IN THE NAME OF GOD

Allergic Rhinitis and co-morbidities in children

By

Tooba Momen

Clinical Allergist and Immunologist

- Rhinitis: Symptomatic disorder of the nose characterized by itching, nasal discharge, sneezing and nasal airway obstruction

- Allergic rhinitis: Induction of rhinitis symptoms after allergen exposure by an IgE-mediated immune reaction; accompanied by inflammation of the nasal mucosa and nasal airway hyperreactivity

- Allergic
- Infectious
- Non allergic and non infectious
- Idiopathic

Infectious Rhinitis

- Acute, commonly precipitated by a viral infection, or chronic, caused more often by bacteria and occasionally fungus
- Children can typically have up to ١١ upper respiratory tract infection episodes per year in infancy, eight episodes at preschool age and four at school age
- ٠٫٢–٢% of these develop into clinically important bacterial sinus infection

- Choanal atresia or stenosis: obstruction without other features of allergic rhinitis(preschool)
- Adenoidal hypertrophy : mouth breathing, discoloured nasal secretions, snoring in the absence of other features of allergic rhinitis(preschool)
- Foreign body: unilateral discoloured nasal secretions, foul smell (preschool)
- Chronic Rhinosinusitis: discoloured nasal secretions, headache, facial pain, poor smell, halitosis, cough (school age and adolescent)

- Cystic fibrosis: bilateral nasal polyps, poor smell, chest symptoms, symptoms of malabsorption, failure to thrive
- Primary ciliary dyskinesia: persisting mucopurulent discharge without respite between “colds”, bilateral stasis of mucus and secretions at the nasal floor, symptoms from birth
- Septal deviation: obstruction in the absence of other features of allergic rhinitis
- CSF leakage, Encephalocele, Immunodeficiency

- Drug-induced: Aspirin, some vasodilators
- Hormonal: Pregnancy, menstruation, hormonal contraceptives, thyroid disorders
- Tumors
- Granulomas: Sarcoid, Wegener's, Midline Granuloma

Allergic rhinitis: impact

- High prevalence
- Impaired quality of life
- Work and school absence
- Impaired learning
- Impaired sleeping
- Associated asthma, sinusitis, otitis

Allergy can affect different children in different ways

Atopic or Allergy March

Natural sequence of allergic clinical conditions appearing during a certain age period and persisting over a number of years from childhood to adulthood

Food Allergy

↓

Atopic Dermatitis

↓

Allergic Rhinitis

↓

Allergic Childhood Asthma

↓

Adult Asthma

Atopy is the inherited tendency to develop harmful immune responses to harmless substances

Allergic Rhinitis

- Allergic rhinitis is clinically defined as a symptomatic disorder of the nose induced by an IgE-mediated inflammation after allergen exposure of the membranes lining the nose
- Most prevalent in Pediatric & Adolescent population
- Traditionally, classified into Seasonal allergic rhinitis (SAR) and Perennial allergic rhinitis (PAR)

Allergic Rhinitis: Classification

Intermittent

- < ۴ days per week
- or < ۴ weeks

Persistent

- > ۴ days per week
- and > ۴ weeks

Mild

- Normal sleep
- No impairment of daily activities, sport, leisure
- Normal work & school
- No troublesome symptoms in untreated patients

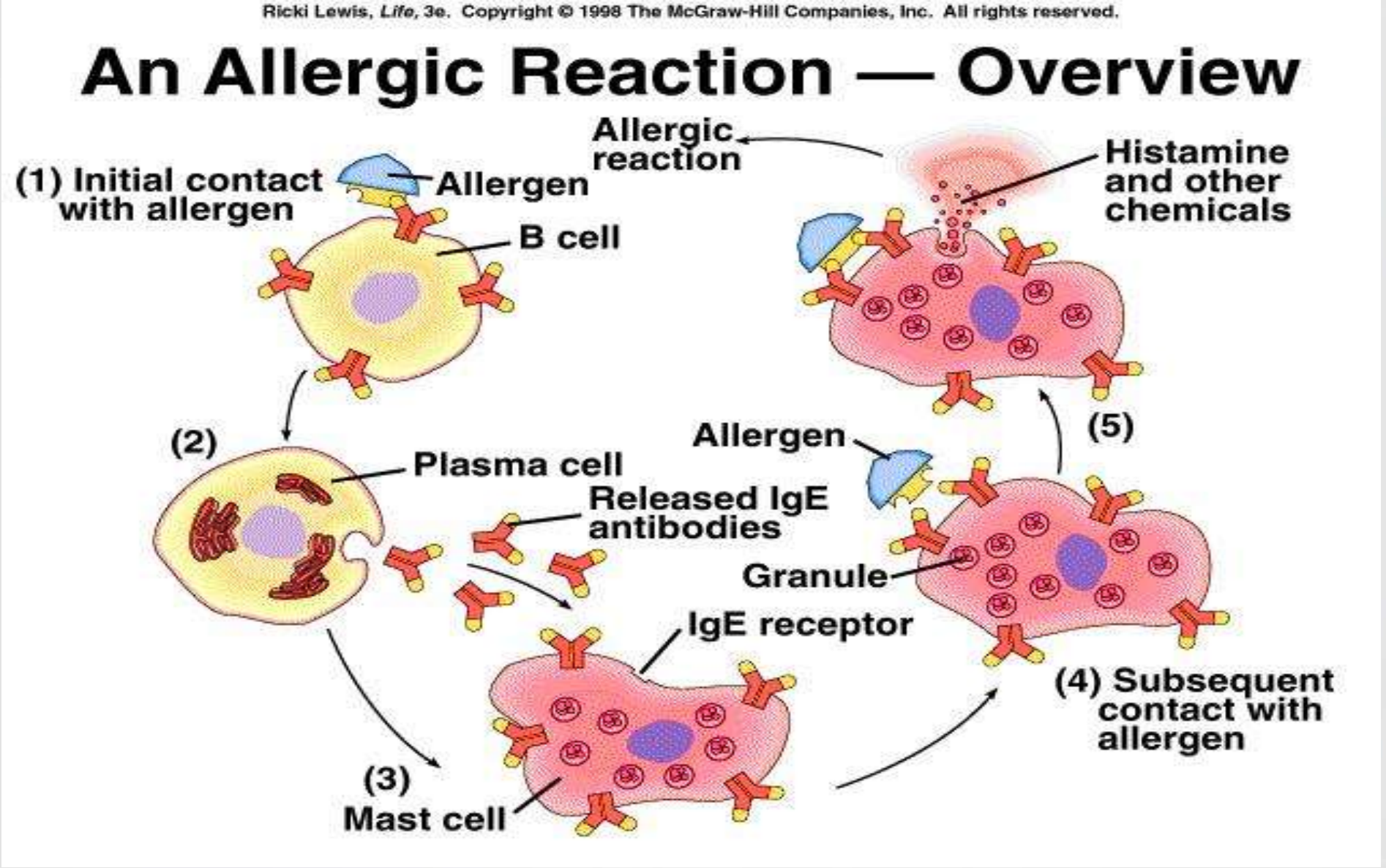
Moderate-Severe

one or more items

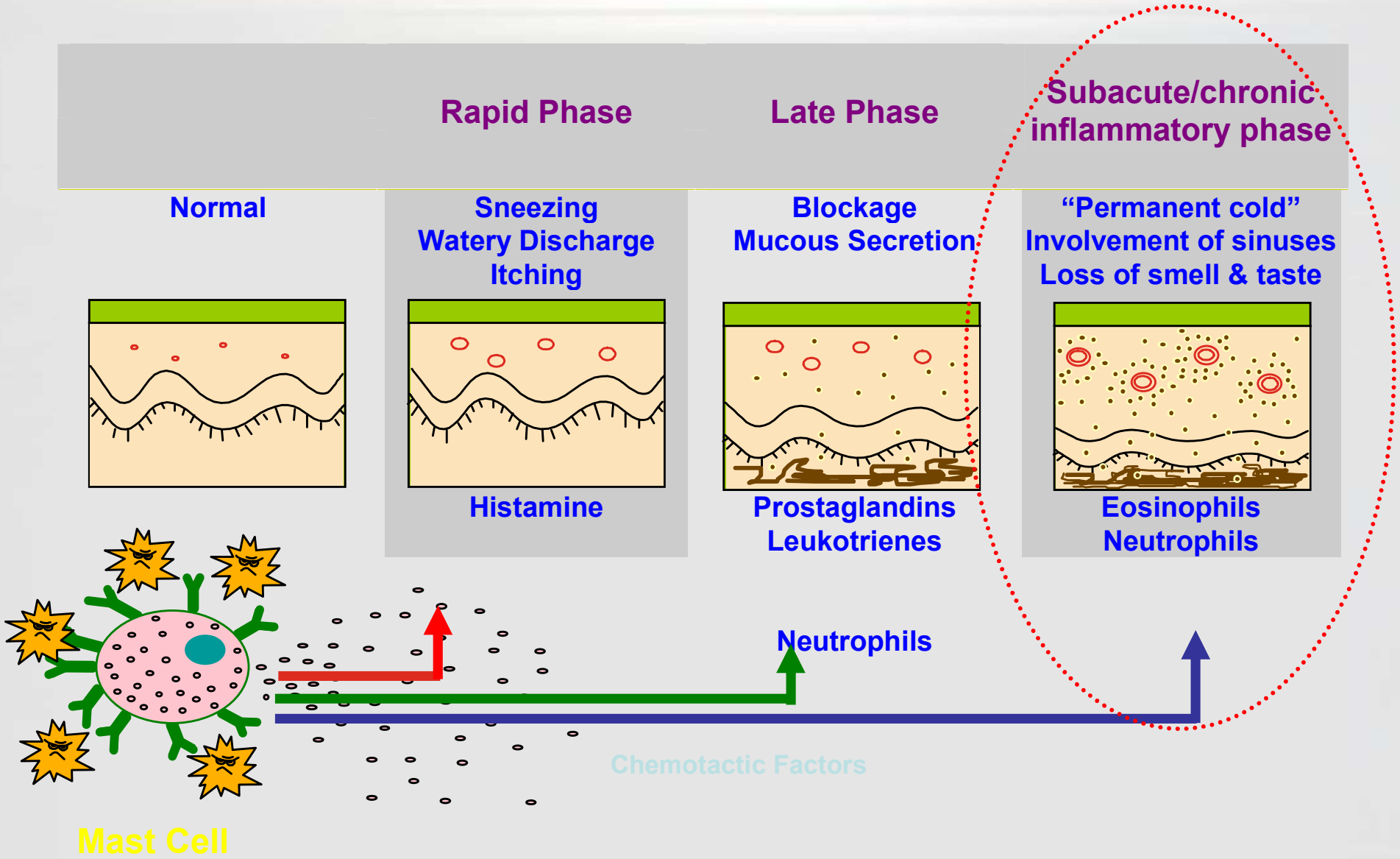
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal work and school
- Troublesome symptoms

J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۱۴۷-۳۳۶.

An Allergic Reaction



Phases of allergy: PINE or MPI



Globally important sources of allergens

- House dust mites
- Grass, tree and weed pollen
- Pets
- Cockroaches
- Molds

Prevalence and epidemiology

- The incidence has increased during last two decades, partecularly in western countries
- The International Study of Asthma and Allergies in Childhood (ISAAC) phase three studies (۱۹۹۹–۲۰۰۴) revealed:
- an average prevalence of rhinitis of ۸٫۵% (range ۱٫۸–۲۰٫۴%) in ۶- to ۷-year-old children
- ۱۴٫۶% (۱٫۴–۳۳٫۳%) for ۱۳- to ۱۴-year-old children

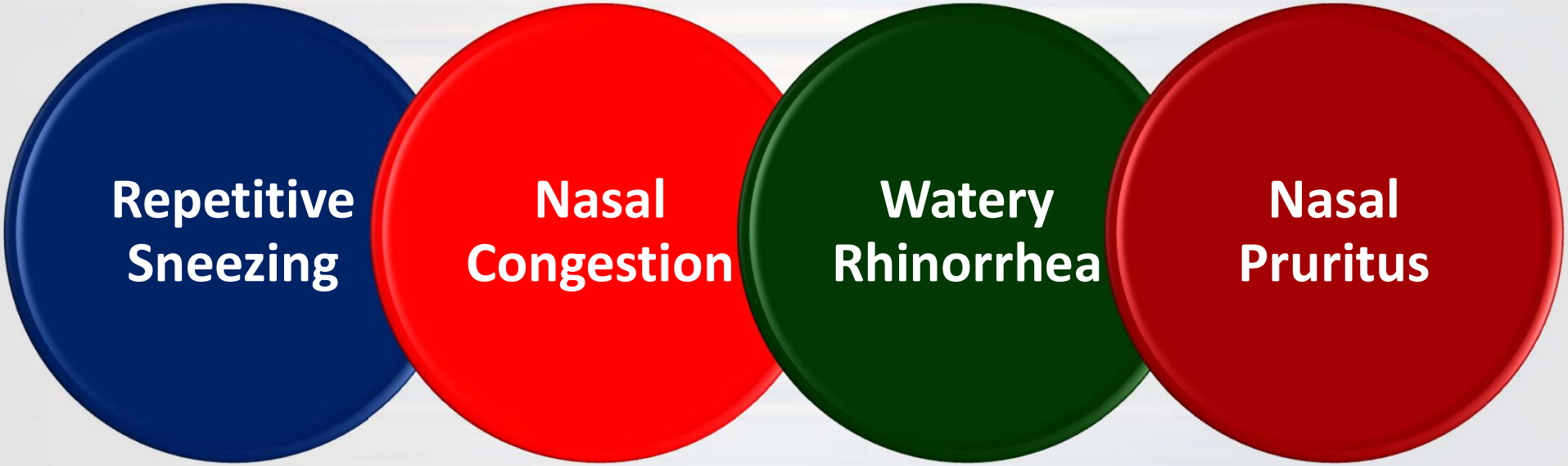
Epidemiology

Race: Allergic rhinitis occurs in persons of all races

Sex: In childhood, allergic rhinitis is more common in boys than in girls, but in adulthood, the prevalence is approximately equal between men and women.

Age: Onset of allergic rhinitis is common in childhood, adolescence, and early adult years, with a mean age of onset ٨-١١ years, but allergic rhinitis may occur in persons of any age. In ٨٠% of cases, allergic rhinitis develops by age ٢٠ years.

Classical Symptoms



Other Manifestations

- Eye Symptoms
- Ear Symptoms
- Post nasal drip

AR in children: Clinical presentation

- Clinical presentation depends on the duration of allergen exposure (perennial versus seasonal and episodic exposure), age of the child, and extent of co-morbid disease.

- AR commonly presents in childhood as recurrent sore throats and upper respiratory tract infections

- Diagnosis of AR is often missed in children, who are thus treated inappropriately with multiple doses of antibiotics.

Lack G. J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۹-۱۵

Allergic Shiners

Allergic Salute and Crease

Allergic Conjuctivitis

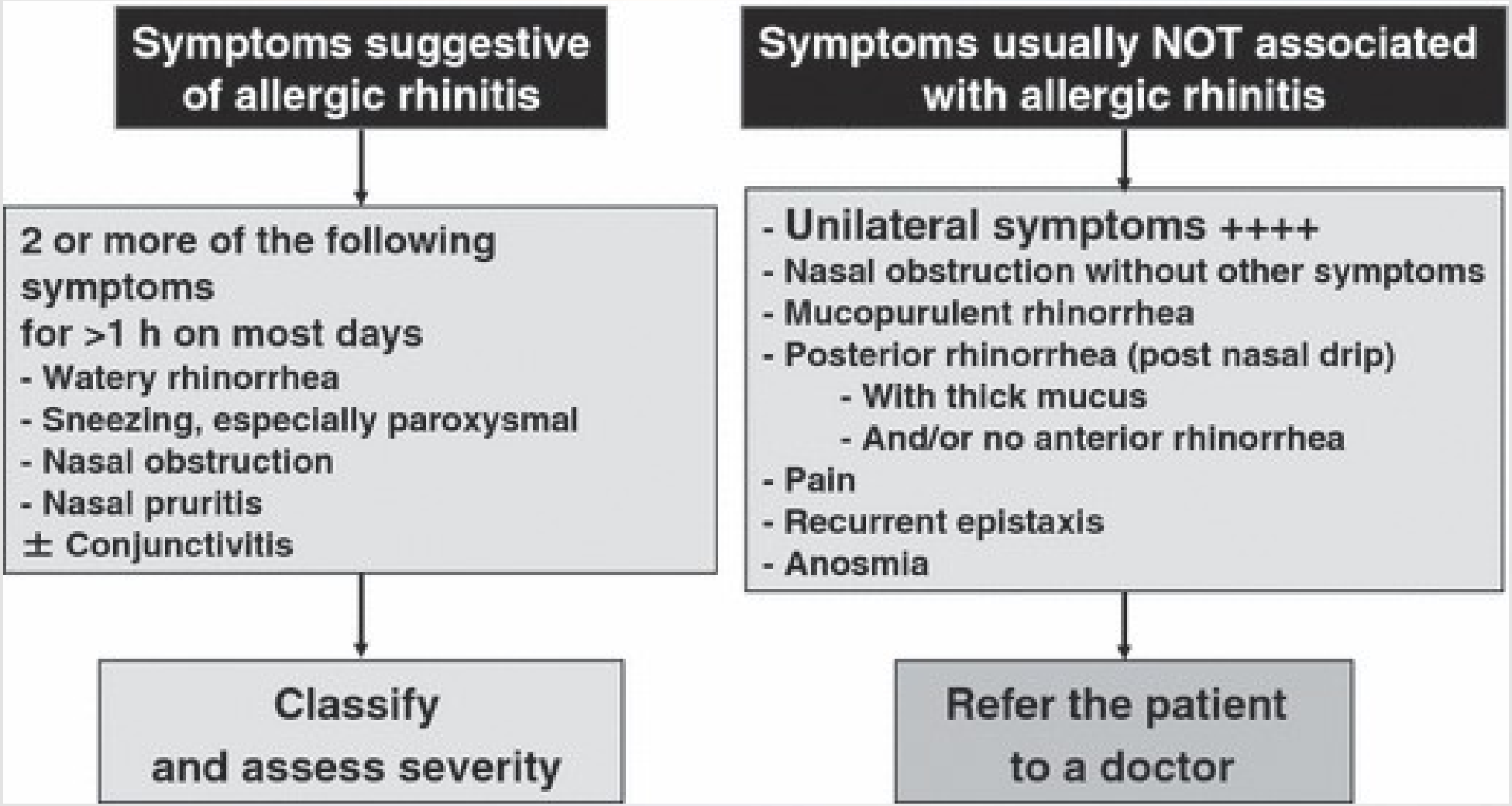
Diagnosis of Allergic Rhinitis

١. History & symptoms of recurrent or persistent rhinitis and/or associated health effects
٢. Signs of atopy and recurrent or persistent rhinitis
٣. Demonstration of IgE allergy
٤. Exclusion of other causes of rhinitis

History

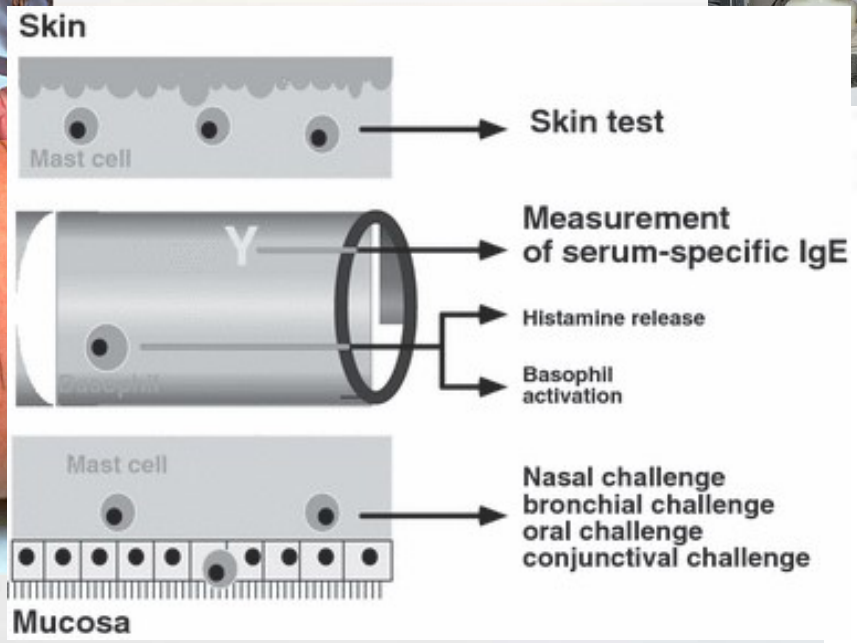
- Evaluation of the nature, duration, and time course of symptoms
- Possible triggers for symptoms
- Response to medications
- Comorbid conditions
- Family history of allergic diseases
- Environmental exposures; occupational exposures; and effects on quality of life

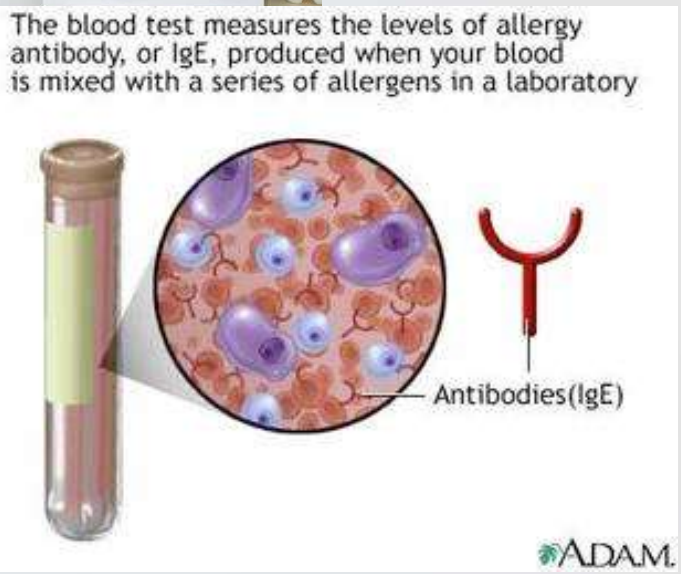
Diagnosis in Primary Care Setting



Diagnosis of Allergic Rhinitis

٣. Demonstration of IgE allergy

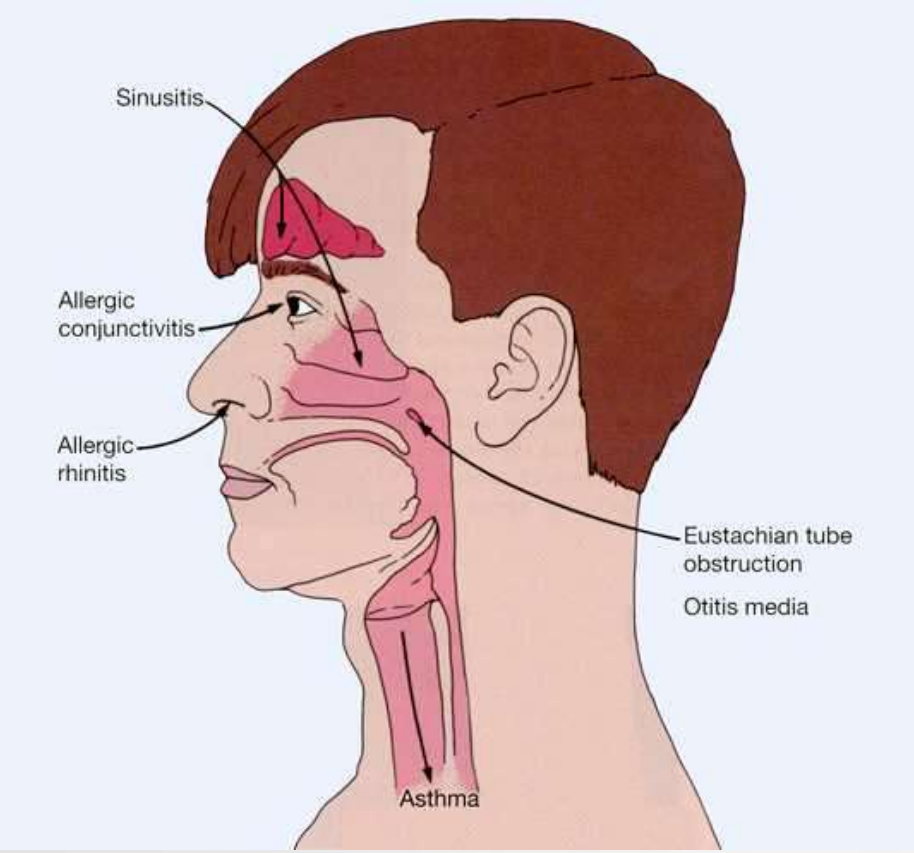


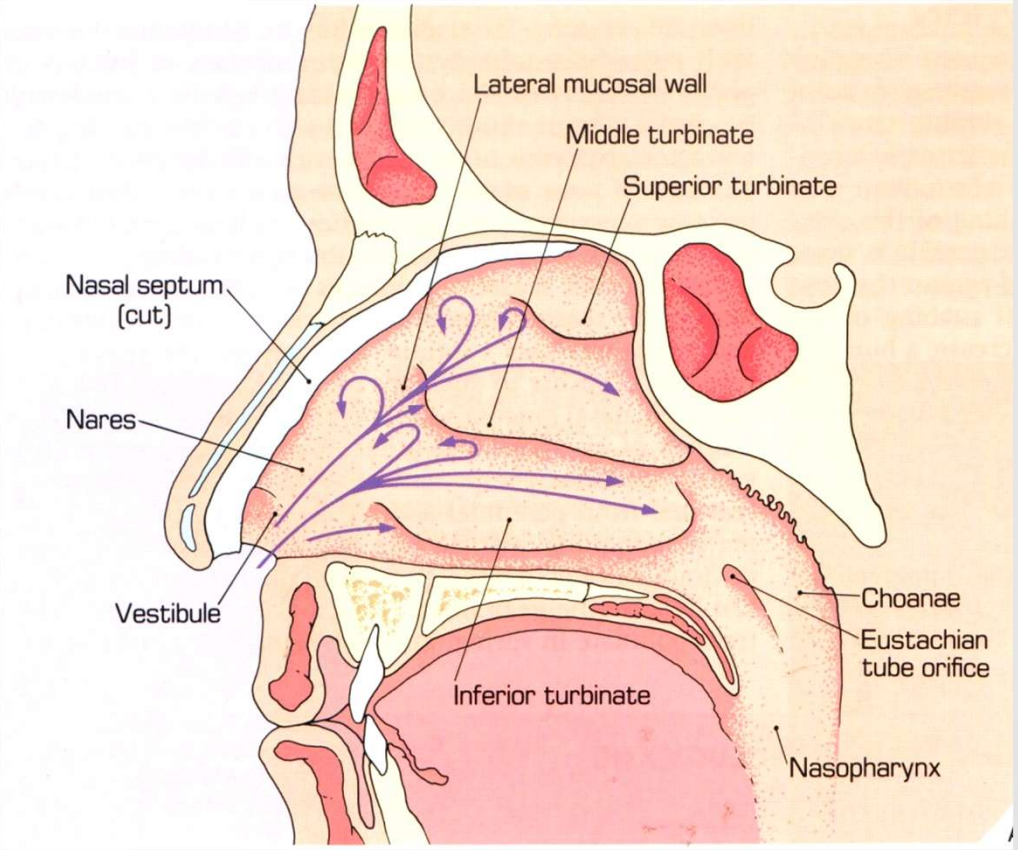


Other diagnostic tests

- Nasal secretion / scraping cytology
- Nasal allergen challenge
- Nasal endoscopy
- CT scan
  - anatomic abnormalities
  - concomitant presence of sinusitis

Allergic Rhinitis and Co-morbidities





"The nose is the part of the lung which can be accessed by the finger"

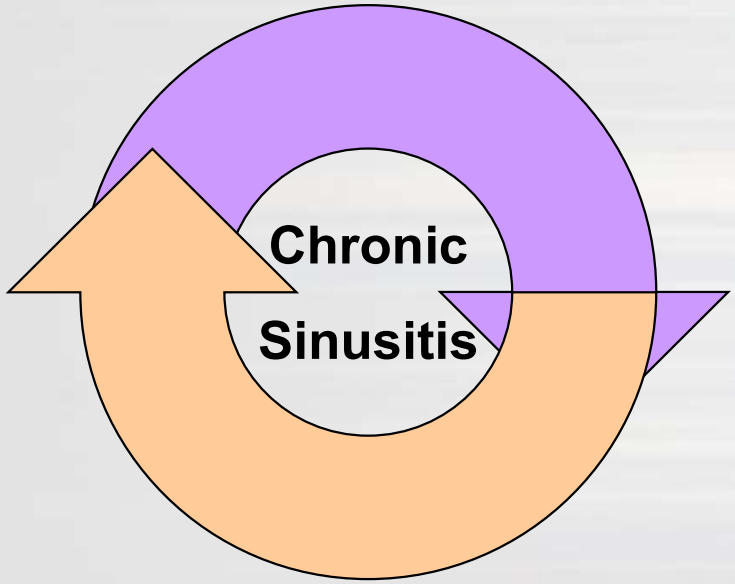
AR and Sinusitis: Pathophysiology

- Rhinosinusitis is common in patients with AR
- ٣٠% of acute sinusitis, ٢٧% of unilateral chronic sinusitis and ٨٠% of bilateral chronic sinusitis have AR
- Impairment in sinus drainage
- A shift to anaerobic conditions and bacterial proliferation

- The relation between Chronic rhino-sinusitis and allergy is more complex and involves anti-staphylococcal IgE antibodies in some

AR and Sinusitis: Pathophysiology

Frontal, Ethmoidal & Maxillary sinuses drain into middle meatus through an opening called ostium (osteomeatal complex)



Allergic Rhinitis → **Nasal inflammation** ← **Viral URTI**

↓

Mucosal swelling

↓

Obstruction of sinus passage

↓

Impedes normal movement of air and secretions

↓

Accumulation of thickened secretions & impaired ciliary movements

↓

Environment for infections

AR and Asthma in children

- Approximately ۴۰% of patients with chronic rhinitis have asthma , and ۸۰% of patients with asthma suffer with persistent nasal symptoms

- AR and Asthma frequently co-exist and are considered as twin expressions of the same disease

Lack G. J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۹-۱۵

Children with chronic cough

Cough-Variant Asthma

- Noctural cough in poorly controlled asthma
- No history of wheezing
- Responsive to brochodilator therapy

Cough Variant Rhinitis

- Cough esp. nocturnal and post nasal drip
- Responsive to allergen avoidance; non-sedating long acting antihistamines; and/or intranasal steroids
- Misdiagnosis may lead to overtreatment inhaled steroids, β۲ agonists and oral steroides

When Asthma & Rhinitis co-exists

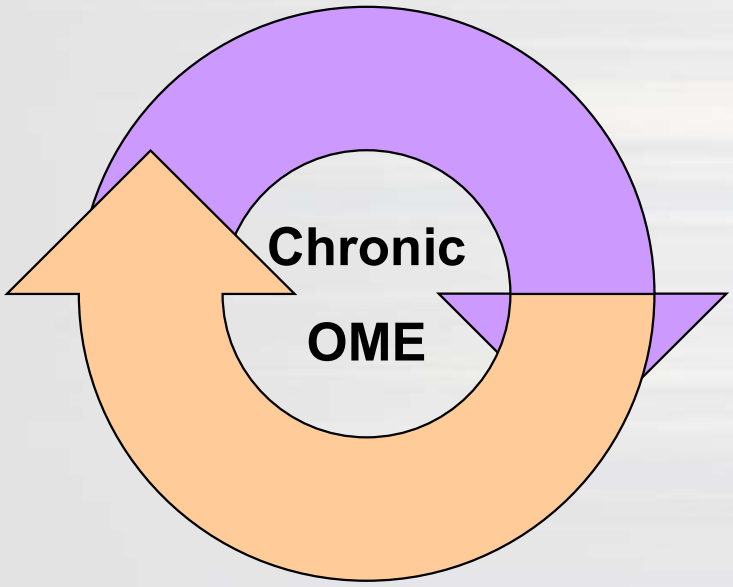
- Asthma may appear to be worse than it is
- Cough may be misattributed to asthma
- This may lead to over-treatment with high dose inhaled steroids
- **Correct diagnosis and treatment of AR has a steroid sparing effect**

Lack G. J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۹-۱۵

AR and Otitis Media: Pathophysiology

Relationship between nasal allergic inflammation and otitis media is caused by a dysfunction of the Eustachian tube

There is anatomic continuity in the form of Eustachian tubes connecting Pharynx and Middle ear



Allergic Rhinitis → Inflammation ← Viral URTI

↓

Mucosal swelling

↓

Obstruction of Eustachian tubes

↓

Increased negative pressure and impaired ventilation in middle ear

↓

Aspiration of fluids in middle ear during transient openings

↓

Acute Otitis media

Complications of AR with Chronic OME

- Chronic middle ear effusions may lead to hearing deficit and speech impairment in children

- ٥١٩ children with Chronic MEE attending a pediatric allergy clinic reported that ٩٨% had associated nasal allergy

- A study of children with seasonal ragweed pollen allergy found an increase in the rate of ETO and clinically significant hearing loss compared with pre-seasonal assessment in the same group of children

Lack G. J Allergy Clin Immunol ٢٠٠١;١٠٨:S٩-١٥

AR & obstructive sleep apnea

- Children with AR usually have lymphoid hypertrophy, particularly evident in the cervical lymph node chain & adenoids

- Children with AR often become mouth-breathers and snore at night as a result of nasal obstruction and adenoidal hypertrophy

- The pediatrician must consider the possibility of AR in the assessment of snoring children

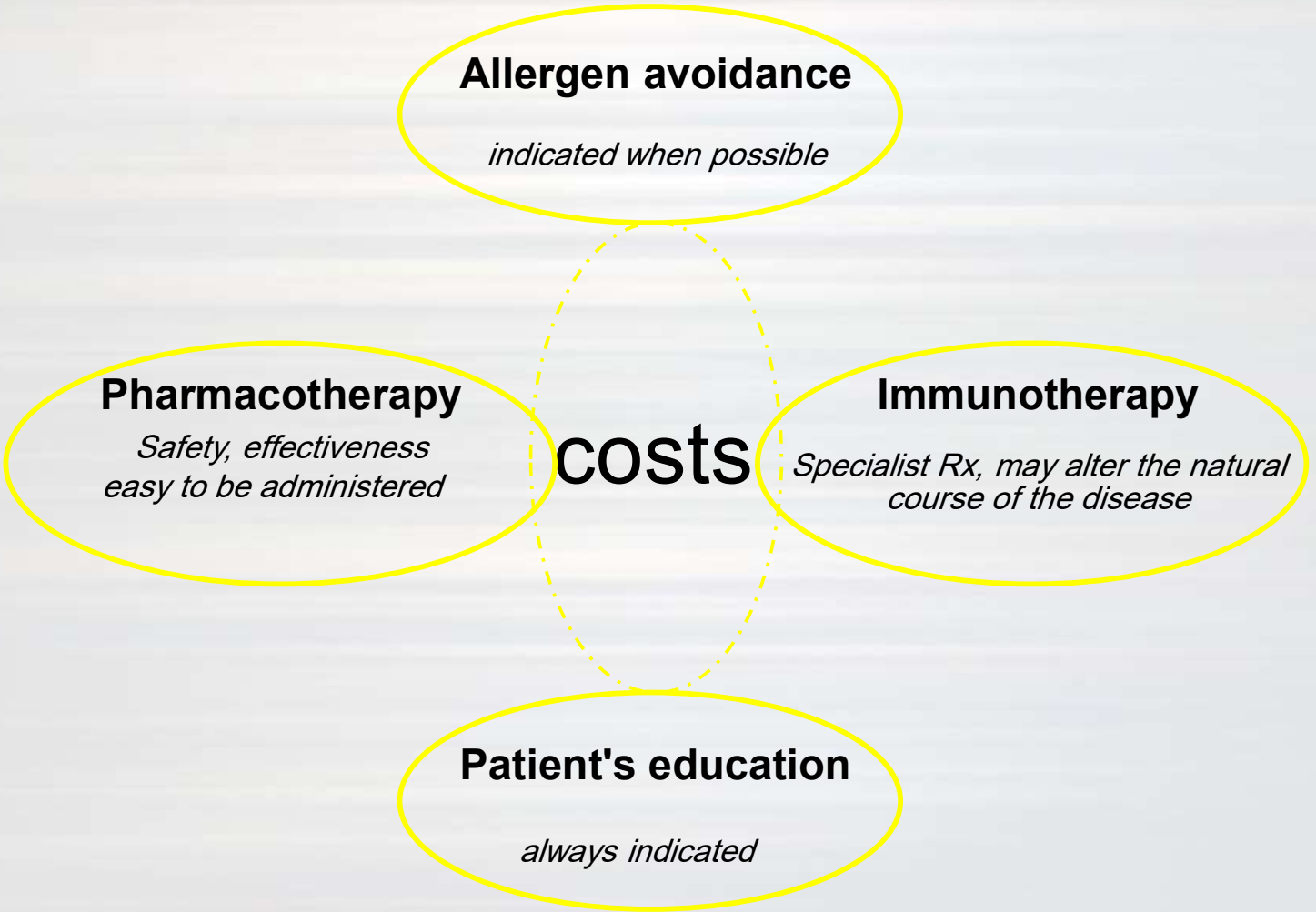
Lack G. J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۹-۱۵

Dental maloclusion

- Persistent, severe rhinitis in children may cause alteration in the palatal anatomy and dental maloclusion ???

MANAGEMENT OF ALLERGIC RHINITIS

ARIA workshop: Therapeutic options



ARIA workshop and children

- Significant correlation between asthma & rhinitis in school going children
- During the ragweed pollen season, ۴۰% of children developed Eustachian tube obstruction
- Gastro esophageal reflux can be associated with rhinitis, especially in children

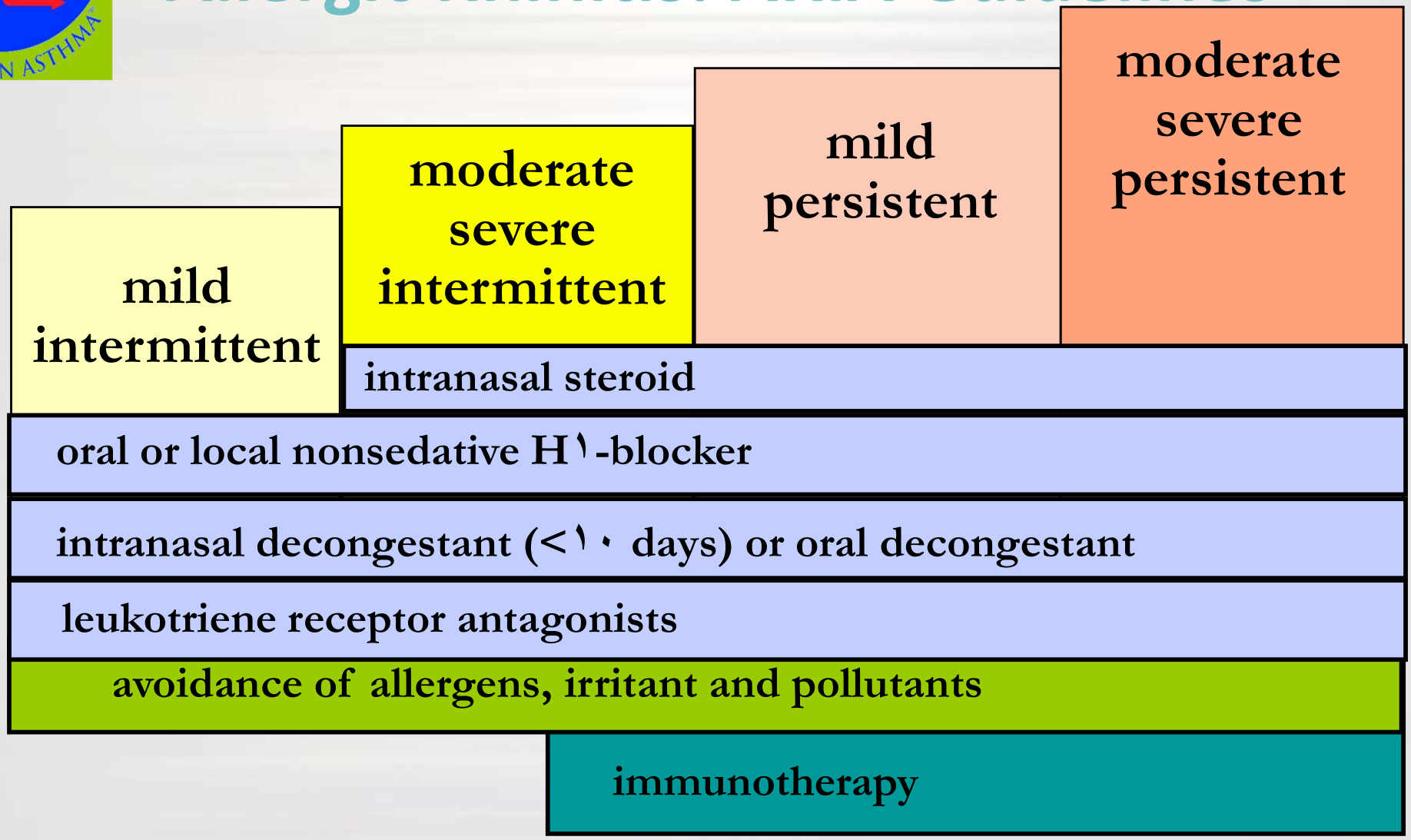
J Allergy Clin Immunol ۲۰۰۱;۱۰۸:S۱۴۷-۳۳۶.

ARIA workshop: Recommendations

- Patients with persistent rhinitis should be evaluated for asthma
- Patients with persistent asthma should be evaluated for rhinitis
- A strategy should combine the treatment of upper and lower airways in terms of efficacy and safety
- Oral H1 antihistamines are the mainstay for management of
  - Mild Intermittent
  - Mild Persistent AR
  - Moderate to severe Intermittent AR

Long term treatment is more effective than on demand treatment

Management of Allergic Rhinitis: ARIA Guidelines



Modified from Bousquet J et al. J Allergy Clin Immunol ٢٠٠١;١٠٨:S١٤٧

Environmental control

١. **Allergens**
   - House dust mites
   - Pets
   - Cockroaches
   - Molds
   - Pollen

٢. **Pollutants and Irritants**

Therapeutic options for AR

Strategy	Action
Allergen control	Simple, effective, and essential means of controlling allergen exposure
Pharmacotherapy[15]	
Antihistamines	Antagonize histamine action
Decongestants	Increase vasoconstriction
Corticosteroids	Anti-inflammatory action
Cromolyn/nedocromil	Stabilize mast cells
Leukotriene antagonists	Inhibition of early allergic response[16]
Immunotherapy	Trigger induction of competing IgG antibodies

Hadley JA. Med Clin North Am. ۱۹۹۹;۸۳:۱۳-۲۵. ۱۶. Busse WW. Clin Exp Allergy. ۱۹۹۶;۲۶:۸۶۸-۸۷۹.

ARIA : Treatment in children

- Long-term continuous treatment with **H_1**-antihistamines may
improve lower respiratory symptoms and may exert a prophylactic effect on asthma onset in children

- Treatment with classical antihistamines often had a further reducing effect upon cognitive function.

- Use of TRULY non-impairing H_1-antihistamines may improve learning ability in allergic rhinitis

PHARMACOTHERAPY OF ALLERGIC RHINITIS

Management of Allergic Rhinitis: ARIA

	sneezing	rhinorrhea	nasal obstruction	nasal itch	eye symptoms
H1-antihistamines					
oral	+++	+++	0 to +	+++	++
intranasal	++	+++	+	++	0
intraocular	0	0	0	0	+++
Corticosteroids	+++	+++	++	++	+
Chromones					
intranasal	+	+	+	+	0
intraocular	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	++

Oral antihistamines

- First generation agents

  Chlorpheniramine

  Brompheniramine

  Diphenydramine

  Promethazine

  Tripolidine

  Hydroxyzine

  Azatadine

- Newer agents

  Acrivastine

  Azelastine

  Cetirizine

  Desloratadine

  Fexofenadine

  Levocetirizine Loratadine

  Mizolastine

Newer generation oral antihistamines

- First line treatment for mild allergic rhinitis
- Effective for
  - Rhinorrhea
  - Nasal pruritus
  - Sneezing
- Less effective for
  - Nasal blockage
- Possible additional anti-allergic and anti-inflammatory effect
  - In-vitro effect > in-vivo effect
- Minimal or no sedative effects
- Once daily administration
- Rapid onset and ٢٤ hour duration of action

Decongestants: alpha-٢ adrenergic agonists

- Oral

  Pseudoephedrine

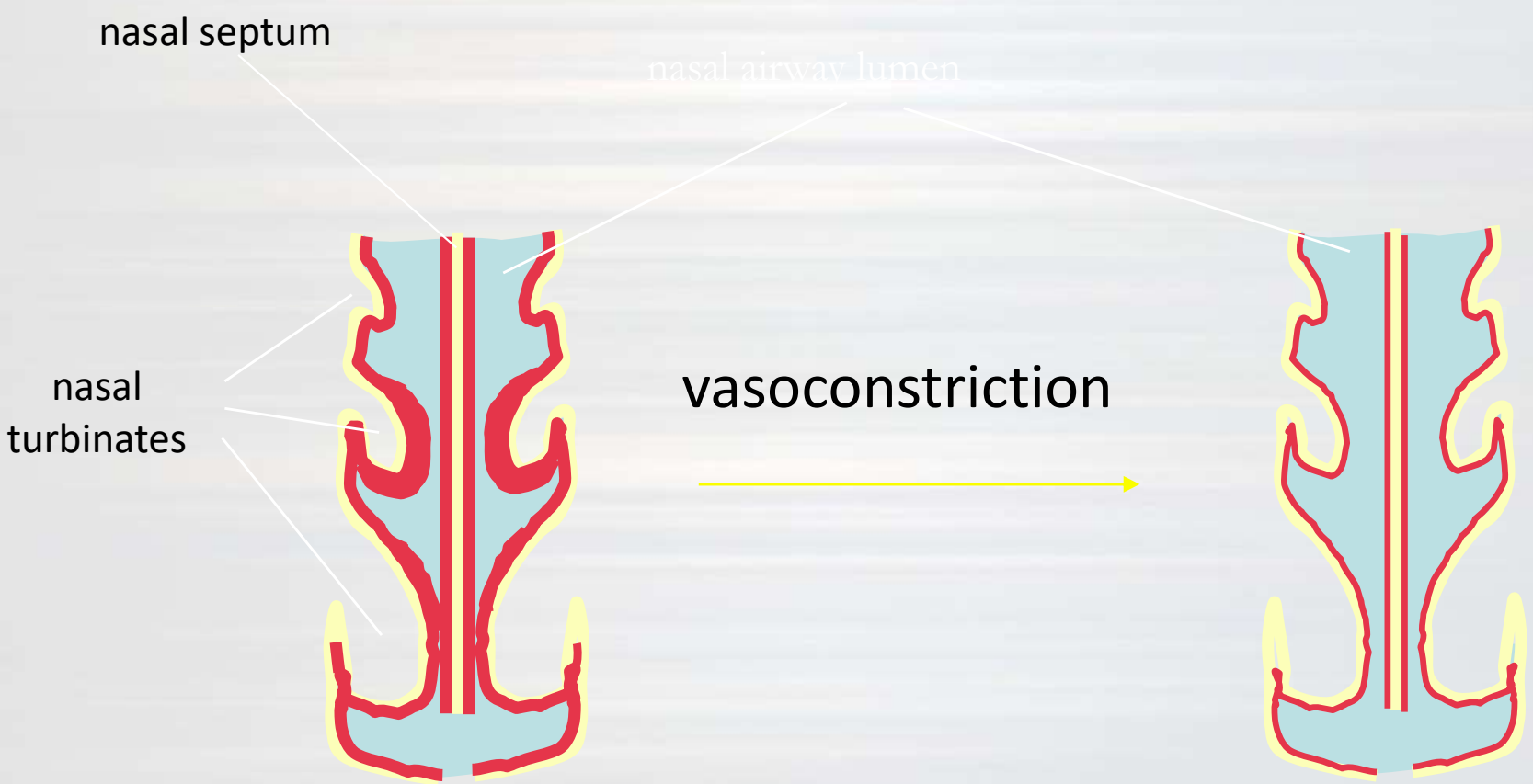
- Nasal

  Phenylephrine

  Oxymetazoline

  Xylometazoline

Decongestants: alpha-۲ adrenergic agonists



Decongestants

EFFICACY:

- Oral decongestants: moderate
- Nasal decongestants: high

ADVERSE EFFECTS:

- Oral decongestants: insomnia, tachycardia, hyperkinesia tremor, increased blood pressure, stroke (?)
- Nasal decongestants: tachyphylaxis, rebound congestion, nasal hyperresponsiveness, rhinitis medicamentosa

Anticholinergic treatment: ipratropium bromide

- Nasal glands are activated by muscarinic, cholinergic receptors
- Ipratropium bromide is a nonselective muscarinic receptor antagonist
- Ipratropium bromide applied intranasally blocks rhinorrhea induced by cholinergic stimulation
- Ipratropium bromide has negligent systemic anticholinergic activity
- Topical adverse effects: excessive dryness, epistaxis

Anti-leukotriene agents

CysLT1 Receptor Antagonists	5-Lipoxygenase Inhibitors
Montelukast *	Zileuton
Pranlukast *	
Zafirlukast	

* Approved for allergic rhinitis

Anti-leukotriene treatment in allergic rhinitis

Efficacy

- Equipotent to H١ receptor antagonists but with onset of action after ٢ days
- Reduce nasal and systemic eosinophilia
- May be used for simultaneous treatment of allergic rhinitis and asthma

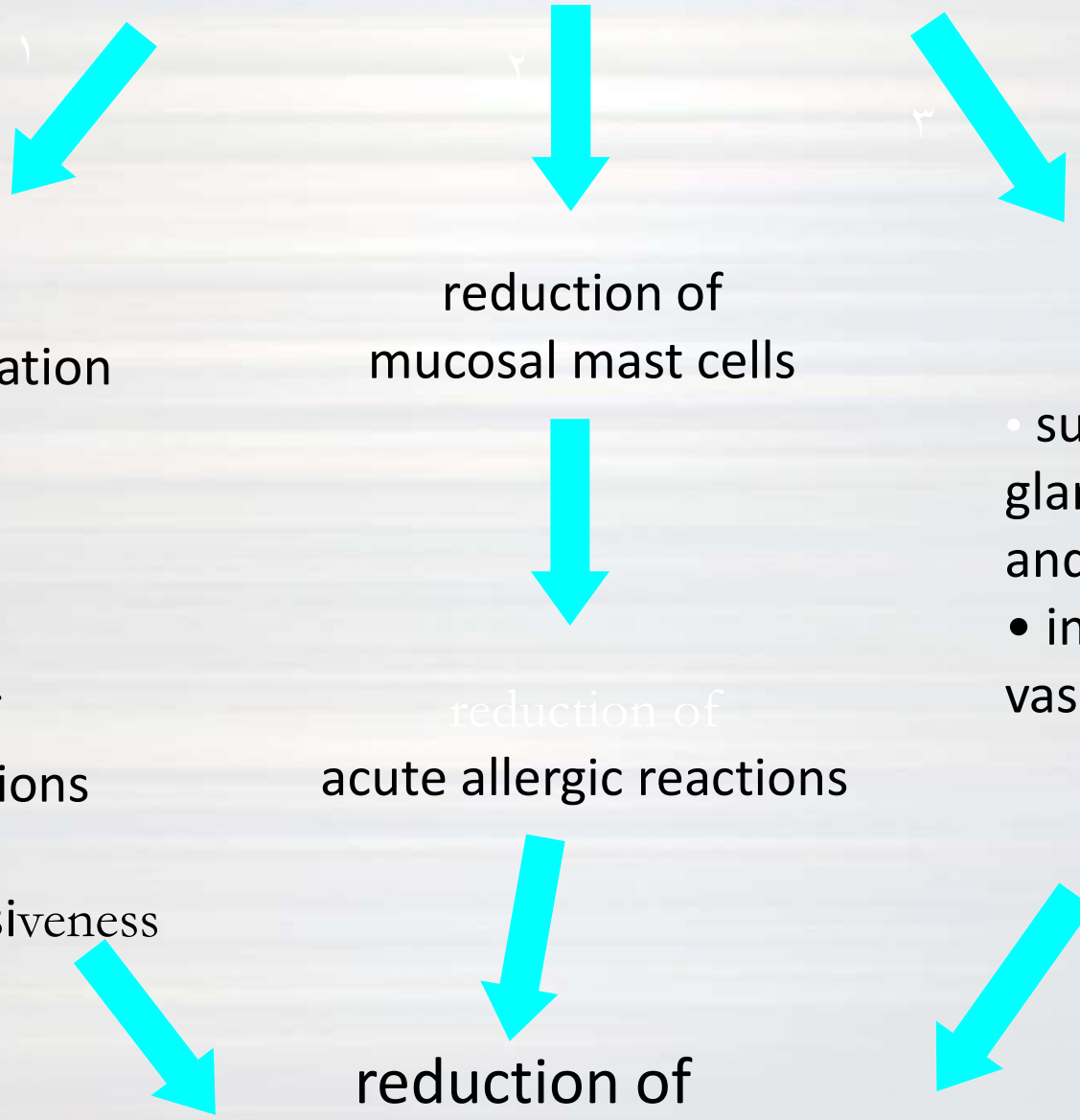
Safety

- Dyspepsia (approx. ٢%)

Nasal corticosteroids

- Most potent anti-inflammatory agents
- Effective in treatment of all nasal symptoms including obstruction
- Superior to anti-histamines and anti-leukotienes
- First line pharmacotherapy for persistent allergic rhinitis

Nasal corticosteroids



Nasal Corticosteroids

Beclomethasone dipropionate

Budesonide

Ciclesonide*

Flunisolide

Fluticasone propionate

Mometasone furoate

Triamcinolone acetonide

* Currently only approved for asthma

Nasal corticosteroids

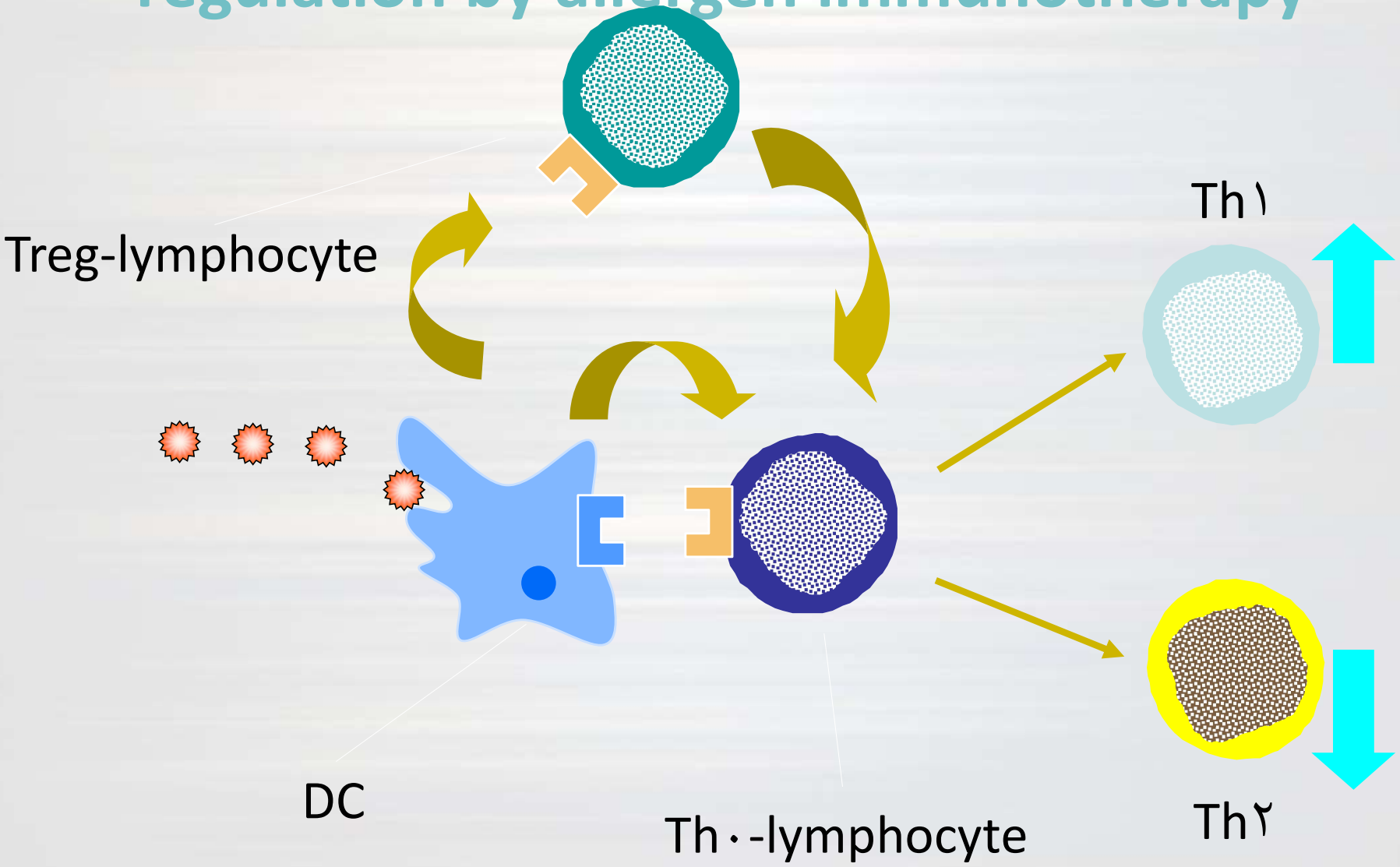
- Overall safe to use
- Adverse Effects
  - Nasal irritation
  - Epistaxis
  - Septal perforation (extremely rare)
  - HPA axis suppression (inconsistent and not clinically significant)
  - Suppressed growth (only in one study with beclomethasone)

Allergen immunotherapy (vaccines)

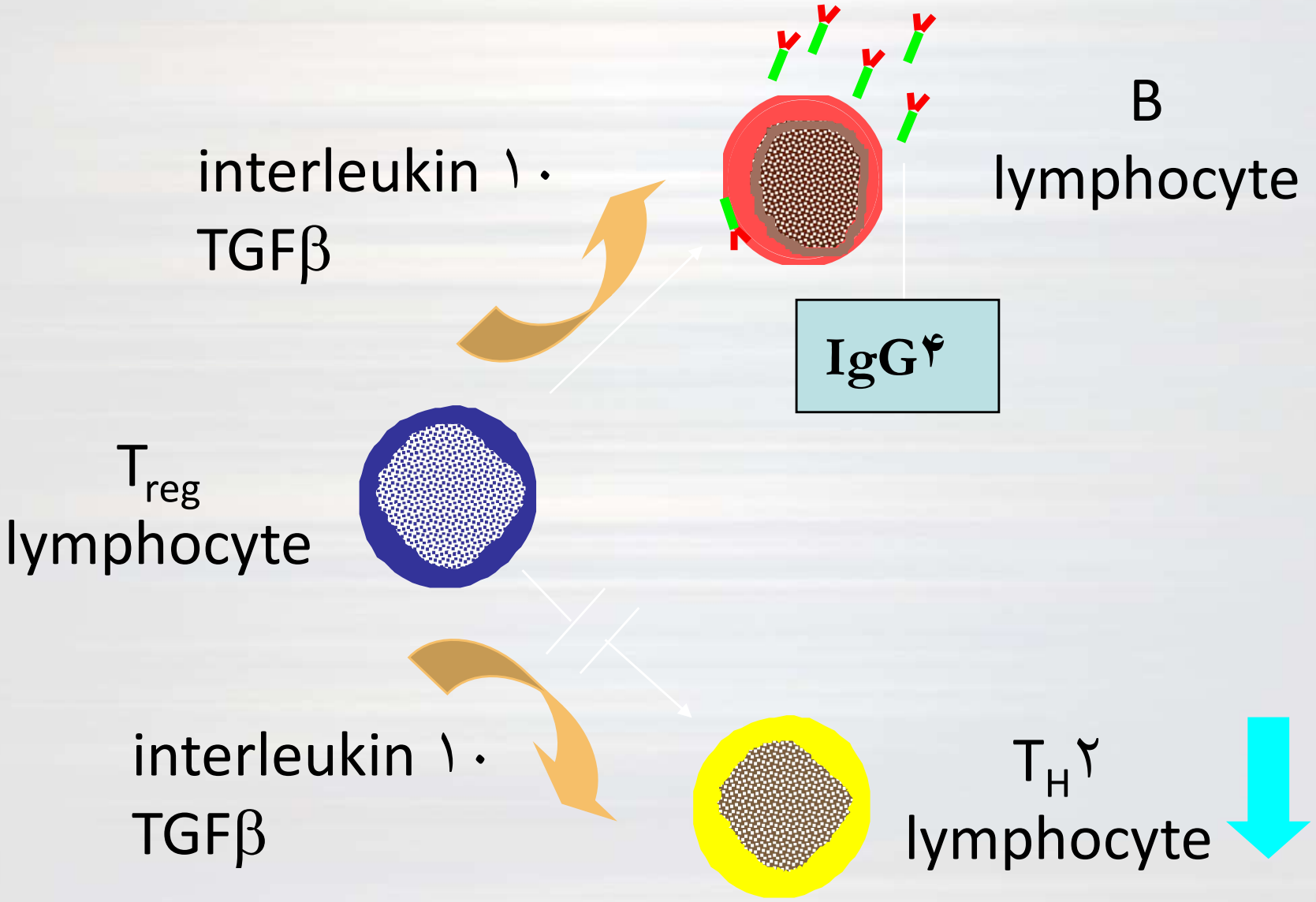
- Subcutaneous
- Sublingual
- Nasal

- Involves the sequential administration of antigen to patients with symptomatic, atopic conditions to induce tolerance to offending antigens
- Effective in treatment of both AR & Asthma
- Generally safe and well tolerated

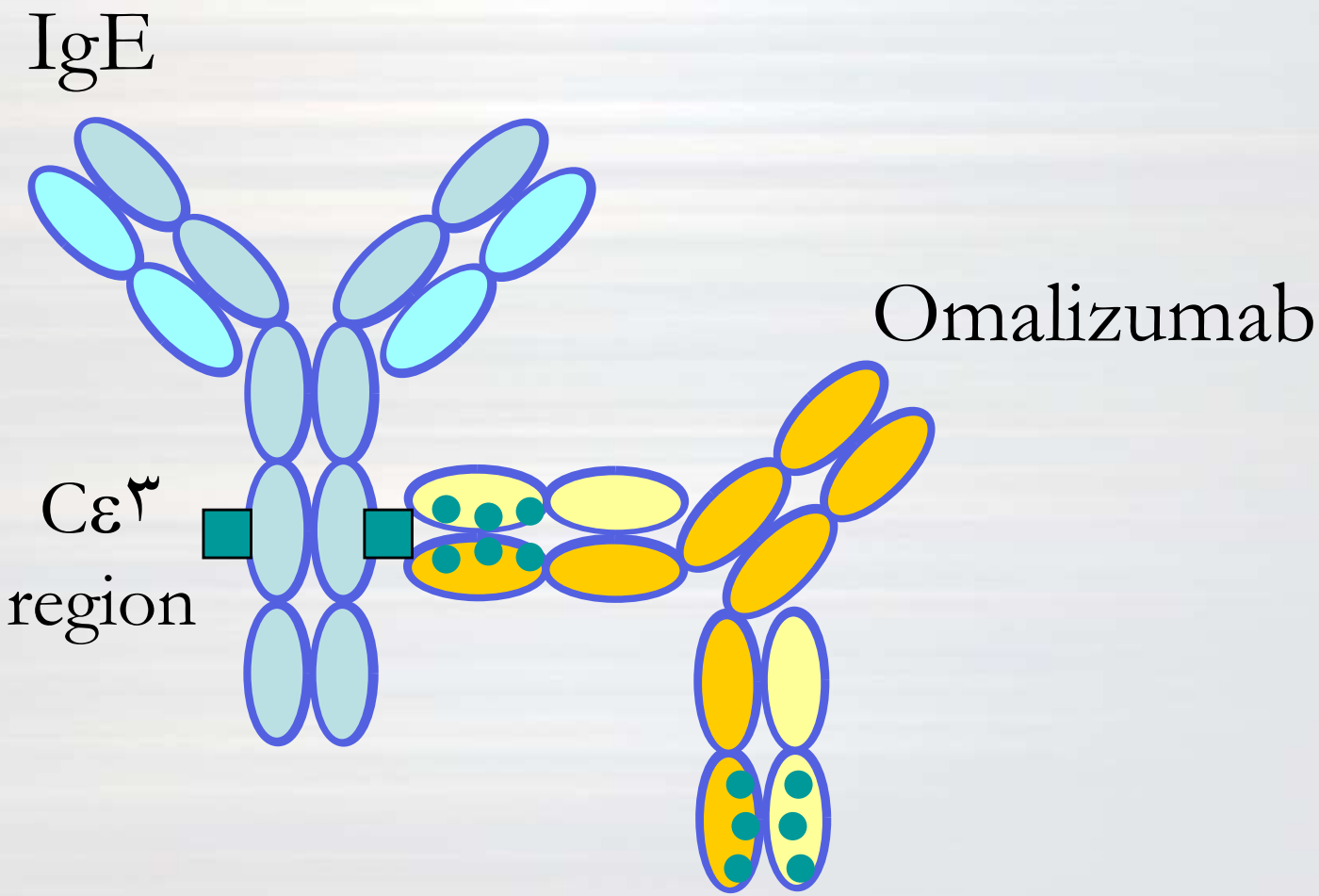
Possible mechanisms of immune response regulation by allergen immunotherapy



Possible mechanism: allergen immunotherapy induces regulatory T-lymphocytes



Humanized monoclonal anti-IgE antibody: omalizumab



Anti IgE - omalizumab

- Not licensed to treat allergic rhinitis
- Could be considered in severe cases unresponsive to conventional treatment
- Could be an adjunct to immunotherapy in severe cases

Algorithm for management of AR

Allergic Rhinitis

Intermittent Symptoms

Mild

- Oral H١ Blocker
- Intranasal H١ Blocker
- Leukotrine modifier

Moderate/Severe

- Intranasal Steroid
- Oral H١ Blocker
- Intranasal H١ Blocker
- Nasal Cromone
- Leukotrine modifier

In PAR Pt. FU after ٢-٤ wks.

If failure step up, if improved continue for one month

Intranasal Steroid

Itch/sneeze add H١ Blocker

Rhinorrhea add Ipratropium

Blockage: add oral decongestant/steroid short term

Persistent Symptoms

Mild

Moderate/Severe

Intranasal Steroid

Follow up after ٢ wks.

Improved

Step down

Failed

Review Dx
Compliance

THANK YOU FOR YOUR ATTENTION