

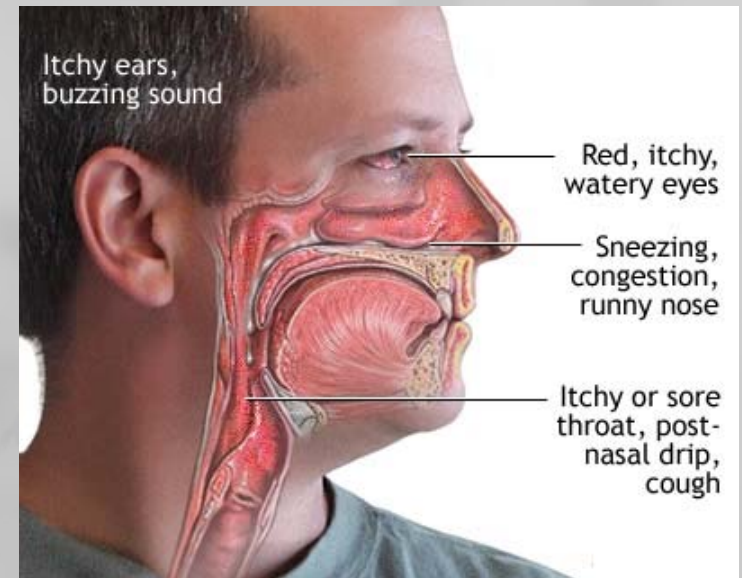
# ALLERGIC RHINOSINUSITIS

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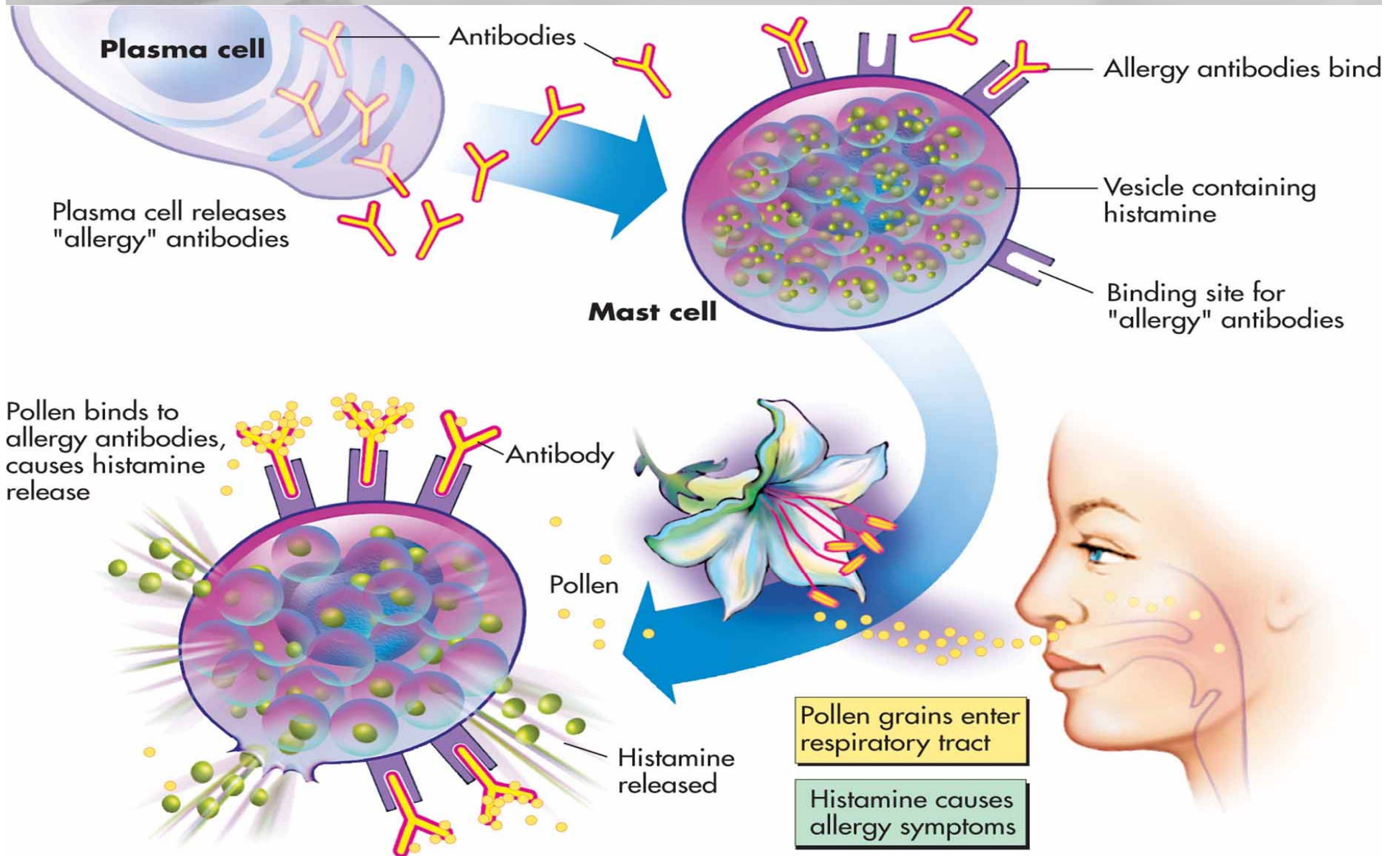




# OVERVIEW

- Pathophysiology
- Goals of therapy
- Approaches to therapy
- Antihistaminics
- Corticosteroids
- Leukotriene modulators
- Decongestants
- Mast cell stabilisers
- Immunomodulation
- Summary

# PATHOPHYSIOLOGY



# GOALS OF THERAPY

- To prevent repeated attacks, enable subject to live as normal life as possible
- **Aim** : To reduce the inflammation
- Therapeutic measures to be taken are
- **Elimination of triggering factors** : allergens, URTI
- **Avoiding respiratory irritants** : smoking, environmental & occupational pollutants
- **Drug therapy**

# APPROACHES TO TREATMENT

- Neutralization of IgE (reaginic antibody) → **Omalizumab**
- Suppression of inflammation – **Corticosteroids**
- Prevention of release of mediators – **Mast cell stabilizers**
- Antagonists to released mediators – **H<sub>1</sub> blockers, LT antagonists, PAF antagonists**
- Immunomodulation **interferon gamma, scissoring effect**

**Drugs used in allergic rhinosinusitis**

Anti histaminics

Loratidine, cetirizine, azelastine

Intranasal steroids

Beclomethasone, budesonide, mometasone

Decongestants

Xylometazoline, oxymetazoline

Leukotriene antagonists

Montelukast, Zafirlukast

Mast cell stabiliser

Cromoglycate sodium

PAF antagonist

Ketotifen

Leukotriene synth inhibitor

Zileuton

Anti IgE antibody

Omalizumab

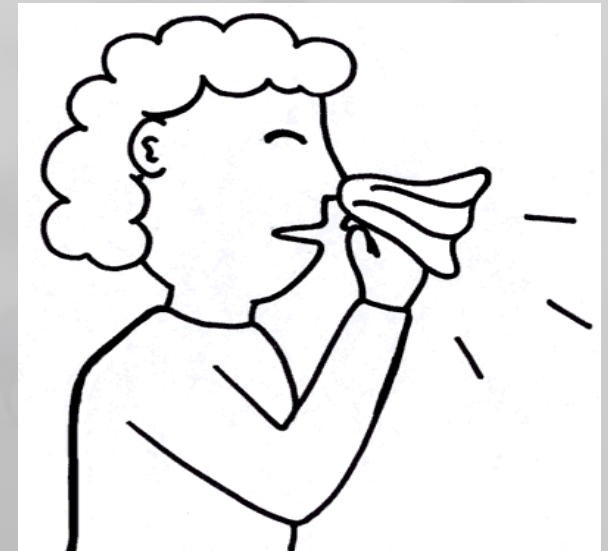
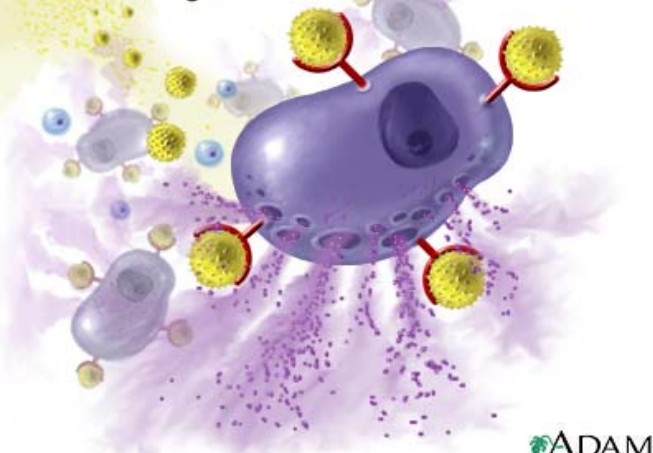
Immunomodulators

# ANTI-HISTAMINICS



- ❖ **Mechanism of action:** competitive antagonism of H<sub>1</sub> receptor
- ❖ **Drugs:** cetirizine, levocetirizine, loratidine, desloratidine, azelastine.

Mast cells release histamines when the allergen is encountered



## 2<sup>ND</sup> GENERATION ANTIHISTAMINICS

Drug	Special features	Dosage	Sedation
Cetirizine	OTC	5–10 mg	Yes
Levocetirizine		5mg	Yes
Loratidine		10mg	No
Desloratidine		5mg	No
Fexofenadine	Approved for SR	120-180 mg	No
Azelastine (IN)	Approved for SR, PR	0.14 mg/puff/day, 2 puffs per day	No
Olapatidine (IN)	Approved for SR	0.667mg/puff/day, 2 puffs BD	No





## Anti histaminics cntd...

- Adverse effects:
  - Dry mouth, sedation at higher than recommended doses.
  - Bitter taste, epistaxis, headache
  - Nasal irritation

# CORTICOSTEROIDS

- ❖ MOA : Inhibits peripheral lymphocytes and macrophages and interferes with gene transcription of inflammatory mediators
- ❖ Inhibits Phospholipase-2
- ❖ Reduces the synthesis of Cyclooxygenase-2
- ❖ Interferes with mast cell degranulation



# INTRANASAL GLUCOCORTICOIDS

Drug	Dose	Use
Beclomethasone dipropionate	1-2 sprays (42 µg/spray) EN, twice daily	Perennial Rhinitis
Budesonide	2 sprays (64 µg/spray) EN, once daily	Allergic rhinitis/ vasomotor rhinitis
Mometasone	2 sprays (50 µg/spray) EN, once daily	Prophylaxis & treatment of Perennial Rhinitis

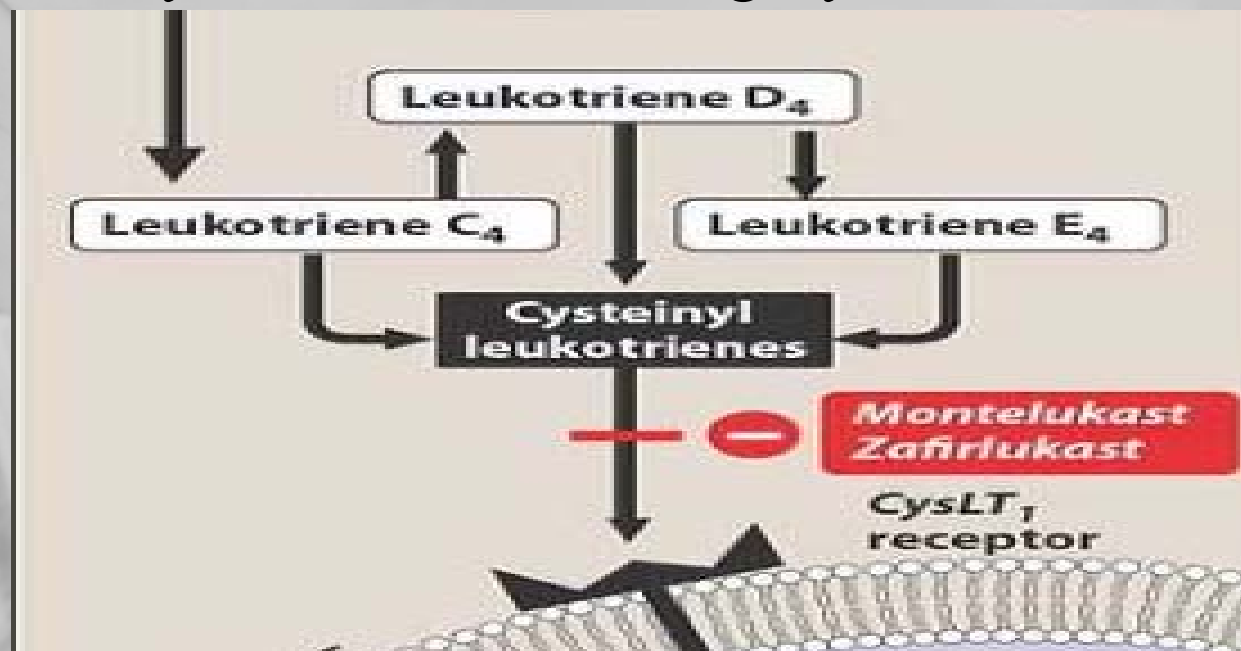


## **ADVERSE EFFECTS**

- Headache
- Throat irritation
- Epistaxis
- Stinging, burning and nasal dryness.

# LEUKOTRIENE RECEPTOR ANTAGONISTS

- Competitively antagonise Cysteinyl LT's  
LTC<sub>4</sub>/ LTD<sub>4</sub> at CysLT<sub>1</sub> receptors
- PK : Orally well absorbed, highly PPB



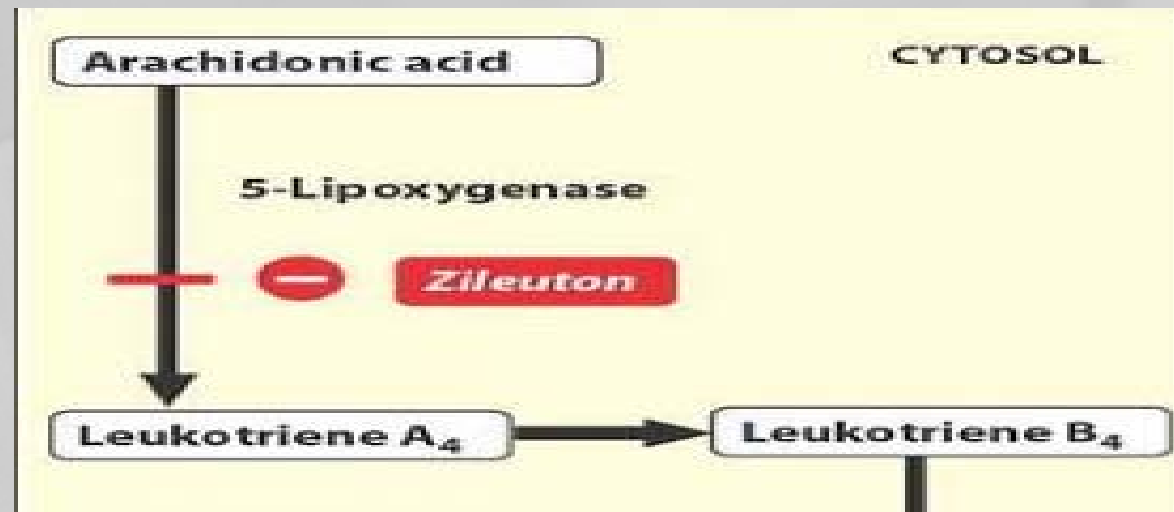
## Leukotriene receptor antagonists cntd..

- **A/E:** Headache, Rashes, rarely –Eosinophilia, Neuropathy, Churg- Strauss syndrome (Eosinophilia & systemic vasculitis)
- **Dose:** Montelukast 10mg OD oral  
Zafirlukast 20mg BD oral.



# LEUKOTRIENE SYNTHESIS INHIBITOR

- **Zileuton** : 5-LOX inhibitor
  - Blocks LTC<sub>4</sub>/D<sub>4</sub> & LTB<sub>4</sub> synthesis
  - Efficacy similar to Montelukast
  - **ADR** : Hepatotoxicity



# MAST CELL STABILIZERS

**Sodium Cromoglycate** (Cromolyn sodium) :

- Inhibits degranulation of mast cells and hence decreases mediators like histamine, LTs, PAF & interleukins

**MOA** : Not clear –by Inhibition of  $Cl^-$  channel and stabilizes mast cell



## Mast cell stabilizers cntd...

- **Pk** : Not absorbed orally, Administered as intranasal preparation 1mg/dose: 2 puffs 4 times a day
- **A/E**: Systemic toxicity minimal, Bronchospasm, Cough, Throat Irritation



# KETOTIFEN

- Platelet activating factor antagonist
- Antihistaminic + cromoglycate like action and inhibits mediator release and inflammatory cells
- **PK** : Orally absorbed, 50% bioavailability due to first pass metabolism with  $t_{1/2}$  - 22hrs.
- **A/E**: Sedation, Dry Mouth, Dizziness, Weight gain
- Dose: 1 to 2 mg OD oral

# DECONGESTANTS

- **Drugs:** oxymetazoline, phenylephrine
- **MOA:**  $\alpha$  receptor agonist
- **Actions:** causes vasoconstriction and thus reduces congestion.
- **A/E:** Sneezing, nasal dryness, atrophic rhinitis.
  - Should not be used for more than 3 days as they may cause rebound congestion.
- **Preparations:** Oxymetazoline: 0.025-0.05% intranasally



# IMMUNOMODULATION

- **Scissoring effect:**

After identifying the allergen using skin prick test, repeated exposure of the patient to small doses of allergen causes increase in IgG4 and IgA levels. These competitively inhibit IgE synthesis and helps in control of the underlying allergy.



## INTERFERON GAMMA

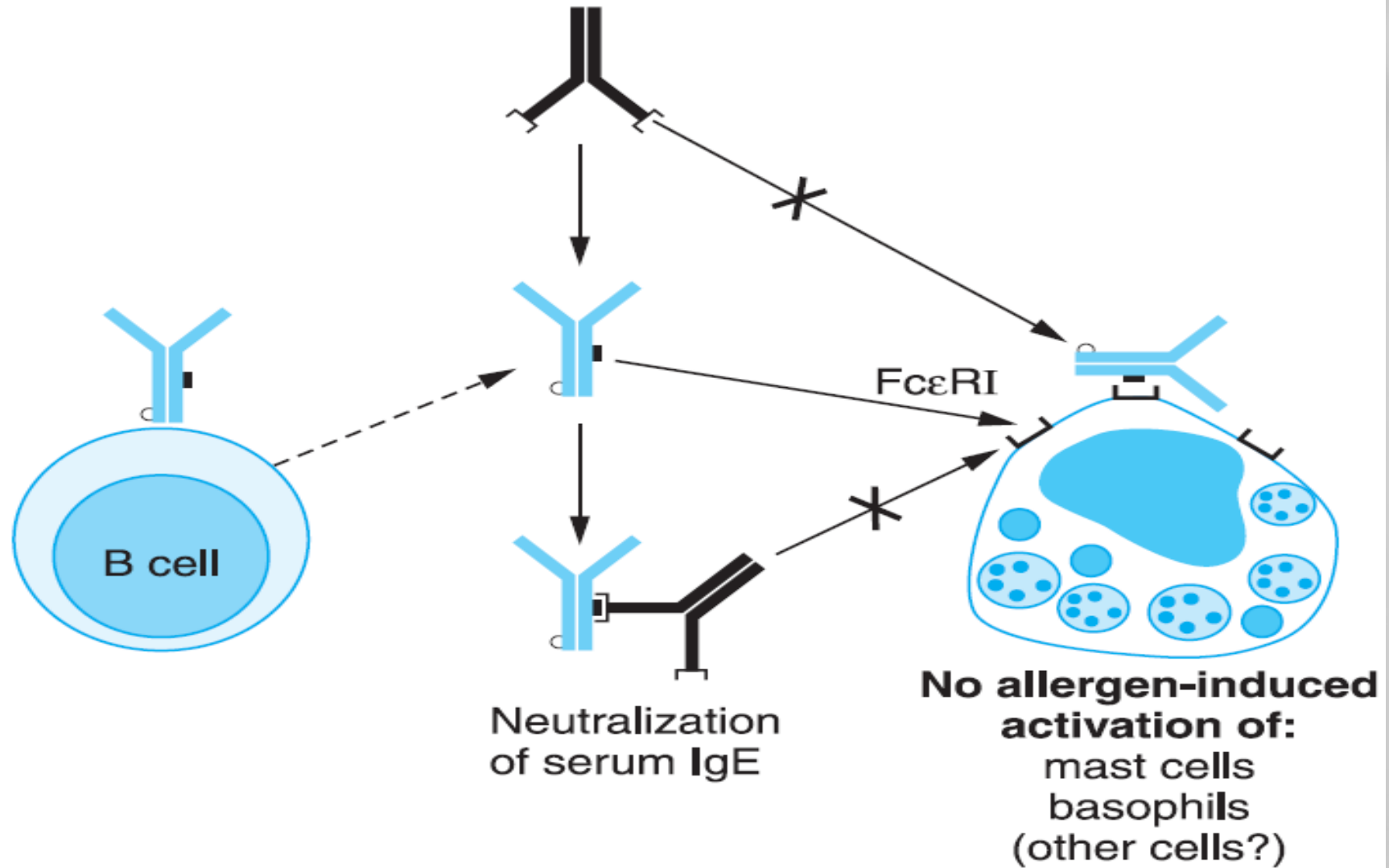
- **MOA:** inhibits stimulation of TH2 cells which modulate the antibody production from B lymphocytes.
- Available as aerosol form
- Highly expensive and not available in India

# OMALIZUMAB

- ❖ **MOA** : Monoclonal antibody against IgE and prevents it from binding to IgE receptors on mast cells & basophils.
- ❖ **ROA** : Given S.C once in 2-4 weeks dose according to IgE titre in the blood.
- ❖ **Use** : Reserved for resistant patients with raised IgE
- ❖ Preparation: 202.5mg as powder
- ❖ Highly expensive and not used below 12 yrs of age.

# Omalizumab cntd...

## Monospecific anti-IgE antibody (Omalizumab)



# TREATMENT BASED ON SYMPTOMS

<i>Treatment type</i>	<i>Ocular symptoms</i>	<i>Nasopharyngeal itching</i>	<i>Sneezing</i>	<i>Rhinorrhoea</i>
Intranasal Corticosteroids	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Oral antihistamines	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Decongestants	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>
Intranasal Cromolyn		<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Leukotriene receptor Antagonists	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>
Immunotherapy	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>



# STEP WISE ALGORITHM

Allergen avoidance



Anti histaminics



Intranasal corticosteroids



Leukotriene modulators

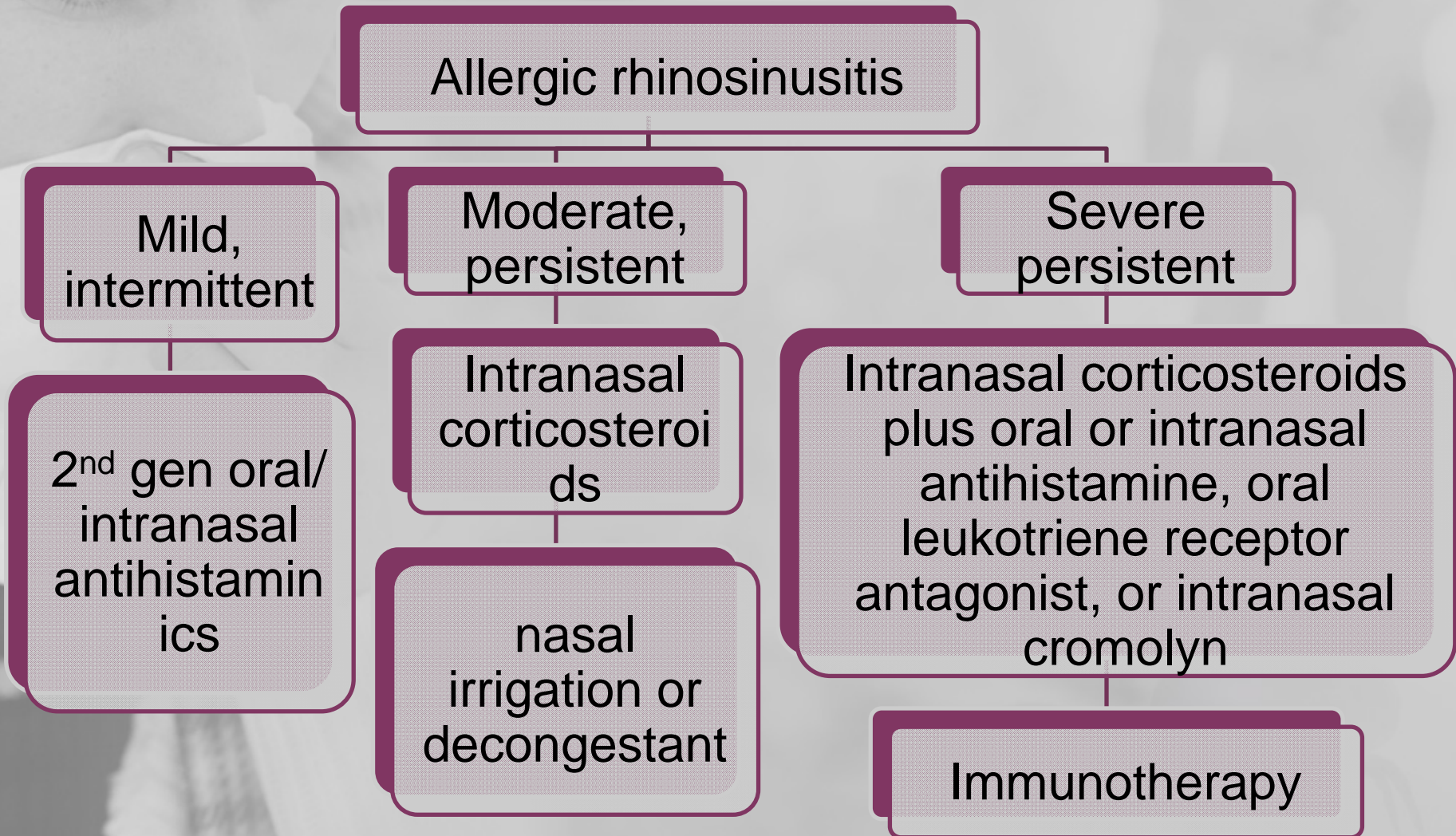


Mast cell stabilisers

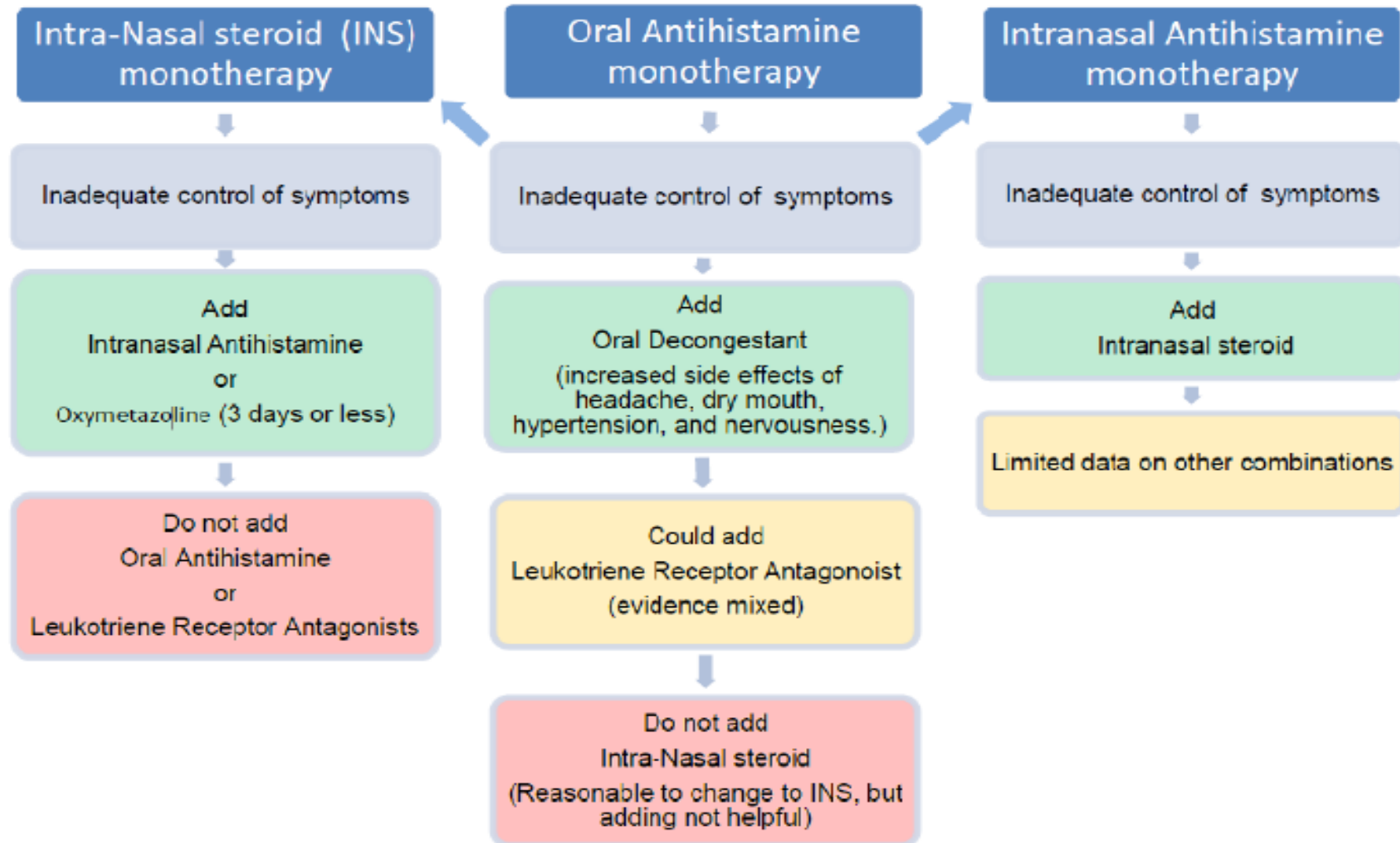


Immunotherapy

# TREATMENT OF ALLERGIC RHINOSINUSITIS



# COMBINATION THERAPY



# SUMMARY

Avoidance of allergen exposure and triggering factors

2<sup>nd</sup> generation antihistaminics

Intranasal corticosteroids

Pharmacotherapy of allergic rhino-sinusitis

Leukotriene modulators

Mast cell stabilisers

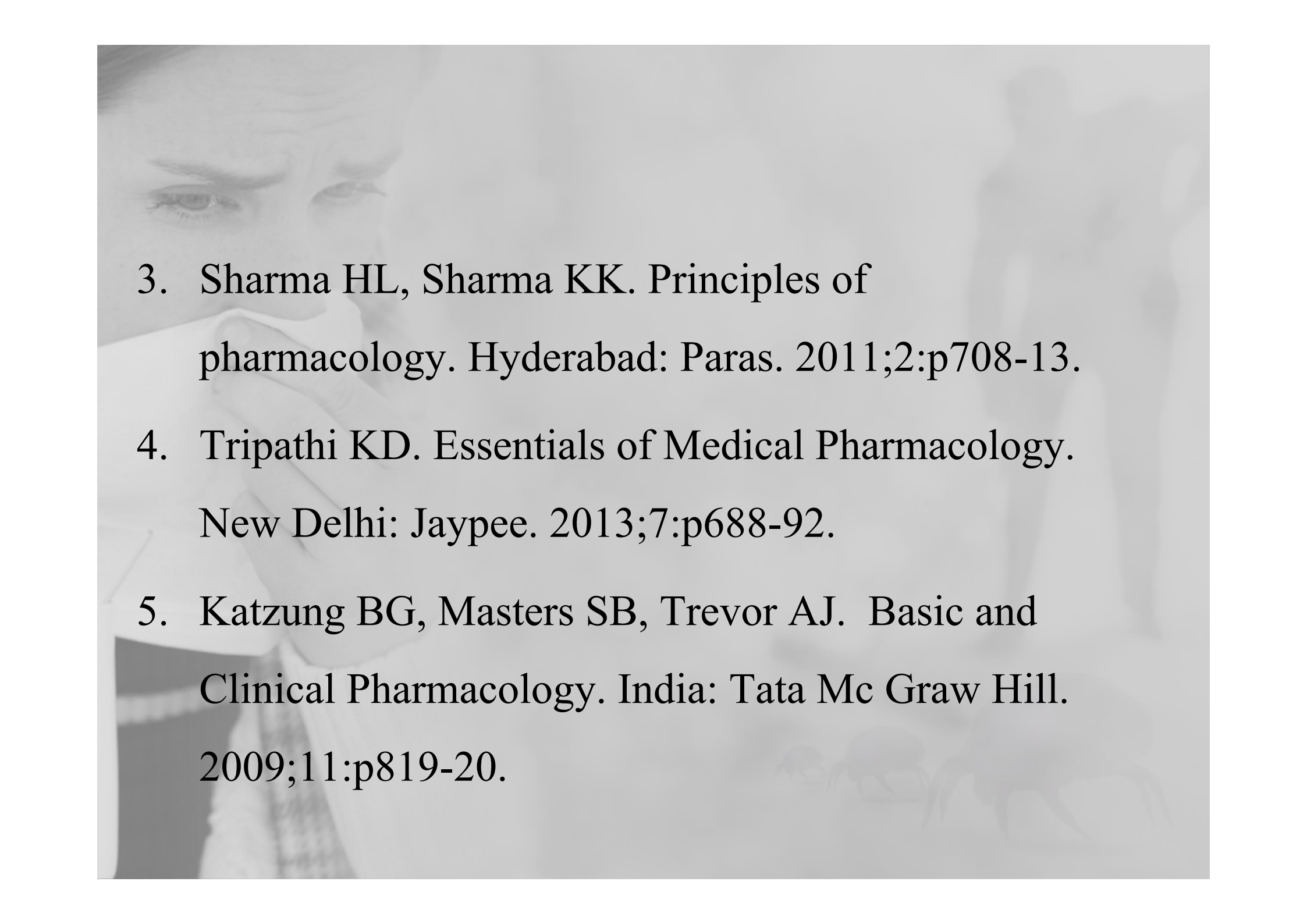
Decongestants

combination therapy of antihistaminics and leukotriene modulators orally



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**Thank you**

