

# Allergic rhinitis

# Introduction

- ▶ Allergic rhinitis (AR) is a chronic inflammatory disorder of the nasal mucosa caused by IgE-mediated early- and late-phase hypersensitivity responses.
- ▶ Symptoms can have significant negative impact on the patients quality of life, often interfere with sleep
- ▶ Treatment for more severe disease employ anti-inflammatory as well as symptomatic medication,
- ▶ Allergy immunotherapy (AIT) should be strongly considered for not only its effectiveness but also its disease-modifying effects.

# Prevalence

- ▶ Allergic rhinitis (AR) is the most common of all atopic conditions, affecting about 10%–30% of adults and up to 40% of children worldwide.<sup>1</sup>
- ▶ 30% of the Indian population suffers from AR, and that 15% develop asthma<sup>1</sup>
- ▶ About 20-30% of Indian population suffers from at least one allergic diseases.<sup>2</sup>
- ▶ Reported incidence of allergic rhinitis in India also ranges between 20% and 30%<sup>2</sup>

1.Jaggi V et al. Lung India 2019;36:411-6.

2.Chandrika D. Int J Otorhinolaryngol Head Neck Surg. 2017

# Classification of allergic rhinitis

Allergic rhinitis was previously subdivided into ■ **Seasonal** ■ **Perennial**

The recent classification:

- Duration: **intermittent** or **persistent** disease
- Severity of symptoms : **mild** or **moderate-severe**

## ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines

### Intermittent

- < 4 days per week
- or < 4 weeks

### Persistent

- $\geq 4$  days per week
- and  $\geq 4$  weeks



### Mild

normal sleep  
& no impairment of daily activities, sport, leisure  
& normal work and school  
& no troublesome symptoms

### Moderate-severe

*one or more items*

- abnormal sleep
- impairment of daily activities, sport, leisure
- abnormal work and school
- troublesome symptoms

# Classification of allergic rhinitis

| Factor                  | Description/type                                                                                                                                                                                                                    |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| IgE-mediated (allergic) | <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</li><li>• Further classified as intermittent or persistent</li></ul> |
| Autonomic               | <ul style="list-style-type: none"><li>• Vasomotor</li><li>• Drug-induced (rhinitis medicamentosa)</li><li>• Hypothyroidism</li><li>• Hormonal</li><li>• Non-allergic rhinitis with eosinophilia syndrome (NARES)</li></ul>          |
| Infectious              | <ul style="list-style-type: none"><li>• Precipitated by viral (most common), bacterial, or fungal infection</li></ul>                                                                                                               |
| Idiopathic              | <ul style="list-style-type: none"><li>• Undetermined etiology</li></ul>                                                                                                                                                             |

# Symptoms of allergic rhinitis in children

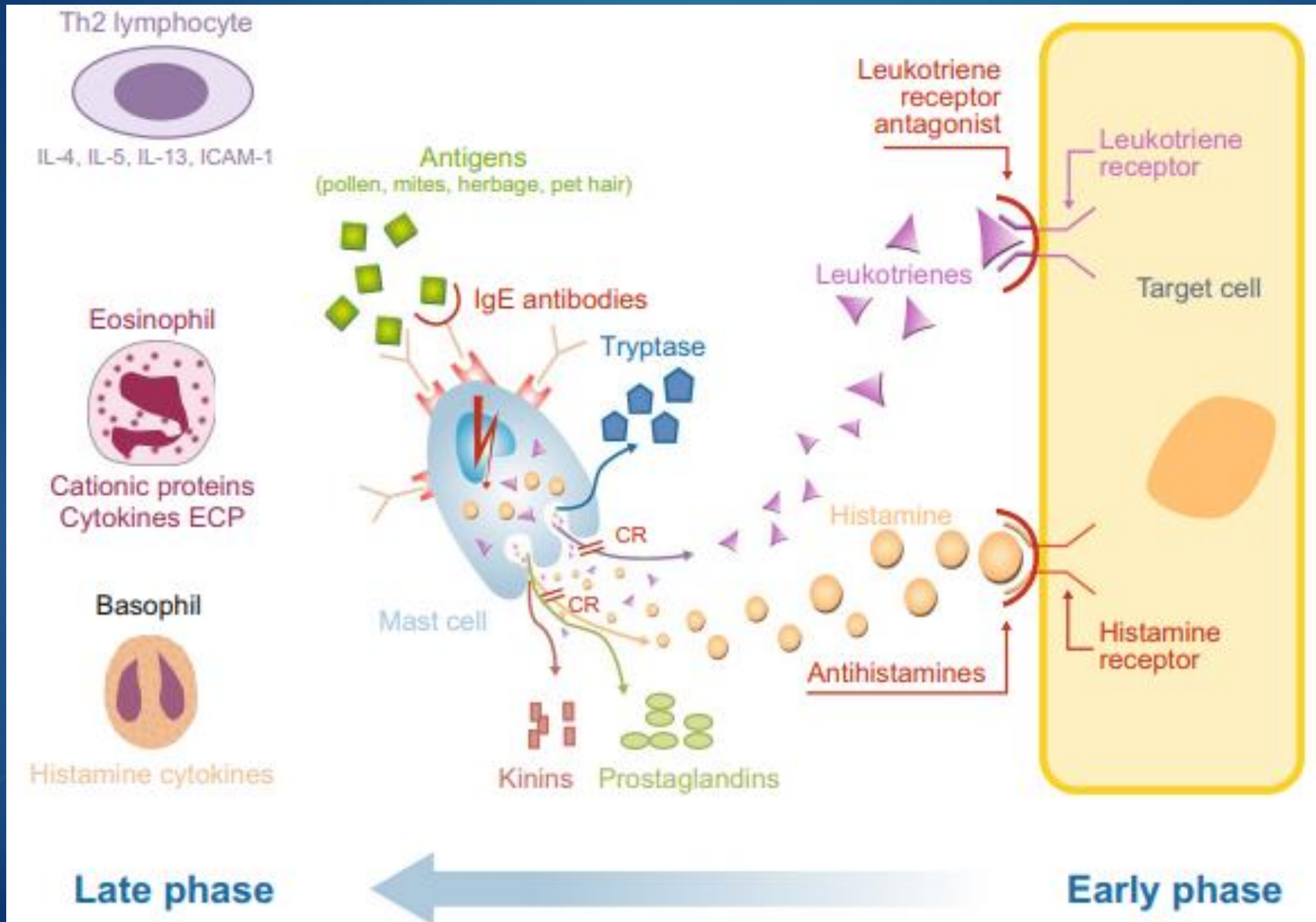
|                                        | Pre-school                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | School | Adolescent |
|----------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|------------|
| Classic symptoms and signs of rhinitis | <b>Rhinorrhoea</b> – clear or discoloured discharge, sniffing<br><b>Pruritus</b> - nose rubbing, the “allergic salute”, “allergic crease”, “sneeze”, may be associated with complaints of an itchy mouth or throat in older children<br><b>Congestion</b> - mouth breathing, snoring, sleep apnoea, allergic shiners                                                                                                                                                                                                                                                      |        |            |
| Potential atypical presentations       | <b>Eustachian tube dysfunction</b> - ear pain on pressure changes (eg flying), reduced hearing, chronic otitis media with effusion<br><br><b>Cough</b> – often mislabelled as asthma<br><b>Poorly controlled asthma</b> – may co-exist with asthma<br><b>Sleep problems</b> - tired, poor school performance, irritability<br><b>Prolonged and frequent respiratory tract infections</b><br><br><b>Rhinosinusitis</b> - catarrh, headache, facial pain, halitosis, cough, hyposmia<br><br><b>Pollen-food syndrome</b> , particularly with pollen driven allergic rhinitis |        |            |

Scadding GK et al. Clin  
Exp Allergy.  
2017;47(7):856-889

# Clinical presentation in allergic rhinitis

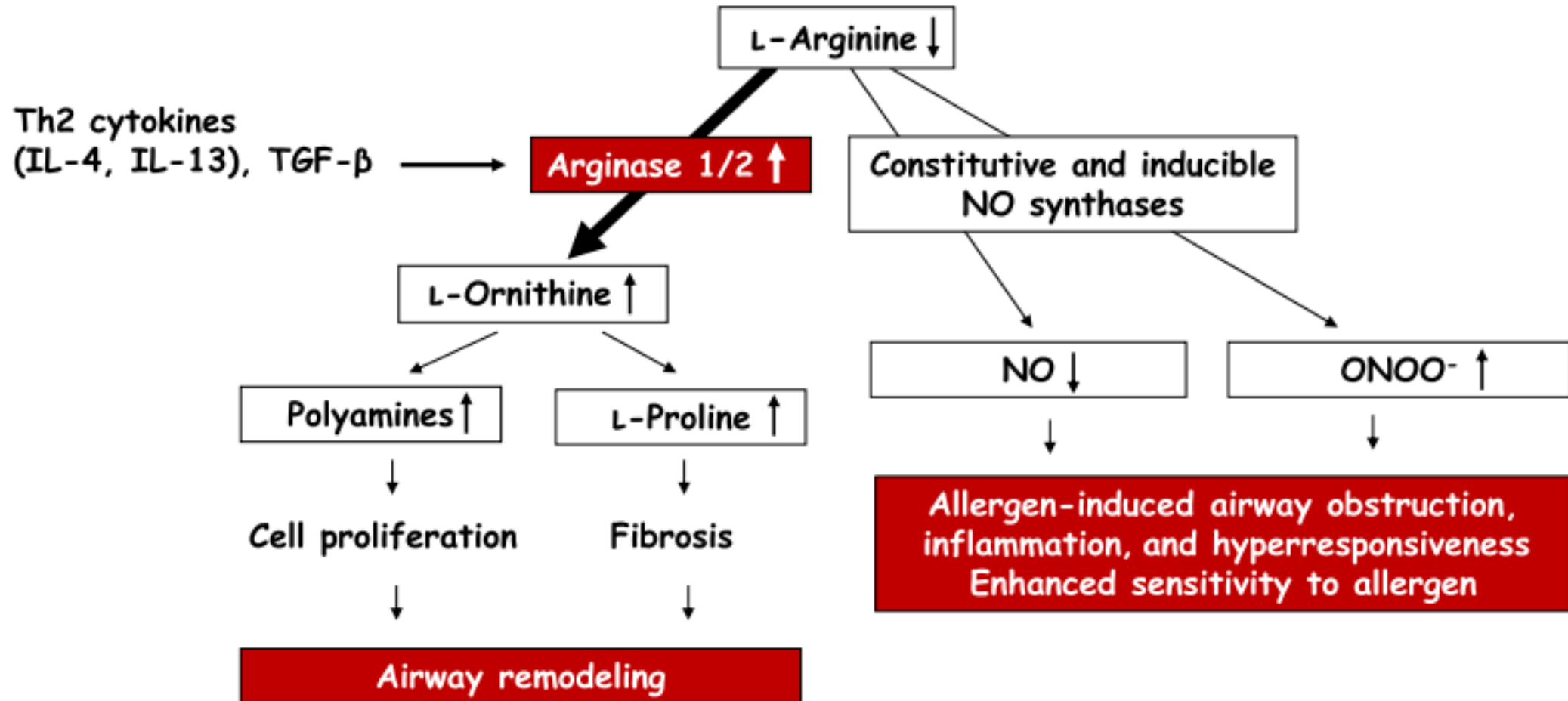
| Symptoms       | Patients with sneezing and Running nose | Patients with nasal blockage                   |
|----------------|-----------------------------------------|------------------------------------------------|
| Sneezing       | Especially paroxysmal                   | Little or none                                 |
| Rhinorrhoea    | Watery anterior and 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                           |                                                |

# Pathophysiology of Allergic rhinitis



ECP : eosinophil cationic protein  
ICAM-1: intercellular adhesion molecule-1  
IgE : immunoglobulin E  
IL : interleukin

# Role of arginine in allergic rhinitis



# Evidence for eosinophil and IL-17 mediated inflammation in allergic rhinitis



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## Abstract

**Background:** The aim was to determine the level of inflammatory cytokines, eosinophil cationic protein and IgE in allergic rhinitis (AR) patients.

**Subjects and methods:** Blood samples were taken from 88 AR patients and 88 healthy controls (HC). Each sample was analysed for eosinophil counts by flow cytometry, IgE by ECLIA, ECP, IL-17, and IL-33 by using ELISA test.

**Results:** There was no significant difference between AR patients and the control group in age and gender. Levels of eosinophils, IgE, ECP, IL-17, IL-33 and the total symptom scores were significantly higher in AR patients than the HC ( $P = 0.0001$ ). Serum ECP correlated with IL-17 ( $P = 0.041$ ,  $r = 0.42$ ), IL-33 ( $P = 0.0001$ ,  $r = 0.80$ ), and IgE levels ( $P = 0.017$ ,  $r = 0.45$ ) in the R patients. There was no correlation between IL-17 and IL-33. There was a correlation between symptom scores and eosinophils ( $P = 0.026$ ,  $r = 0.52$ ), and IgE ( $P = 0.001$ ,  $r = 0.60$ ) in the patients. No correlation was observed between symptom scores and ECP, IL-17, and IL-33 in the AR patient.

**Conclusions:** Patients with AR have significant higher serum levels of ECP, IL-17, and IL-33 than healthy controls. This indicates that these markers could be used to in order to diagnose AR and to monitor disease. Inhibitory molecules to IL-17 and IL-33 may be considered as novel treatment strategies.

**Keywords:** Allergic rhinitis, Immune system, ECP, IL-17, IL-33, IgE

# Physical examination in Allergic rhinitis

- ▶ Mouth breathing
- ▶ Rubbing the nose/transverse nasal crease
- ▶ Frequent sniffing and/or throat clearing
- ▶ Allergic shiners (dark circles under eyes)
- ▶ Nose
  - Mucosal swelling, bleeding
  - Pale, thin secretions
  - Polyps or other structural abnormalities
- ▶ Sinuses
  - Palpation of sinuses for signs of tenderness

- ▶ Ears
  - Pneumatic otoscopy to assess for Eustachian tube dysfunction
  - Valsalva's maneuver to assess for fluid behind the ear drum
- ▶ Posterior oropharynx
  - Postnasal drip
  - Lymphoid hyperplasia ("cobble stoning")
  - Tonsillar hypertrophy
- ▶ Chest and skin
  - Wheezing

# BSACI Guideline for Diagnosis of allergic rhinitis

## ROUTINE TESTS:

### Nasal airway assessment

- ▶ Peak nasal inspiratory flow (PNIF)

### Allergy tests

- ▶ Skin
- ▶ Serum-specific IgE

# BSACI Guideline for Diagnosis of allergic rhinitis

## **ADDITIONAL TESTS:**

### Endoscopy

- ▶ Rigid
- ▶ Flexible

### Radiology

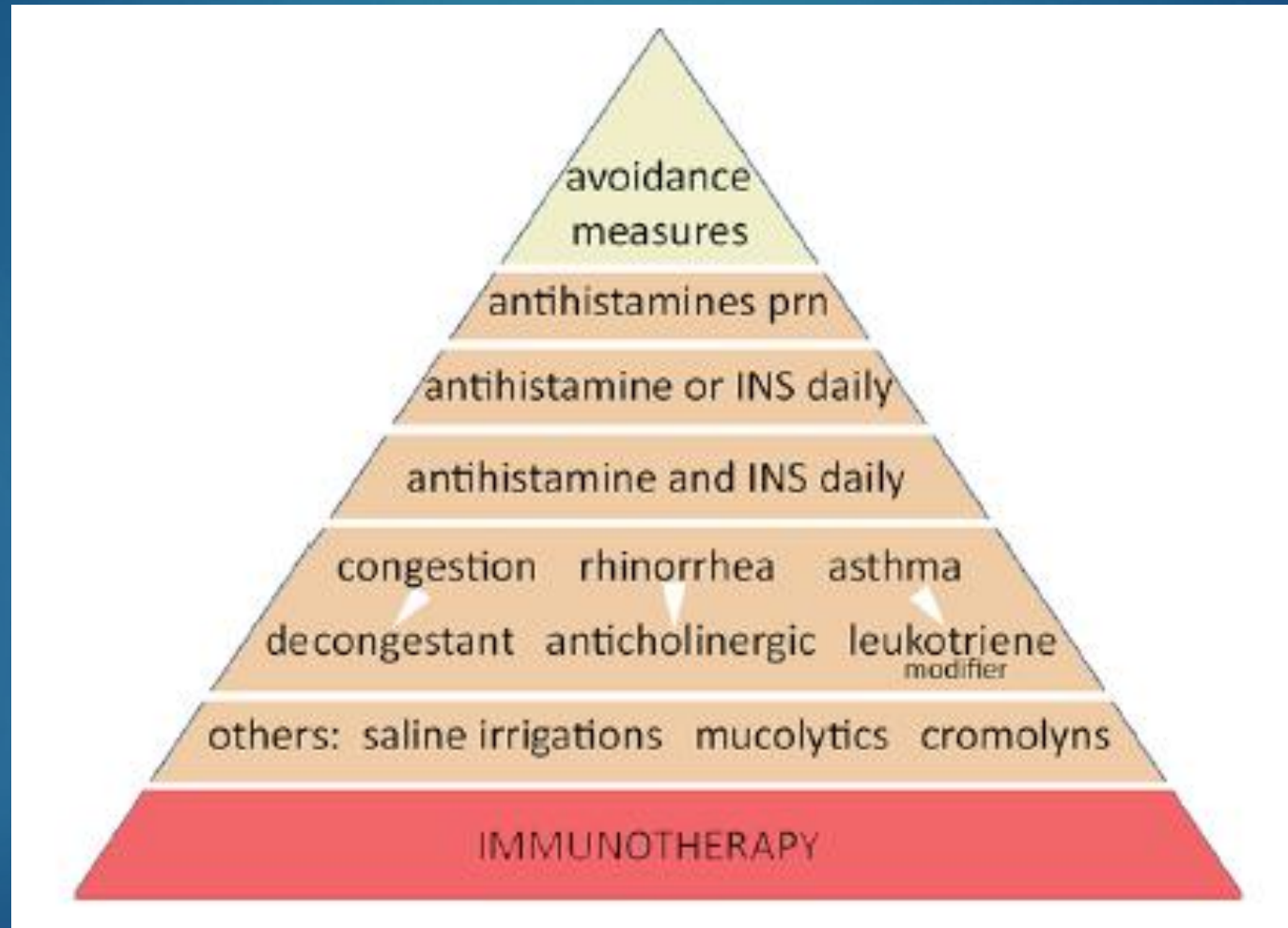
- ▶ CT scan

# BSACI Guideline for Diagnosis of allergic rhinitis

## OPTIONAL TESTS:

- ▶ Nasal challenge: Allergen, Lysine aspirin
- ▶ Nasal samples: Cytology/nasal secretions, Nasal biopsy, Nasal swab  
Radiology: MRI
- ▶ Mucociliary function: Nasal mucociliary clearance (NMCC), Ciliary beat frequency, Electron microscopy
- ▶ Nasal airway assessment – Rhinomanometry (anterior, posterior), Acoustic rhinometry
- ▶ Exhaled nitric oxide (FeNO=fractional exhaled nitric oxide) :Normal levels are less than 20 ppb, elevated in eosinophilic lower respiratory tract inflammation

# Allergy treatment pyramid



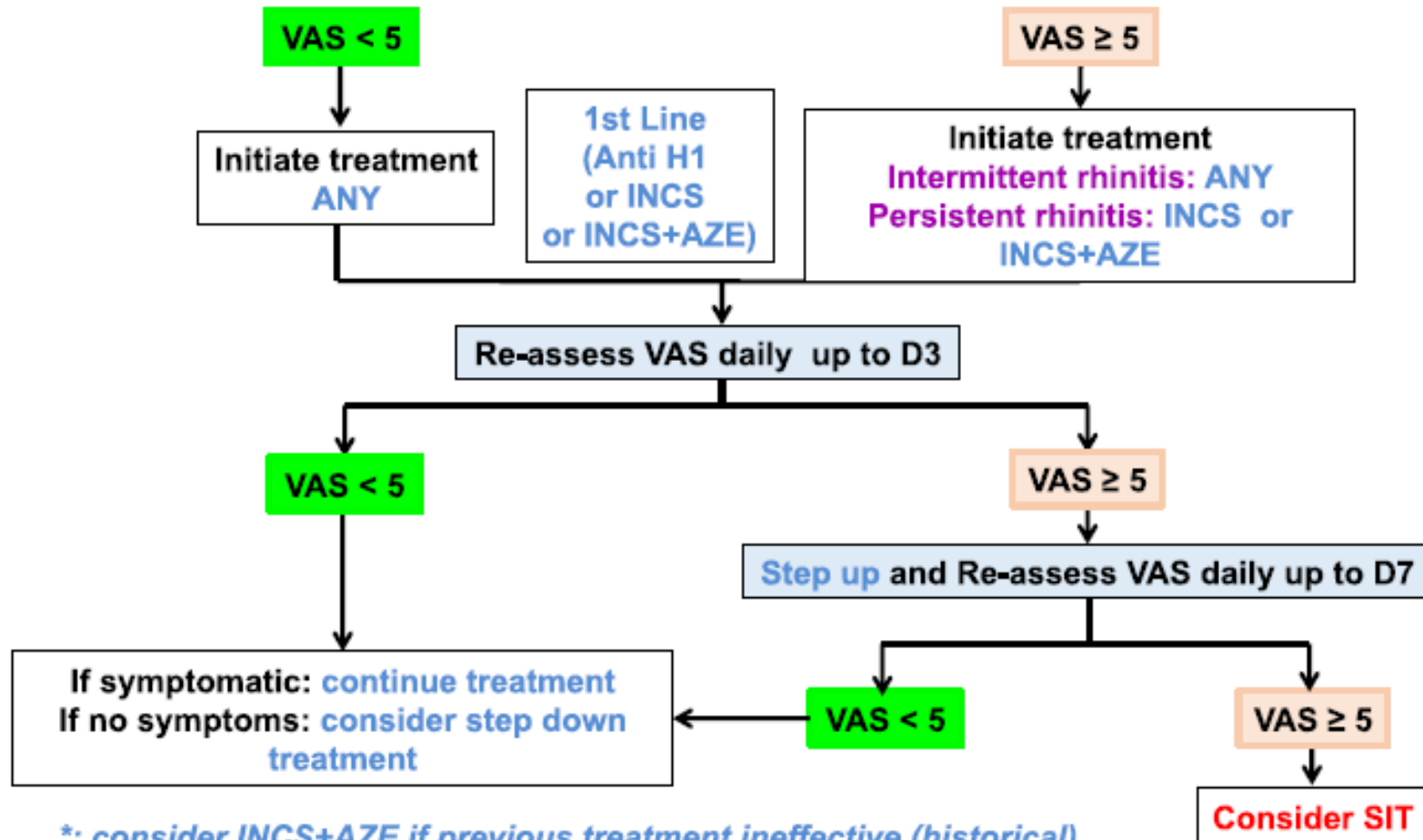
Platt M. Pharmacotherapy for allergic rhinitis. In International forum of allergy & rhinology 2014 ; 4 (2): S35-S40.

# Treatment

- ▶ Allergen avoidance
- ▶ Isotonic saline irrigation in both adults and children.
- ▶ Carbon dioxide washing: use of a ten second burst of carbon dioxide from a pressurized container into the nasal airway, with the mouth open, reduces all symptoms of rhinitis within minutes.
- ▶ Oral H1-antihistamines: on neurally mediated symptoms of itch, sneeze and rhinorrhoea and only a modest effect on nasal congestion.
- ▶ Intranasal corticosteroids
- ▶ Intranasal corticosteroids + oral antihistamine or plus a leukotriene receptor antagonist
- ▶ Systemic glucocorticoids

# Step up algorithm in untreated allergic rhinitis according to ARIA guidelines

## Assessment of control in untreated symptomatic patient

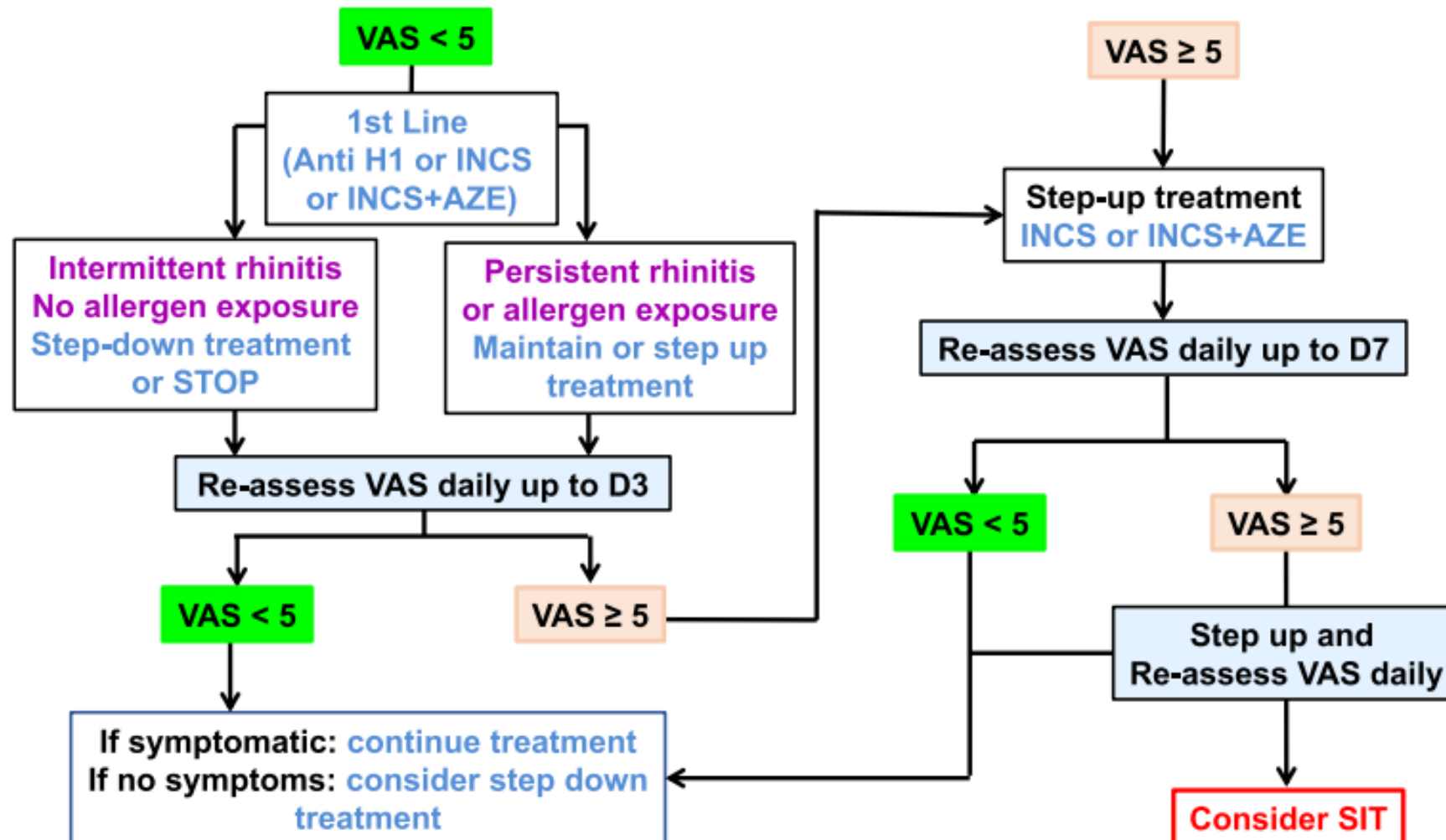


AZE: Azelastine  
INCS: Intranasal Corticosteroids  
AIT: allergen-specific immunotherapy  
LTRA: Leukotriene Receptor Antagonist  
VAS: Visual Analog Scale  
SIT: Specific Immunotherapy

Bousquet J et al. J Allergy Clin Immunol. 2020;145(1):70-80.e3

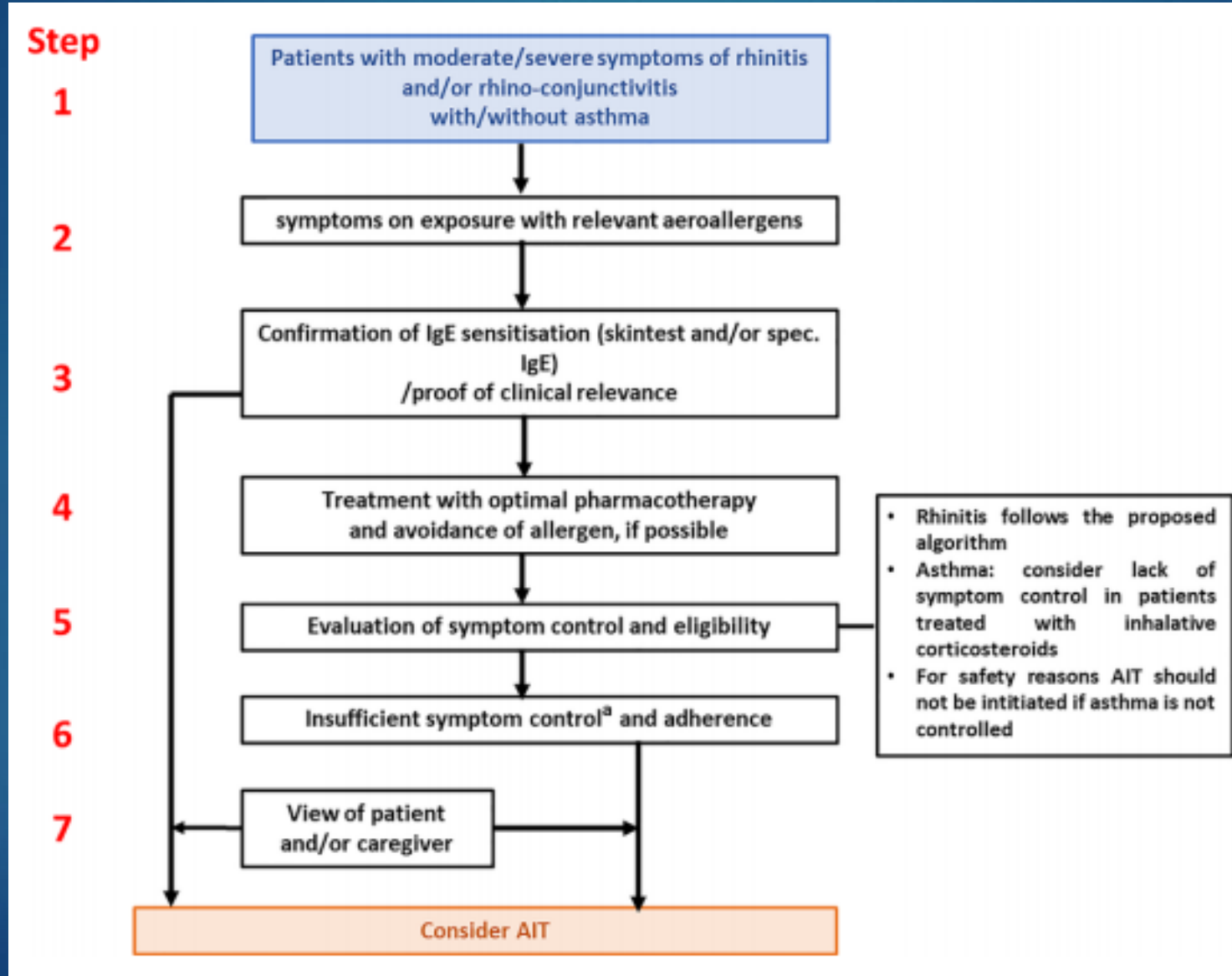
# Step up algorithm in untreated allergic rhinitis according to ARIA guidelines

## Assessment of control in treated symptomatic patient



AZE: Azelastine  
INCS: Intranasal  
Corticosteroids  
AIT: allergen-  
specific  
immunotherapy  
LTRA: Leukotriene  
Receptor  
Antagonist  
VAS: Visual  
Analog Scale  
SIT: Specific  
Immunotherapy

# Step by step approach to indication for Allergy specific Immunotherapy

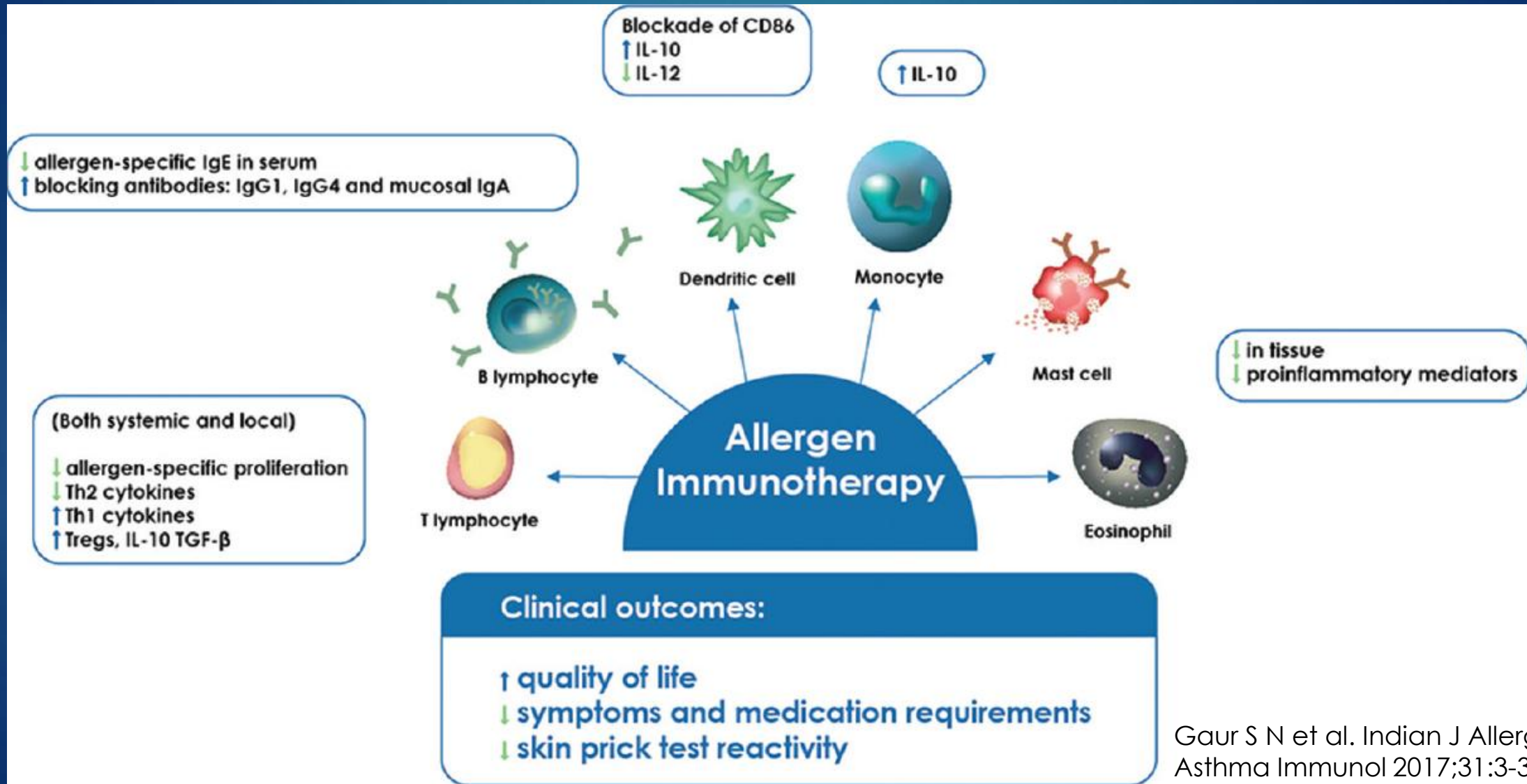


AIT: Allergy  
specific  
Immunotherapy

# Allergic / Specific Immunotherapy (AIT/SIT)

- ▶ Allergen immunotherapy (AIT) is an immunomodulatory method for the treatment of immunoglobulin E (IgE)-mediated allergic diseases.
- ▶ It control symptoms and decrease the sensitivity toward allergen(s) by sequentially increasing dose of antigen(s) to induce a shift of the immunological response from TH2 to TH1.
- ▶ AIT is a therapy with disease-modifying effects and is currently used for the treatment of allergic rhinitis, rhinoconjunctivitis, allergic asthma, and venom hypersensitivity.
- ▶ It is the only method to prevent the onset/progression of asthma in patients suffering from allergic rhinitis/rhinoconjunctivitis

# Mechanism of Allergy specific Immunotherapy



# Indications of Allergy specific Immunotherapy

IgE-mediated disease in patients'  $\geq 5$  years with no limit on the upper age (i.e., presence of sensitization on a skin prick test\* with clinical correlation to the symptoms)

- Allergic rhinoconjunctivitis

  - Moderate-severe intermittent rhinitis

  - Mild to moderate-severe persistent rhinitis

- Allergic asthma (controlled)

- Large local reactions to insect venom

- Atopic dermatitis in patients with aeroallergen sensitivity (low level of evidence)

Symptoms are of sufficient duration and severity

Allergen avoidance not possible or if symptom relief is inadequate

Availability of standardized or best as technically possible allergen extracts

Proof of efficacy of the planned AIT for the respective indication and age group

*\*In vitro* tests may be used only in situations in which skin testing is not possible and for diagnostic work-up in children below 5 years. AIT - Allergen immunotherapy

# Contraindications of Allergy specific Immunotherapy

| Absolute contraindications                                                   | Relative contraindications                      |
|------------------------------------------------------------------------------|-------------------------------------------------|
| Uncontrolled persistent asthma (FEV <sub>1</sub> <70% in spite of treatment) | β-blockers                                      |
| Malignant neoplasias                                                         | Cardiovascular diseases                         |
| Pregnancy (only for the initiation of AIT)                                   | HIV (A, B; CD4 > 200/μL)                        |
| Children (<2 years of age)                                                   | Children (2–5 years of age)                     |
| AIDS                                                                         | Psychiatric or mental disorders                 |
|                                                                              | Chronic infections                              |
|                                                                              | Autoimmune disorders                            |
|                                                                              | Immunodeficiencies or use of immunosuppressives |

FEV<sub>1</sub> - Forced expiratory volume 1 s, AIT - Allergen immunotherapy, AIDS - Acquired immunodeficiency syndrome

# Allergens of proven efficacy in allergen immunotherapy trials globally

| Allergen          | Level of evidence | Availability of data |
|-------------------|-------------------|----------------------|
| House dust mite   | A                 | ++++                 |
| Pollen            | A                 | ++++                 |
| Mold              | A                 | ++                   |
| Animal epithelia  | A                 | ++                   |
| Hymenoptera venom | A                 | ++                   |
| Cockroach         | B                 | +                    |

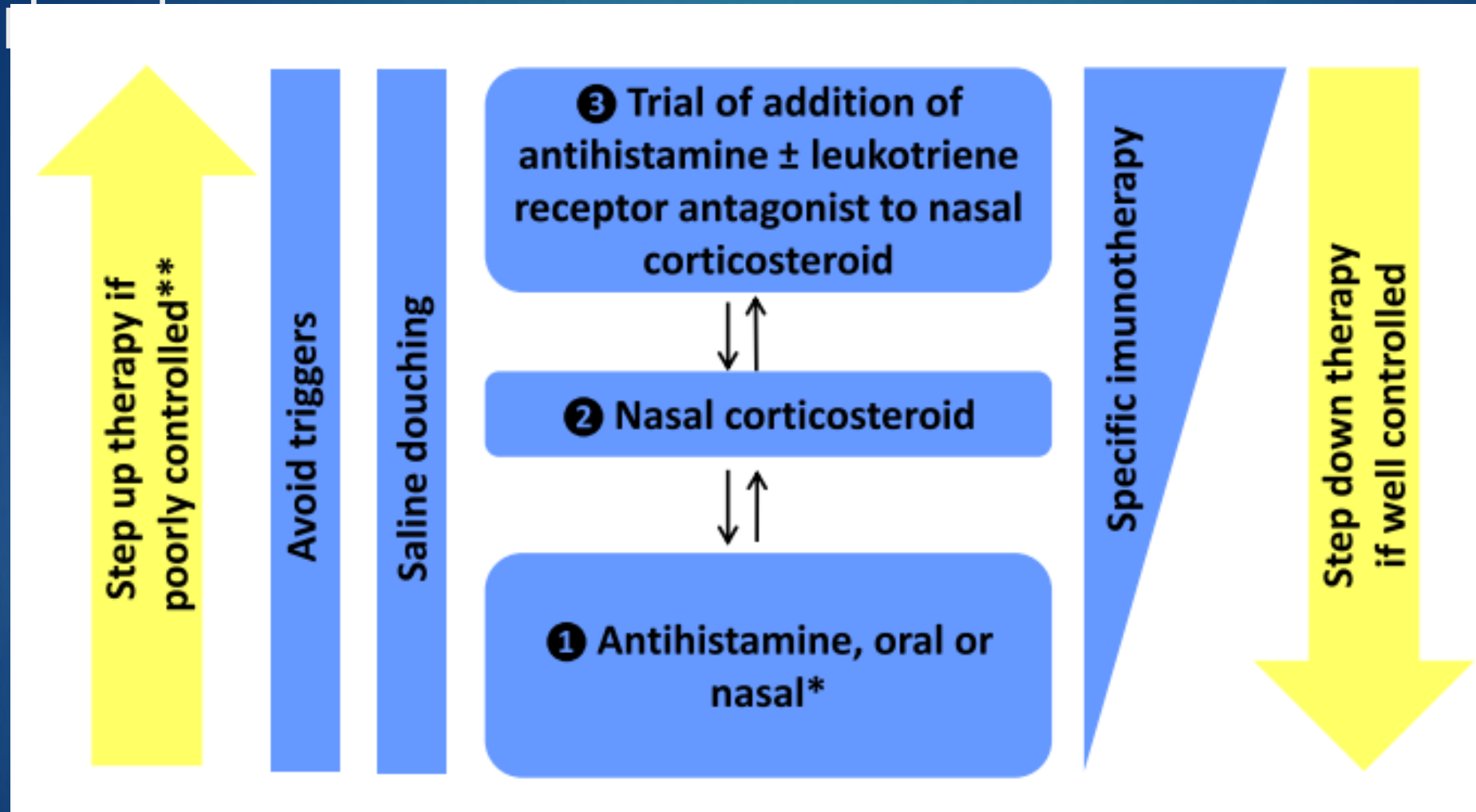
A - Evidence from meta-analysis of RCTs or at least 1 RCT, B - Evidence from at least 1 controlled study without randomization or at least 1 other type of quasi experimental study, ++++ - Multiple long-term RCTs available, ++ - Few RCTs available, + - Limited data, RCTs - Randomized controlled trials

# Pharmacotherapy effects on individual rhinitis symptoms

|                                                       | Sneezing | Rhinorrhea | Nasal obstruction | Nasal itch | Eye symptoms |
|-------------------------------------------------------|----------|------------|-------------------|------------|--------------|
| H1-antihistamines                                     |          |            |                   |            |              |
| Oral                                                  | ++       | ++         | +                 | +++        | ++           |
| Intranasal                                            | ++       | ++         | +                 | ++         | 0            |
| Eye drops                                             | 0        | 0          | 0                 | 0          | +++          |
| Corticosteroids                                       |          |            |                   |            |              |
| Intranasal                                            | +++      | +++        | ++                | ++         | ++           |
| Chromones                                             |          |            |                   |            |              |
| Intranasal                                            | +        | +          | +                 | +          | 0            |
| Eye drops                                             | 0        | 0          | 0                 | 0          | ++           |
| Decongestants                                         |          |            |                   |            |              |
| Intranasal                                            | 0        | 0          | ++++              | 0          | 0            |
| Oral                                                  | 0        | 0          | +                 | 0          | 0            |
| Anti-cholinergics                                     | 0        | ++         | 0                 | 0          | 0            |
| Anti-leukotrienes                                     | 0        | +          | ++                | 0          | ++           |
| Intranasal steroids and<br>Intranasal antihistamine 1 | +++      | +++        | +++               | +++        | +++          |

Scadding GK et al. Clin Exp Allergy. 2017;47(7):856-889

# Approach to therapy in pediatric allergic rhinitis



# A new generation antihistamine - Bilastine

- ▶ Bilastine is a non-sedating, long-acting histamine antagonist.
- ▶ The affinity for the H1 receptor of Bilastine is 3 and 6 times higher than for cetirizine and fexofenadine, respectively.
- ▶ Bilastine had a rapid onset of action, a long duration of action, well tolerated

# A new generation antihistamine - Bilastine

- ▶ Brain H1 receptor occupancies of bilastine is nearly 0%, minimally penetrate into the brain.
- ▶ Studies have shown that it faster onset of action and acts for longer duration than Fexofenadine in treatment of allergic rhinitis
- ▶ Bilastine shows a favourable safety profile with a low incidence of adverse events

# COMPARATIVE TABLE OF ANTIHISTAMINES

| Characteristic                          | Bilastine | Cetirizine                           | Desloratadine               | Fexofenadine | Levocetirizine                       | Loratadine         |
|-----------------------------------------|-----------|--------------------------------------|-----------------------------|--------------|--------------------------------------|--------------------|
| H <sub>1</sub> receptor selectivity     | +++       | +                                    | ++                          | +            | ++                                   | +                  |
| Dosage adjustment in renal impairment?  | ✗         | ✓ (in moderate to severe)            | Caution (severe impairment) | ✗            | ✓ (in moderate-to-severe)            | ✗                  |
| Dosage adjustment in hepatic impairment | ✗         | ✓ (if concomitant renal dysfunction) | Not mentioned               | ✗            | ✓ (if concomitant renal dysfunction) | ✓ (severe disease) |
| Contraindications                       | None      | Severe renal impairment              | None                        | None         | Severe renal impairment              | None               |



Clinical trials

# Bilastine 20 mg compared with cetirizine 10mg in the treatment of perennial allergic rhinitis

**Aim:** Multicenter study in patients with perennial allergic rhinitis (PAR) were evaluated.

## **Method:**

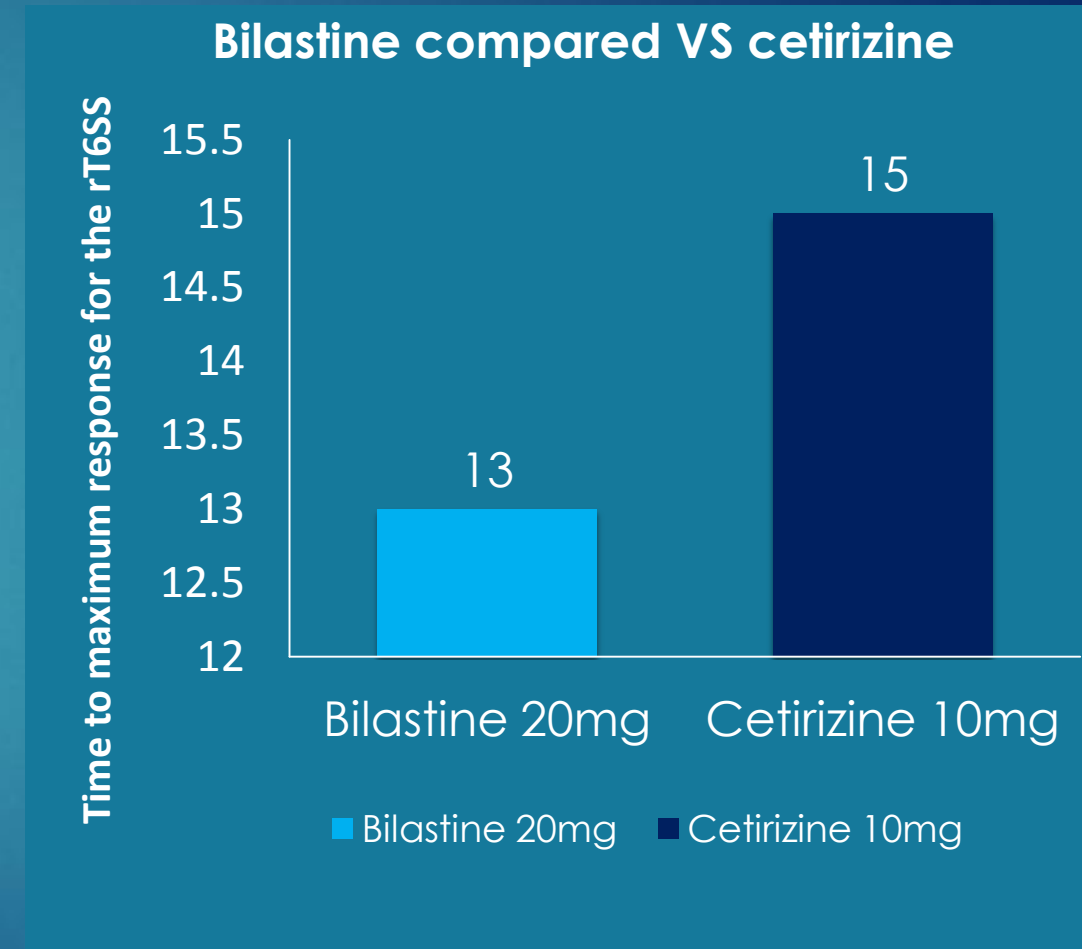
The patients were administered with Bilastine 20mg or cetirizine 10mg for one year.

## **Results:**

- ▶ Time to maximum response for the reflective total 6-symptom score(rT6SS) was less with Bilastine
- ▶ Total 4-nasal symptom score was low with Bilastine

## **Conclusion:**

**Bilastine is more effective in patients with PAR and shown to be well-tolerated.**



# Bilastine vs Fexofenadine on allergen-induced nasal and ocular symptoms

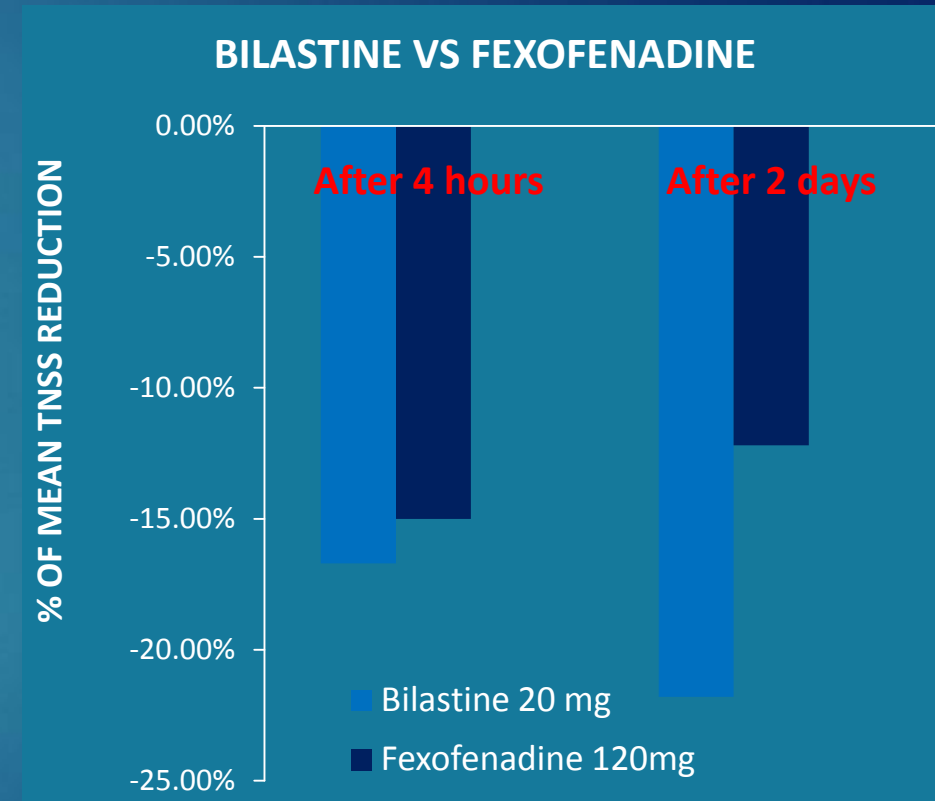
**Aim:** This study compared the potential of Bilastine and Fexofenadine to relieve the symptoms of allergic rhinitis.

## Method:

- ▶ 75 subjects were tested after 2 days of allergen provocation
- ▶ Total nasal symptom scores (TNSS) were assessed

## Results and Conclusion:

- Bilastine has rapid onset of action, within 1 h, and a long duration of action, greater than 26 h.
- Fexofenadine was similar on day 1 but less effective on day 2, indicating a shorter duration of action.



# Bilastine 20 mg vs Desloratadine 5 mg in seasonal allergic rhinitis

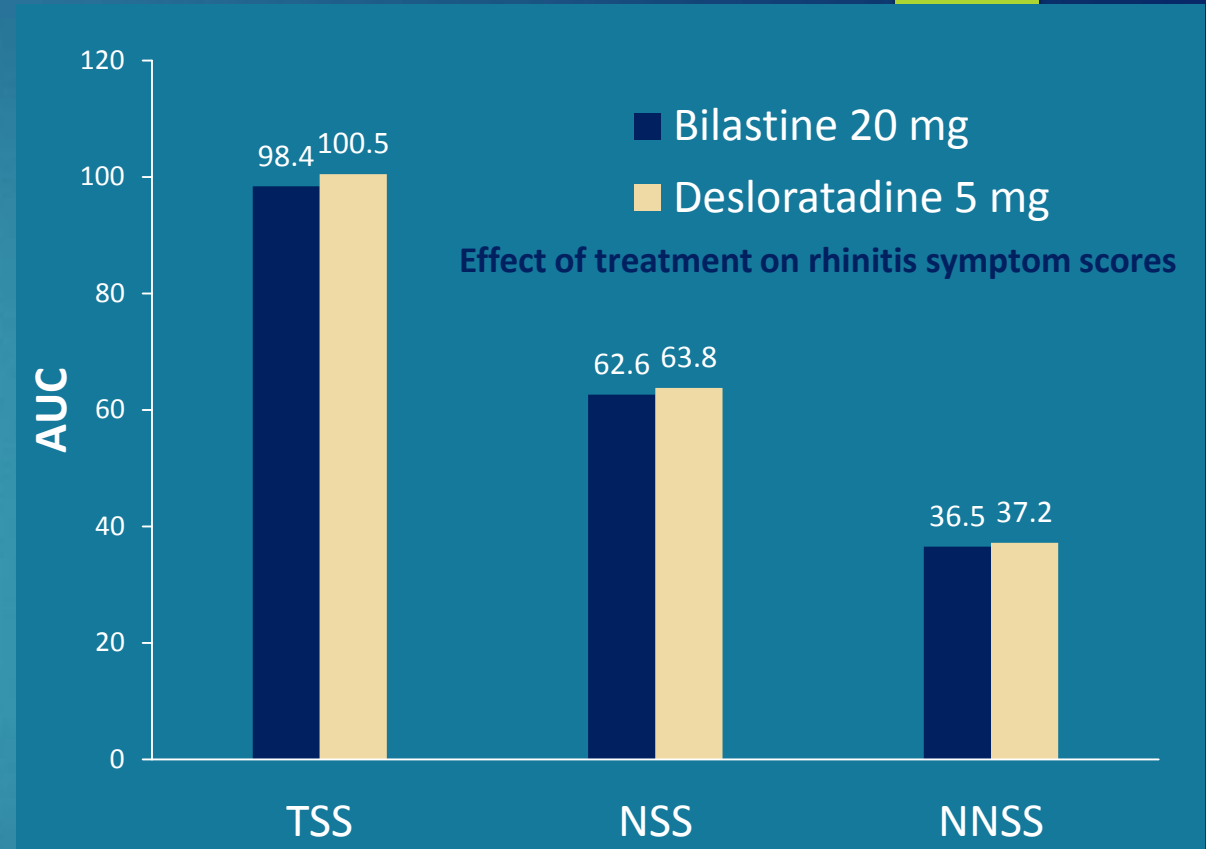
## Method:

- ▶ Symptomatic SAR patients were treated with bilastine, or desloratadine
- ▶ Nasal and nonnasal symptoms were assessed on a predetermined scale to provide a total symptom score (TSS)

## Result:

- ▶ Bilastine 20 mg reduced TSS to a greater degree and improved the QOL of patients, as measured by RQLQ

**Conclusion:** Bilastine effectively relieved the symptoms of SAR and improved the quality of life



- NSS-Nasal Symptom Score,
- NNSS-Non nasal symptom score,
- RQLQ- Rhinoconjunctivitis quality of life questionnaire
- QOL- quality of life

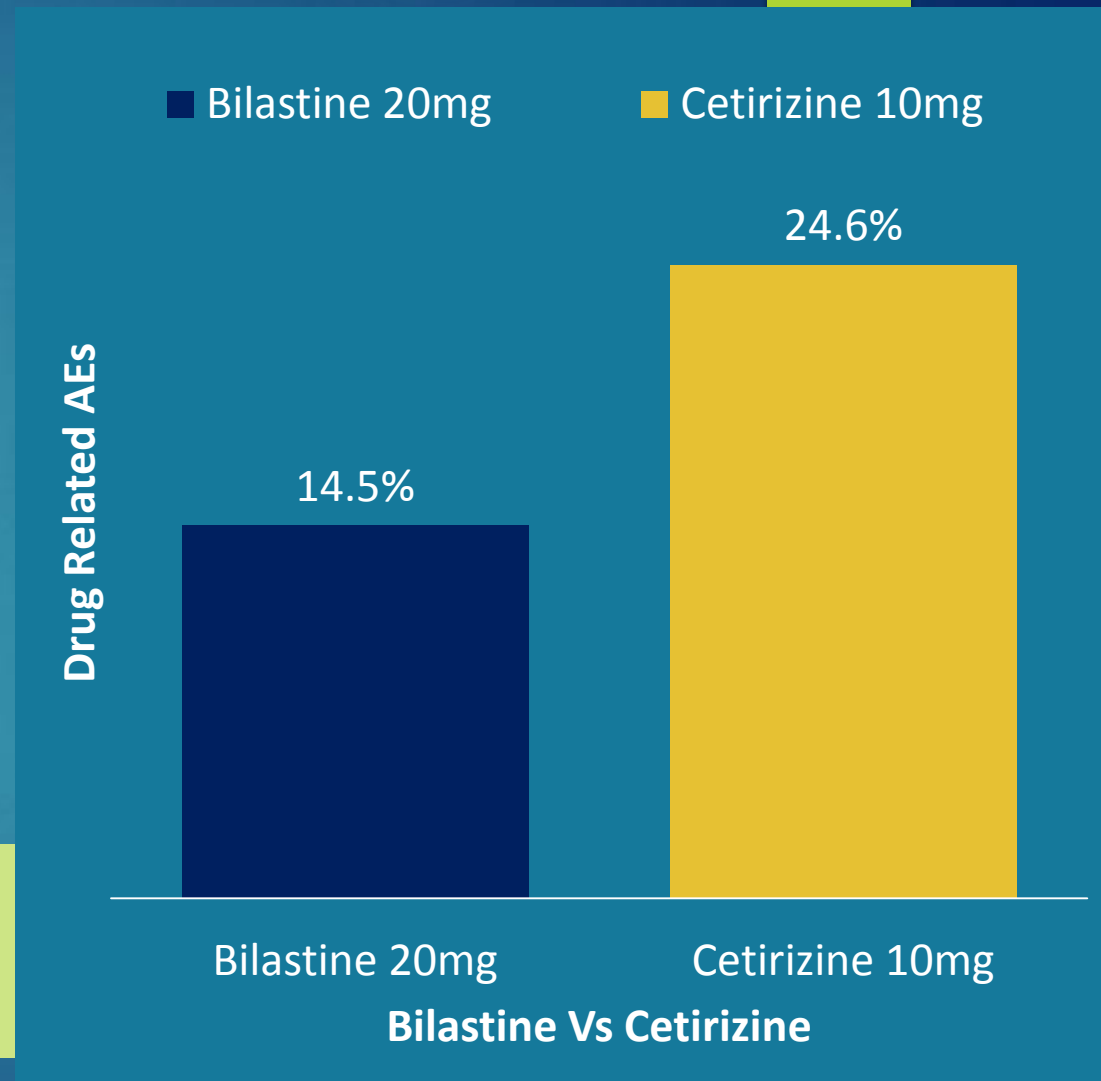
# Bilastine 20mg compared with cetirizine 10mg in seasonal allergic rhinitis

**Aim:** To assess and compare the efficacy and safety of bilastine 20 mg vs. cetirizine 10 mg in relieving the symptoms of seasonal allergic rhinitis (SAR).

## Methods:

- ▶ 683 SAR patients, aged 12–70 years, were given bilastine 20mg, cetirizine 10mg once daily for 14 days.
- ▶ Nasal and non-nasal symptom scores were recorded

**Conclusion:** Bilastine 20 mg once daily significantly relieve symptoms of SAR, demonstrated a significantly better AE profile than cetirizine.



# Newer surgical options for Allergic rhinitis -

## Mini Inferior Turbinoplasty



Endoscopic View of the Right Side Inferior Turbinate  
Convex Shape of Inferior Turbinate



Creating a window in the Inferior Turbinate with  
a 4mm Microdebrider Blade



Debrider Used for Removal of the Right  
Hypertrophic Inferior Turbinate Soft tissue  
& Bony Component



Tunneling Technique  
Removal of Additional bony component using Tilley Nasal  
forceps through Tunnel Created allowing Endoscopic  
Visualization of Right Inferior Turbinate.

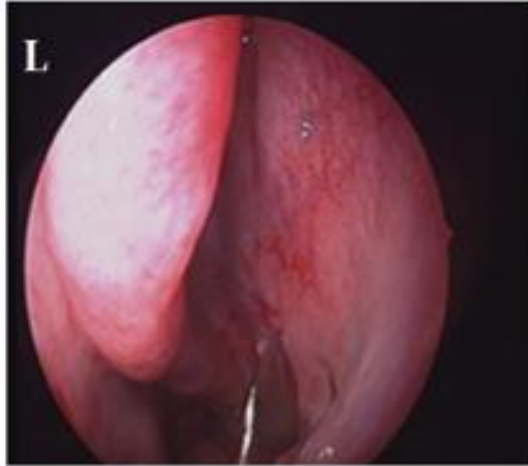


Post removal of soft tissue and bony component of Right  
Inferior turbinate. After approximating soft tissue  
surface at the site of window created. Concave shape  
Right Inferior Turbinate

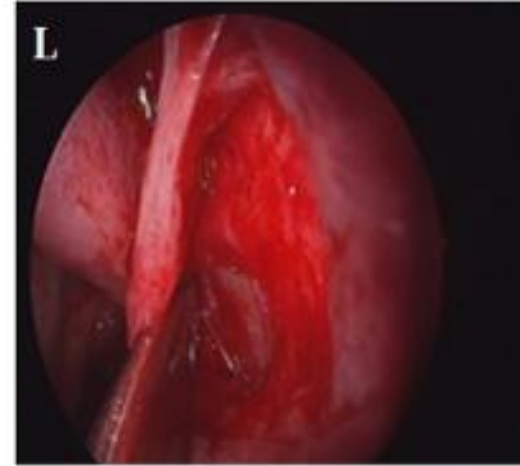
Nagalingeswaran A, Kumar  
RD. Indian J Otolaryngol  
Head Neck Surg. 2020 ; 72  
(1) : 133-139

# Newer surgical options for Allergic rhinitis -

## Endoscopic Posterior Nasal Neurectomy (PNN)



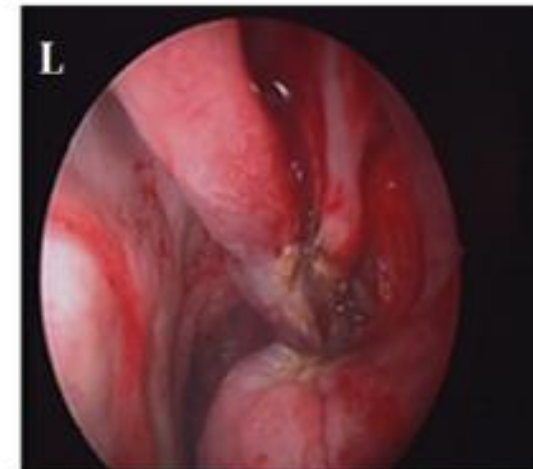
Left side nasal cavity, Incision Site



Flap elevation & identification of the nerve



Monopolar suction cauterization of  
Posterior Nasal Nerve



Repositioning of Mucoperiosteal Flap

Nagalingeswaran A, Kumar  
RD. Indian J Otolaryngol  
Head Neck Surg. 2020 ; 72  
(1) : 133-139

# Summary

- ▶ Individuals with AR is assessed for the presence of associated conditions like asthma, atopic dermatitis, sleep-disordered breathing, conjunctivitis, rhinosinusitis, and otitis media.
- ▶ Specific IgE testing (blood or skin) is performed for patients with a clinical diagnosis of AR not responding to empiric treatment, or diagnosis is uncertain, or when determination of specific target allergen is needed.
- ▶ Oral second-generation antihistamines are prescribed for patients with AR and primary complaints of sneezing and itching.
- ▶ Intranasal antihistamines may be prescribed for patients with seasonal, perennial, or episodic AR.
- ▶ Immunotherapy is recommended for patients with AR who have inadequate response to pharmacologic therapy.
- ▶ Inferior turbinate reduction may be considered for patients with AR with nasal airway obstruction and enlarged inferior turbinates with failed medical management.