

# Recent Trends in the Diagnosis and Management of Allergic Rhinitis

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## Summary

Allergic rhinitis is a global health issue and its prevalence is increasing. Allergic rhinitis and asthma coexist in many patients. Allergic rhinitis is an Ig E mediated reaction. Prostaglandins and Leukotriens do not play a significant role in the pathogenesis of allergic rhinitis. Skin prick test and Enzyme linked immunosorbent assays (ELISA) are useful as diagnostic tests. The three major modalities of treatment for allergic rhinitis are allergen avoidance, pharmacotherapy and immunotherapy.

**Key Words:** Allergic rhinitis, Diagnosis, Management, Pharmacotherapy, Immunotherapy, Asthma

## Introduction

Allergic rhinitis is one of the global health issues affecting 10% to 25% of the world's population<sup>1</sup>. Epidemiological studies indicate that the prevalence of allergic rhinitis may be increasing<sup>2</sup>. Allergic rhinitis has a significant morbidity on account of the widespread mucosal inflammation affecting several target organs and the generalized malaise it causes, it impairs the work and school performance. The socio-economic impact of allergic rhinitis is substantial, if we take the cost of managing these patients as well as the reduced productivity and absenteeism from work due to allergic rhinitis<sup>3</sup>. One or more of the following symptoms namely sneezing, rhinorrhoea, itching and nasal congestion characterizes allergic rhinitis. It may also be associated with itching of the eyes, ears and throat and postnasal drip.

## Classification

Allergic rhinitis can be classified as seasonal or perennial based on the timing and duration of allergen exposure. Seasonal allergic rhinitis is common in UK and other European countries, whereas in other parts

of the world, perennial variety is very common. In Malaysia perennial variety is the commonest. A new classification has been proposed based on the ARIA (allergic rhinitis and its impact on asthma) guidelines<sup>4</sup>. The new classification divides allergic rhinitis into "intermittent" or "persistent" disease. Intermittent means the symptoms are present less than 4 days a week or for less than 4 weeks. Persistent means the symptoms are present more than 4 days a week and for more than 4 weeks.

## Allergic rhinitis and asthma

Allergic rhinitis and asthma often co-exist. Approximately 75% of patients with allergic asthma and 40% of the patients with non-allergic asthma have persistent rhinitis. Twenty percent of the patients with persistent allergic rhinitis have signs of asthma<sup>5</sup>. In a study done in Malaysia<sup>6</sup> 65% of the adult asthma patients had associated rhinitis.

## Pathological feature

Allergic rhinitis is characterized by two-phase allergic reaction. Initial sensitization phase where allergen

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presentation results in antibody (IgE) formation and triggering of humoral response. In the second clinical disease phase, there is manifestation of symptoms in response to subsequent antigen exposure. The early phase of clinical disease is largely mediated through mast cells and in the late phase there is involvement of cellular infiltration and mediator release<sup>7</sup>. In the early phase, the mast cells release mediators as a result of antigen cross linking of adjacent IgE molecules bound to mast cell surfaces. This results in degranulation of mast cells, leading to the characteristic symptoms of rhinitis, which include rhinorrhoea, nasal obstruction, nasal itching, and sneezing.

Prostaglandin and leukotrienes are implicated in conditions of upper and lower airways. A recent study<sup>8</sup> has shown that level of prostaglandin and leukotriene are lower in patients with allergic rhinitis and the authors conclude that these mediators do not play a significant role in the pathogenesis of rhinitis.

#### **Diagnosis**

**History:** Keystone of diagnosis is a proper history, which should include pattern, chronicity, seasonal, precipitating factors, occupational, and environmental history. Pre-existing, co-existing conditions and medication history also should be elicited<sup>9</sup>.

**Physical examination:** Nasal mucosa may be oedematous and it may appear pale or purplish in colour. The nasal secretion will be clear or watery and mucoid. There may be associated nasal polyps. Ears have to be examined for the presence of retraction of the tympanic membrane or fluid in the middle ear. Ocular examination may show conjunctival congestion. Children may have infraorbital skin discolouration, and transverse nasal crease because of repeated rubbing of the nose.

#### **Diagnostic tests**

**Non-specific tests:** Total IgE level and circulating eosinophil counts are not much useful in the diagnosis. Nasal cytology smear for eosinophils may be useful in some cases.

#### **Test specific for IgE mediated rhinitis:**

Skin prick test is the most widely used initial test for inhaled allergens. This method has high sensitivity, but the problem is false positive results. There is a small risk of anaphylaxis associated with intra dermal testing.

#### **In Vitro testing:**

Enzyme linked immunosorbent assays (ELISA) performed on a serum sample has a high specificity and sensitivity, though it is expensive.

#### **Treatment of Allergic Rhinitis**

Three major modalities of treatment for allergic rhinitis are allergen avoidance, pharmacotherapy and immunotherapy.

##### **1. Allergen avoidance**

Cat fur, poultry feather, house dust and house dust mite are the common allergens in Malaysia<sup>10,11</sup>. The most commonly implicated food in Malaysia is shrimp<sup>12</sup>. Avoidance of allergy is one of the guiding principle in the management of allergic rhinitis.

##### **House dust mite**

Several measures have proven to be efficacious in the control of house dust mite and are: (i.) Encasing pillows and mattress in vapor permeable covers, (ii.) Encasing mattress and box springs in vinyl or plastic (iii) washing bedding weekly in hot water (130°F) and (iv) removing stuffed toys from the bedroom. Weekly vacuuming and making sure that the bags are quality ones has been effective in controlling the allergens<sup>13</sup>.

##### **Animal Dander**

The best treatment for animal allergy is abstaining contact with the animals to which a person is allergic<sup>13</sup>.

##### **2. Pharmacotherapy**

The central role of the airway epithelial cell in generating a whole host of pro-inflammatory cytokines, which assist in the amplification of the ongoing inflammatory response and eventually lead on to chronicity of the underlying disease process. Manipulation of the cytokine release from the airway epithelial cells by therapeutic agents constitutes one approach in the management of allergic rhinitis<sup>14</sup>.

##### **(i) Antihistamines:**

First generation antihistamines like chlorpheniramine malleate, though effective and cheap, has the limitation of causing sedation and anticholinergic effects. Now newer Histamine H<sub>1</sub>-receptor antagonists have superseded them and which have minimal side effects<sup>15</sup>.

Second generation antihistamines, has the advantage of being non-sedating and better patient compliance

because of once a day regime. The following antihistamines are available now: Cetrizine (10mg/day), Loratidine (10mg/day), Fexofenadine (60mg/twice daily) and Desloratidine (5mg / day).

Recently, nasal antihistamine spray, Azelastine (274µg twice daily) has been introduced; however, its exact role as either an alternative therapy or adjuvant to oral antihistamines remains to be established.

### **(ii) Nasal Corticosteroids:**

Corticosteroids affect the late phase inflammatory reaction but also overtime may reduce the early phase response also. They cause vasoconstriction, reduce mediator release, and inhibit the influx of inflammatory cells such as eosinophils into the tissues. They are extremely effective and exhibit better overall symptom control in allergic rhinitis. Adverse effects of nasal corticosteroids include nasal irritation, epistaxis and rarely nasal septal perforation<sup>16</sup>.

The following nasal corticosteroids are available: Beclomethasone (42µg 1-2 bid), Budesonide (32µg 2 bid), Flunisolide (25µg 2bid), Fluticasone propionate (50µg 2 od), Mometasone furoate (50µg 2 od) and Triamcinolone acetonide (55µg 2 od).

### **(iii) Oral decongestants:**

Oral decongestants may be useful in patients with severe nasal congestion. Long-term therapy with topical nasal decongestants should be avoided because they may induce a rebound effect leading to more nasal congestion<sup>17</sup>.

### **(iv) Chromones:**

Sodium cromoglycate, has a mast cell stabilizing property and is more of a prophylactic treatment. It is useful in seasonal rhinitis rather than perennial rhinitis.

A summary of the pharmacological treatment for allergic rhinitis based on the ARIA guidelines<sup>18</sup> is provided in the Table I.

## **3. Immunotherapy**

Immunotherapy is useful for individuals who cannot avoid allergen exposure, whose symptoms cannot be

controlled by medications, or who experience significant adverse effects of pharmacotherapy. Contra indication for immunotherapy includes patients receiving β-adrenoreceptor antagonist therapy. Immunotherapy has been shown to be effective in the treatment of pollen-induced rhinitis<sup>19</sup>. Allergy immunotherapy has been shown to prevent the development of asthma in patients with moderate to severe allergic rhinitis<sup>20</sup>.

### **Role of Omalizumab in Perennial allergic rhinitis:**

Omalizumab is a molecularly cloned humanized monoclonal antibody inhibiting human IgE. It binds specifically to the region of the IgE molecule that binds to the IgE receptor on the mast cell or basophils. Studies have shown that Omalizumab is effective in the treatment of seasonal allergic rhinitis<sup>21</sup>.

### **Treatment of allergic rhinitis during pregnancy:**

The best first line approach is the avoidance of allergens. If medication is indicated intranasal chromone should be considered as first line approach, with its excellent safety profile. If chromone is ineffective first generation (chlorpheniramine and tripelemamine) and second generation (cetirizine and loratidine) antihistamine can be given<sup>22</sup>. In a meta-analysis examining the safety of first-generation antihistamines in pregnancy, 200,000 first trimester exposures failed to show increased teratogenic risk<sup>23</sup>. In a cohort of 2147 women who were exposed to second generation antihistamine (Loratidine), does not appear to increase the risk of major congenital malformations<sup>23</sup>. Intranasal steroids (beclomethasone dipropionate and budesonide) can be added to first line therapy especially for severe nasal obstruction. Immunotherapy has not been proven to be teratogenic and can be used in cases, not responding to pharmacotherapy<sup>22</sup>. A retrospective cohort study done on 141 pregnant women reported a negative association between immunotherapy during first trimester of pregnancy and congenital malformations<sup>24</sup>. According to the World Health Organisation Position Paper, subcutaneous immunotherapy should not be commenced during pregnancy but maintenance therapy may continue if it is providing benefit without causing systemic reactions<sup>25</sup>.

**Table I: Efficacy and properties of drug treatments in allergic rhinitis.**

Characteristic	Oral anti-histamine	Nasal anti-histamine	Nasal steroids	Nasal decongestant	Nasal chromone
Rhinorrhoea	++	++	+++	0	+
Sneezing	++	++	+++	0	+
Itching	++	++	+++	0	+
Blockage	+	+	+++	++++	+
Eye symptoms	++	0	++	0	0
Onset of action	1 h	15 min	12 h	5-15 min	variable
Duration	12-24 h	6-12 h	12-48 h	3-6 h	2-6 h

+, marginal effect; +++, substantial effect

## Conclusion

Allergic rhinitis is a common condition affecting 20% or more of individuals. The best first-line approach in the management of allergic rhinitis is avoidance of allergens. Nasal corticosteroids are very effective, but

prolonged treatment may have adverse effects. Antihistamines are also useful but may not control nasal congestion. Immunotherapy is beneficial for patients who are allergic to pollens. Anti IgE antibody therapy is very useful adjunctive therapy in allergic rhinitis.

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### MCQ'S

1. The following are the symptoms of allergic rhinitis:
  - a. Sneezing
  - b. Nasal congestion
  - c. Rhinorrhoea
  - d. Itching
  - e. Postnasal drip
  
2. The following test/ tests are very useful in the diagnosis of allergic rhinitis:
  - a. Total IgE level
  - b. Eosinophil count
  - c. Nasal smear for eosinophils
  - d. Skin prick test
  - e. Enzyme linked immunosorbent assays
  
3. Regarding antihistamines:
  - a. First generation antihistamines have anticholinergic effects.
  - b. Second generation antihistamine causes sedation.
  - c. Histamine H<sub>1</sub>- receptor antagonists have more side effects.
  - d. Patient compliance is better in the second generation antihistamines.
  - e. Antihistamine is available as a nasal spray
  
4. Nasal Corticosteroids:
  - a. Affect late phase inflammatory reaction
  - b. Cause vasodilatation
  - c. Reduce mediator release
  - d. Are very effective in controlling nasal symptoms
  - e. Can rarely cause nasal septal perforation.
  
5. Immunotherapy:
  - a. Is the first line therapy in allergic rhinitis
  - b. Is contra indicated in pregnant patients
  - c. Is effective in pollen induced allergic rhinitis
  - d. Is contra indicated in patients receiving  $\beta$ - adrenoreceptor antagonist therapy.
  - e. Has been shown to prevent the development of asthma in patients with moderate to severe allergic rhinitis.