations: Nasal saline irrigation**

- Beneficial as adjunctive therapy in the management of AR in both children and adults
- It may help in reducing the need of pharmacotherapy

### **c) Allergen Immunotherapy (AIT)**

Allergen Immunotherapy (AIT) is the administration of gradually increasing quantities of an allergen vaccine to an allergic subject, reaching a dose which is effective in ameliorating the symptoms associated with subsequent exposure to the causative allergens.<sup>48</sup>

AIT is the only treatment that can modify the course of an allergic disease either by preventing the development of new sensitivities or by altering the natural history of disease or disease progression.<sup>48</sup>

AIT provides a window of opportunity of multiple benefits. Following are the benefits of AIT:

- AIT is the only available curative tool
- AIT can alter the course of allergic disease for good
- AIT is capable of changing the Th2 status (allergic) to Th1 status (normal)

- AIT is capable of impeding the onset of asthma in cases of allergic rhinitis
- AIT can impede poly-sensitization
- AIT is capable of providing medication-sparing effect
- There is enough evidence that the benefit of AIT continues to be present for a long tenure even after concluding the therapy
- AIT has the capacity to provide long-term protective benefit against development of various other allergic conditions

For an effective AIT, a proper specific diagnosis must be established. History and clinical examination are crucial but it is erroneous to make a specific diagnosis based on history alone. Causative allergens have to be determined by conducting specific allergy detection tests and must be correlated with clinical manifestations.

Skin Prick Tests (SPT) can provide evidence of causative allergens and will demonstrate the presence of allergen-specific IgE. Serum specific IgE (ssIgE) estimation can provide a quantitative evidence of the antigen-specific antibodies in the blood circulation of an allergic individual. Advantage of ssIgE estimation is that one blood sample is enough for the assay. Availability of normal skin is not a requirement. There need not be a curfew on immunosuppressive drugs when the test is conducted. Result of ssIgE may be negative but the patient may have potential allergy. A positive result is an excellent evidence of specific allergen sensitivity. SPT done with good quality allergens is the best diagnostic option. SPT offers both qualitative and quantitative measure of an allergen activity. It is fairly simple, safe, cost-effective and reliable. SPT is hardly an invasive procedure.

Subcutaneous AIT (SCIT) or Sublingual AIT (SLIT) as a choice is left to the clinician and the patient considering various angles of therapy and tenure. Possibility of systemic reactions and anaphylaxis that is a major concern in SCIT, is eliminated in SLIT. Proper diagnosis, good quality allergens, compatible and proper combination of allergens and compliance are crucial to successful treatment by AIT.

With evidence of SLIT providing excellent therapeutic benefit to patients of AR and allergic asthma and especially with its safety profile, it has emerged and has become the option of choice for AIT. SCIT has to be administered by a medical professional. The best option for SCIT is it being administered by the allergy specialist who would have done diagnostic evaluation and would have prescribed AIT. In India, it is practically not feasible. Patient has to commute and spend mandatory time in the doctor's office. So SCIT demands quite a bit of time and effort for administration of each dose. In the initial and build-up phase, injections are quite frequent. If the scheduled gap between injections is prolonged for any reason and if the following higher dose is administered, there is a risk of a systemic reaction especially if the sensitivity is high. Danger of anaphylaxis is a possibility. For AIT to become effective, effort is necessary to reach highest possible concentration and dose. So, compliance and safety are a major concern in SCIT. **For food allergy and at present SCIT is not the accepted option.**

Considering all these difficulties, SLIT appears to be a safe and viable option. Much higher dose and concentration need to be achieved in SLIT for it to become therapeutically effective. Proper combination of allergens in the SLIT vaccine is necessary. Treatment happens in the comforts of the patient's home. It is the biggest benefit. This itself must not become a hindrance to the maintenance of treatment. SLIT works on trust. Patient and the family must be made to understand this fundamental aspect. Patient must also be made to understand that SLIT contains the same allergens to which the patient is allergic and that it is directed to shift the patient's status of allergy to normalcy, and that it does not directly relieve the symptoms like the medication does. SLIT can be started above 5 years of age under discretion of the allergy specialist and the recommended duration of SLIT is 5 years.

Process of AIT commences from the very first dose but it generally takes some time for its beneficial effect to reflect on the symptoms. Allergic Rhinitis, Allergic Conjunctivitis, Allergic Asthma, Sting Reactions are the classical indications for AIT. AIT may be a good option in some selected cases of drug allergy. Anaphylaxis and angioedema are conditions where AIT if possible, would be a boon to the patient and may actually be a life-saving tool. AIT has been approved as a major option of management for Atopic Dermatitis. When atopic dermatitis is so severe that it affects social and professional life of a patient, even if reasonable benefit can be obtained, AIT will be great. Selected cases of Migraine and Meniere's disease especially with co-morbid allergy conditions, would be worth the while candidates for AIT<sup>49-60</sup>.

Beneficial effect of AIT will not be appreciable if it is administered in cases of mild allergy conditions. When the disease is persistent and when the symptoms are moderate or moderate-severe, AIT would be a great option in addition to medical management.

Successful AIT will initiate a marked enhancement of protective blocking IgG antibodies. AIT will blunt the serum concentration of specific IgE antibodies. There will be a down-regulation of inflammatory cell recruitment, activation and mediator release. These will modify the T-Lymphocyte response to the benefit of the patient. Th2 response will get down-regulated resulting in enhanced Th1 response.<sup>61</sup>

Poly-sensitization is a common feature in patients.<sup>62</sup> Poly-sensitization happens over a course of period. Poly-sensitization can be prevented by institution of AIT early. Children are the best candidates. Remodulation of the airways that happens due to persistent allergic inflammation is prevented with effective and early AIT. AIT also makes it cost effective in the long run. In patients where SPT results show positive response to too many allergens, only major allergens must be chosen considering cross reactivity profile and clinical correlation. This is to be decided by the allergy specialist.

### **Allergens and Triggers:**

Allergens have to be differentiated from non-allergic triggers. A clear distinction is necessary. Non-allergic triggers must never be included in prescriptions for immunotherapy. In fact, they should not even be included in the tests for allergy. Many of them are inanimate subjects. They do not contain any allergen themselves. Various dusts other than house dust, smokes, fumes, perfumes, dhoop, incense, plastic, paper, cement, gravel, nylon and polyester are such

substances. Low molecular substances like monosodium glutamate (MSG), colouring agents and food additives are not to be included in SPT and hence AIT.

Allergens are substances which initiate and cause an allergic reaction in an individual who has developed specific IgE antibodies to those substances. They are protein in nature. They can be broadly classified into three main groups. They are injectants, ingestants and inhalants. In AR and other airway allergic conditions, inhalants are the predominant allergens.

### **SLIT as Food Allergen Immunotherapy:**

With SLIT, the food protein is delivered sublingually in a liquid form and then usually held for 2 minutes and swallowed. SLIT is thought to capitalize on the tolerogenic antigen-presenting cells in the oral mucosa. It is further thought that SLIT efficacy can be enhanced by exposure to the food protein in its intact form before possible epitopes are broken down through gastric digestion.<sup>63,64</sup>

Both in adults and in children, a judicious combination of AIT, medical management and correction of allergen-rich environment have become the hallmark of providing complete solution to the persistent suffering of allergy patients. Wherever necessary, an effort must be made to change the existing life style to suit the prevailing condition to achieve best results. With better understanding, better techniques and better quality of allergens, AIT can only become a more powerful and sustaining tool and option of management of allergic diseases.

### **Allergens for SLIT:**

**Allergen products are restricted to only trained physicians/professionals who have obtained practical training in allergy diagnosis and immunotherapy.**

In India, SLIT is also used as off label treatment. It can be considered legal for trained physicians to prescribe it and for a patient to take it as prescribed. **Indian drug rules permit a doctor to prescribe, compound, dispense or dilute FDA approved products for his patients but cannot sell or commercialize.**

### **The Drug Rule states:**

THE DRUGS AND COSMETICS RULES, 1945 as corrected up to the 30th November, 2004, which clearly indicates that private practitioners and hospitals are exempted from obtaining a license for dispensing drugs to their patients.

Chapter IV of the Drugs and Cosmetics Act, 1940, Amended Act, 1955, 1960, 1962, 1964, 1972, 1982, 1986, 1995

Part XI of The drugs and Cosmetics Act, 1945 (as corrected up to 30th Nov. 2004) deals with exemption of IV of the Drugs and Cosmetics Act, 1940

### **Extent and Conditions of Exemption:**

All the provisions of Chapter IV of the Act and the Rules made there under, subject to the following conditions:

5[(1)The drugs shall be purchased only from a dealer or a manufacturer licensed under these rules and records of such purchases showing the names and quantities of such drugs

together with their batch numbers and the names and addresses of the manufacturers shall be maintained. Such records shall be open to inspection by an Inspector appointed under the Act, who may, if necessary, make enquiries about purchases of the drugs and may also take samples for test.

#### **Recommendations: Allergen Immunotherapy**

- Proper diagnosis, good quality allergens, compatible and proper combination of allergens and compliance are crucial to successful treatment by AIT
- AIT is a great option in addition to medical management in persistent cases and the symptoms are moderate or moderate-severe,
- Causative allergens must be identified by conducting specific allergy detection tests and must be correlated with clinical manifestations
- SPT done with good quality allergens is the best diagnostic option before AIT. It is fairly simple, safe, cost-effective and reliable
- Although a clinician can choose between SCIT or SLIT, the safe and viable option is SLIT as SCIT has the possibility of systemic reactions and anaphylaxis
- SLIT can be started above 5 years of age under discretion of the allergy specialist and the recommended duration of SLIT is 5 years

#### **d) Surgical management of allergic rhinitis**

In patients with allergic rhinitis, the predominant complaint of nasal obstruction can be very distressing. In the management of allergic rhinitis, surgical interventions are aimed at the underlying nasal obstructive component and other anatomical changes, especially in patients with nasal obstruction refractory to clinical treatment, and for those who exhibit inferior turbinate hypertrophy.<sup>65,66</sup> The inferior turbinate has proven to be the most important contributor to nasal obstruction. The main objective of the surgical treatment is to augment the nasal airway by primarily reducing turbinate tissue to improve nasal obstruction and reduce static obstruction.<sup>65</sup> Observational studies have demonstrated clinical benefits of surgery as indicated by potential improvement in breathing and consequent improvement in quality of life, as well as better distribution of topical medications in the nasal cavity.<sup>67</sup> Surgery may also be indicated for anatomic obstruction, such as septal spurs, polyposis, chronic sinusitis, which are concomitant with allergic rhinitis.<sup>65</sup>

Sinonasal imaging, particularly CT scan is essential to define sinus anatomy prior to surgery in patients with acute rhinosinusitis, nasal polyposis, chronic rhinosinusitis, or complicated rhinosinusitis. CT imaging allows visualization of bony anatomy of the sinuses and patterns of bone destruction, as well as any formation of cartilaginous or bone matrix.<sup>67</sup>

A meticulous operative technique considering the superficial mucosal layers should be employed with conservative reduction of lower turbinate tissue in order to reduce adverse outcomes such as empty nose syndrome and maximizing surgical outcomes and improving symptoms.<sup>68</sup>



## Surgical techniques

Reduction of the inferior turbinate is the primary means of augmenting the nasal airway in allergic rhinitis patients.<sup>65</sup> A number of techniques for turbinate reduction have been performed, including partial or total turbinate resection, cauterization, cryotherapy, laser therapy, and radiofrequency ablation. These traditional techniques have disadvantages like bleeding, crusting, synechia formation, osteitis, inadequate volume reduction, and atrophic rhinitis.<sup>69</sup>

There is no gold standard surgical technique for treatment of nasal obstruction in allergic rhinitis; instead the surgeon should be familiar with an armamentarium of surgical techniques.<sup>65</sup> Individualized approach for selection of surgical technique is employed; which depends on the factors such as greater or lesser bony or mucosal components of the inferior turbinate, surgeon's experience, available equipment, and cost.<sup>67</sup>

- a) **Turbinoplasty** may be effective in patients with persistent allergic rhinitis refractory to intranasal steroids and antihistamines.<sup>70</sup> The respiratory mucosa is essential for proper physiologic functioning of the turbinates, such as warming and humidification of inspired air and mucociliary clearance. Thus, an ideal turbinate surgery effectively reduces the volume of the submucosal stromal tissue and preserves the overlying respiratory epithelium and prevents complications.<sup>69</sup>
- b) **Submucosal turbinectomy**, a form of turbinectomy, has an excellent effect on reduction of nasal congestion, sneezing, and rhinorrhoea in patients with perennial allergic rhinitis. The major advantage of this technique, is that it reduces the infiltration of various inflammatory or allergy-related cells.<sup>71,72</sup> In addition, surgical damage to a peripheral nerve fibre (branch of postnasal nerve) might reduce the allergic symptoms such as sneezing and hypersecretion.<sup>71</sup>
- c) **Radiofrequency turbinoplasty** has demonstrated significant subjective and objective improvement in nasal congestion through rhinomanometry, compared to intranasal steroids even after 12 months from surgery.<sup>70</sup>
- d) **Turbinoplasty in combination with medical therapy** i.e. intranasal corticosteroid and antihistamine, demonstrates greater efficacy in improving the nasal flow, when compared with medical treatment alone in persistent moderate-to-severe AR.<sup>73</sup>
- e) **Radiofrequency turbinoplasty is an effective and safe tool for treating allergic rhinitis refractory to medical therapy.**<sup>74</sup> It has been associated with significant improvement in nasal stuffiness, nasal obstruction and mouth breathing.<sup>75</sup> The outcome of radiofrequency turbinoplasty has been observed to decline and worsen with time.<sup>74,75</sup> However, the improvement in symptom scores was significant 5 years after surgery.<sup>74</sup>
- f) **Septoplasty** alone has little role in the treatment of nasal obstruction for allergic rhinitis. **Endoscopic sinus surgery** is an important treatment method for allergic rhinitis when it contributes to chronic sinusitis, nasal polyposis, or allergic fungal disease.<sup>65</sup>

In addition, vidian neurectomy and posterior nasal neurectomy is also essential. They are helpful in refractory cases and are being used in many centres.<sup>76</sup>

### **Recommendation: Surgery for management of AR**

- In allergic rhinitis, the major complaint of nasal obstruction significantly impacts the quality of life of the patients
- Surgery is not a conventional treatment method for allergic rhinitis. It may only be exercised as an adjunctive option for relieving nasal obstruction in perennial allergic rhinitis, that is not responding to medical therapy alone
- No gold standard surgical treatment method exists. Most of the existing literature centres on reduction of the inferior turbinate for symptomatic improvement in patients afflicted with allergic rhinitis
- Endoscopic sinus surgery and septoplasty have hardly any advantage in the management of allergic rhinitis, unless when observed in conjunction with other conditions such as rhinosinusitis or polyposis
- Surgical management hardly finds any mention in international guidelines for allergic rhinitis and the evidence can be best described as 2A

### **Referral to a specialist**

Referral to a specialist is indicated in the following cases –

- Nasal blockage unrelieved by pharmacotherapy or structural abnormalities, such as septal deviation, sufficient to render nasal therapy difficult should be seen by a surgeon<sup>11</sup>
- Patients with unilateral symptoms, heavily blood stained discharge or pain, new onset nasal polyps, pressure effects on orbit or orbital cellulitis<sup>5</sup>
- Persistent symptoms despite aggressive medical therapy in order to confirm the diagnosis of AR versus mixed or non-AR and/or for consideration of allergen immunotherapy, if appropriate<sup>11</sup>

### **Prevention of allergic rhinitis**

The primary prevention measure in AR is total allergen avoidance. Secondary prevention halts the progression of disease in individuals who are at high risk for the development of allergy, for example, the prevention of asthma in individuals with rhinitis, or evidence of allergen sensitization. The objective of tertiary prevention is to prevent exacerbations and improve disease control and reduce medication.<sup>77</sup>

#### **Probiotics in allergic disorder**

Although health benefits of taking probiotics have been reported in allergic disorders, it is still early to draw any conclusions. In 2015, the World Allergy Organization (WAO) applied Grading of Recommendations, Assessment, Development and Evaluation approach to develop evidence-based recommendations for using probiotics in the prevention of allergic diseases. Findings were reported in a systemic review of 29 RCTs by Cuello-Garcia et al. The panel observed that there is insufficient evidence to support recommendation to use probiotics in primary prevention of allergic diseases. However, they suggested the use of probiotics in pregnant/lactating women and infants with a family history of allergic

disease. Although strain-specific activity of different bacterial species is recognized, no recommendations were made by the WAO regarding strain or dose of probiotics in light of insufficient evidence.<sup>78</sup>

#### **Recommendations: Prevention of AR**

- Breast-feeding for 6 months for all infants irrespective of their family history of atopy
- No antigen avoidance diet in pregnant or breast-feeding women for prevention of development of allergy in children
- Total avoidance of environmental tobacco smoke or passive smoking in children and pregnant women
- Reduction of early life exposure to house dust mite in infants and preschool children
- Specific prevention measure for eliminating or reducing occupational allergen exposure for individuals exposed to occupational agents
- Physical and chemical preventative measures to reduce exposure to house dust mites in patients with AR and/or asthma sensitive to house dust mite allergens
- Avoid exposure to indoor molds in patients with allergy to molds
- Avoid exposure to animal dander in patients with AR caused by animal dander
- Immediate and total cessation of exposure to occupational allergen in patients with occupational asthma

#### **D) Comorbid conditions in AR**

Allergic rhinitis is a long-lasting condition, which has a significant impact on the quality of life of the patients.<sup>2</sup> It usually goes undetected in the primary care setting, which further complicates the condition. Moreover, patients themselves are unable to recognize the impact of the condition on their daily functioning.<sup>2</sup> Besides nasal and extra nasal symptoms, patients may often complain of experiencing generalized symptoms such as fatigue, mood changes, depression, anxiety, etc. Severe cases of allergic rhinitis have been associated with significant impairment of school performance in children and work productivity in adults.<sup>79</sup>

Quality of life (QOL) is defined as 'the subjective value a person places on satisfaction with his or her life'.<sup>80</sup> According to World Health Organization, QOL includes 'psychological and social functioning as well as physical functioning. It also comprises positive aspects of well-being as well as negative aspects of disease or infirmity'.<sup>79</sup> Health-related QOL (HRQOL), on the other hand, focuses on a part of QOL which is influenced by the disease. HRQOL focuses on the patient's perception about the functional effects of a disease and the treatment and it measures impairments which significantly impact the patient's life. Overall, HRQOL can be described as a patient's subjective perception of the impact of the disease and its treatment on their physical, psychological and social functioning and overall well-being.<sup>79,80</sup>

It is a patient's perception of the burden of the disease on his/her life that forms the basic motivation to seek medical assistance and undergo appropriate therapy. This disease burden is usually described by patients in terms of symptoms and impact on QOL.<sup>80</sup>

In patients with allergic rhinitis, adverse effects of the condition on the QOL include



impairment of physical and social functioning, disturbed sleep, daytime somnolence and fatigue, irritability, depression; and attention, learning, and memory deficits.<sup>80</sup>

**a) AR and the physical domain of QOL**

In patients with AR, sleep disturbances including difficulty falling asleep, staying asleep, and awakening refreshed, are one of the significantly impaired component, mediated via nasal obstruction.<sup>80</sup>

**b) AR and the emotional domain of QOL**

There have been multiple reports of associations of nasal allergies with mood and anxiety syndromes. Several proposed mechanisms have suggested allergic reactions to trigger the immune system and cytokines and then exacerbate psychiatric symptoms.<sup>80,81</sup>

**c) AR and the mental domain of QOL**

Allergic rhinitis significantly impairs attention and learning, thus negatively affecting cognitive functioning and decreased day-time school performance.<sup>80</sup>

**d) AR and other domains of QOL**

In patients with AR, impaired QOL can also be linked to reduced sense of smell. It may affect a patient's ability to taste, and loss of pleasures of eating. It may also risk a person's health as a result of inability to estimate quantity of sugar and salt in food, and ending up adding larger quantities, or inability to identify spoiled food or recognize gas leakage.<sup>80</sup>

Lastly, allergic rhinitis can interfere with family and social relationships and also increase health-care associated medical costs.<sup>80</sup>

**Comorbidities of allergic rhinitis**

**1) Asthma**

Allergic rhinitis and asthma frequently coexist. Their association is clinically significant as indicated by common epidemiologic, physiologic, and pathologic mechanisms.<sup>82,83</sup> Both these conditions are systemically linked by common and interrelated inflammatory processes of the upper and lower airways.<sup>84</sup> In addition, treatment for one entity results in beneficial effect against the other. According to the survey reports, 38% of patients with allergic rhinitis have asthma; and up to 78% of asthma patients have allergic rhinitis.<sup>82</sup>

Concomitant allergic rhinitis in patients with asthma has been associated with poor asthma control, including higher rate of asthma attacks, increased asthma exacerbations, more emergency room visits, higher medical costs compared with asthma patients without AR.<sup>84</sup>

Therefore, it is suggested that patients with persistent allergic rhinitis should be evaluated for asthma on the basis of history and chest examination and pulmonary function tests.<sup>83</sup>

**2) Associated rhinosinusitis**

Studies have demonstrated a strong correlation between nasal allergies and sinus issues, indicating nasal allergies to be a common contributing factor to acute or chronic sinus problems. It has been reported that 50% of adults and 43% of children (4- 17 years) diagnosed with AR had sinus problems.<sup>85</sup>

### **3) Allergic conjunctivitis**

Observational studies have demonstrated that 52% of allergic rhinitis patients (women more often than men) report ocular symptoms, including troublesome symptoms such as itchy eyes (51%), watery eyes (39%), red eyes (7%) and swollen eyelids (4%).<sup>86</sup> In patients with allergic rhinitis, ocular symptoms may result from allergen contact with the eye and nasal ocular reflexes; both the mechanisms trigger a significant inflammatory response.<sup>87</sup>

### **4) Associated skin rashes**

Atopic dermatitis and allergic rhinitis are atopic disorders sharing common pathogenesis i.e. IgE sensitization in response to environmental triggers.<sup>88</sup> Atopic dermatitis is an important risk factor in the development of other allergic reactions.<sup>89</sup> The combined frequency of atopic disorders including AR, dermatitis, skin rashes, etc. is estimated to be 20%.<sup>89</sup>

### **5) Otitis media**

Otologic symptoms such as ear fullness and pressure, otalgia or ear pain, etc. are commonly experienced by patients with AR.<sup>90</sup> Epidemiological studies have reported prevalence of AR in patients with chronic or recurrent otitis media with effusion to be 24% to 89%.<sup>91</sup> Moreover, AR and otitis media are associated by the involvement of type 1 IgE-mediated inflammation in the middle ear space, epidemiological associations, and the beneficial effect of AR treatment on clinical outcomes of otitis media.<sup>90</sup>

### **6) Chronic upper airway cough syndrome (also referred to as postnasal drip syndrome)**

Persistent allergic stimulation can cause direct mucosal effects in the larynx; leading to mucus production in both the upper and lower respiratory systems and mucus trafficking, which results in a range of laryngeal symptoms, including cough.<sup>92</sup> Cough sensitivity in patients with allergic rhinitis may result from subclinical inflammatory changes within the lower airways.<sup>93</sup>

### **7) Associated gastroesophageal reflux**

The impact of AR on GERD has been evaluated by a few studies. AR on nasal mucosa can cause similar effects on laryngeal mucosa including congestion, oedema and excessive mucous secretion, which leads to symptoms of laryngopharyngeal reflux (LPR), a subgroup of GERD. In patients with AR, throat itching and posterior nasal dripping lead to increased frequency of swallowing, which exacerbate the reflux. However, more conclusive research is required.<sup>94</sup>

### **8) Associated headaches**

Headaches are one of the most common bothersome symptoms associated with nasal allergy attacks.<sup>85</sup> Although, headache is not a typical symptom of allergic rhinitis, however, it may cause sinus headache.<sup>95</sup>

### **9) Sleep disturbances**

Sleep-related symptoms are commonly observed in patients with allergic rhinitis.<sup>96</sup> Nasal obstruction is an independent risk factor for obstructive sleep apnoea. Rhinitis alone is associated with mild obstructive sleep apnoea, but commonly causes micro-arousals and sleep fragmentation.<sup>97</sup> Sleep disturbances majorly contribute to the overall disease morbidity and the loss of work productivity associated with allergic rhinitis.<sup>96</sup>

## 10) Associated sexual dysfunction

Decrease or loss of sexual function in many chronic diseases, including allergic disorders, have significant impact on the quality of life. Clinical studies demonstrate significantly lower scores of the Female Sexual Function Index in women with symptomatic allergic rhinoconjunctivitis; and higher scores of International Index of Erectile Function in men with treated allergic rhinoconjunctivitis and controls compared to symptomatic patients.<sup>86</sup>

### Recommendations: Comorbid condition

- Allergic rhinitis frequently coexists with comorbid conditions like asthma, rhinosinusitis, conjunctivitis, atopic dermatitis, sleep problems, etc.
- A step-wise diagnostic and treatment approach for each suspected comorbid condition is recommended.

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