ALLERGIC RHINITIS AND CO-MORBIDITIES IN CHILDREN

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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
- < 4 days per week
- or < 4 weeks

Persistent
- > 4 days per week
- and > 4 weeks

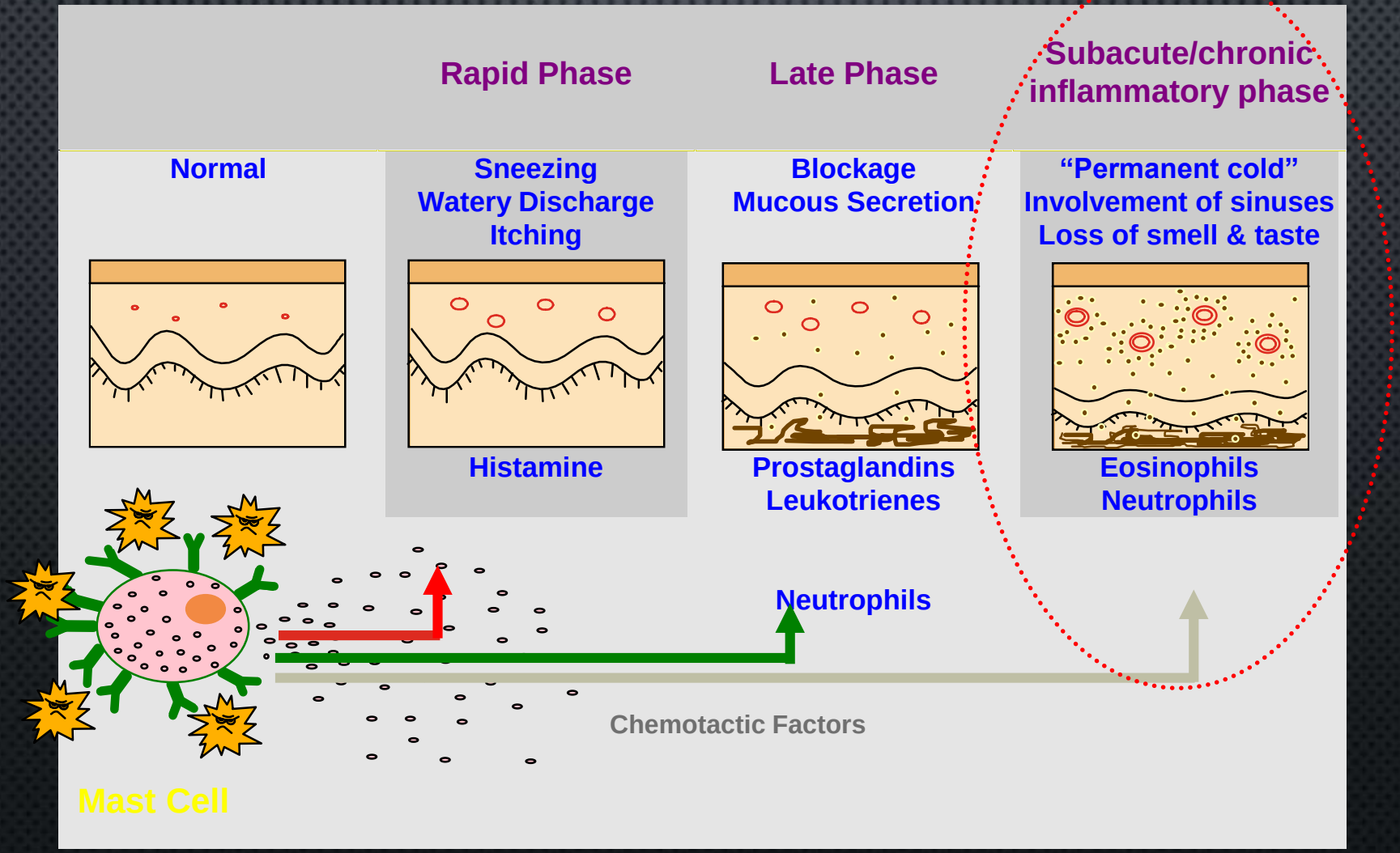
Mild
- Normal sleep
- No impairment of daily activities, sport, leisure
- Normal work & school
- No troublesome symptoms in untreated patients

Moderate-Severe

one or more items
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Abnormal work and school
- Troublesome symptoms

J Allergy Clin Immunol 2001;108:S147-336.

Phases of allergy: PINE or MPI



Allergic Rhinitis in Children

- Pediatric rhinitis: Range of symptoms
  - Cough
  - Sneezing
  - Nasal pruritus
  - Nasal congestion
  - Sore throats – recurrent infections
  - Halitosis
  - Respiratory distress – infant
  - Hypernasality
  - Behavioral problems
- Pediatric AR and its comorbid disorders
  - Conjunctivitis
  - Pharyngitis
  - Sinusitis
  - Asthma
  - Eczema
  - Otitis media
  - Lymphoid hypertrophy/obstructive sleep apnea
  - Speech impairment
  - Failure to thrive
  - Reduced quality of life

Lack G. J Allergy Clin Immunol 2001;108:S9-15

AR in children: Clinical presentation

- Allergic rhinitis (AR) : Multiplicity of symptoms in the child
- 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.
- Chronic cough is common symptom of AR or sinusitis in children resulting from postnasal drip and irritation of the larynx.

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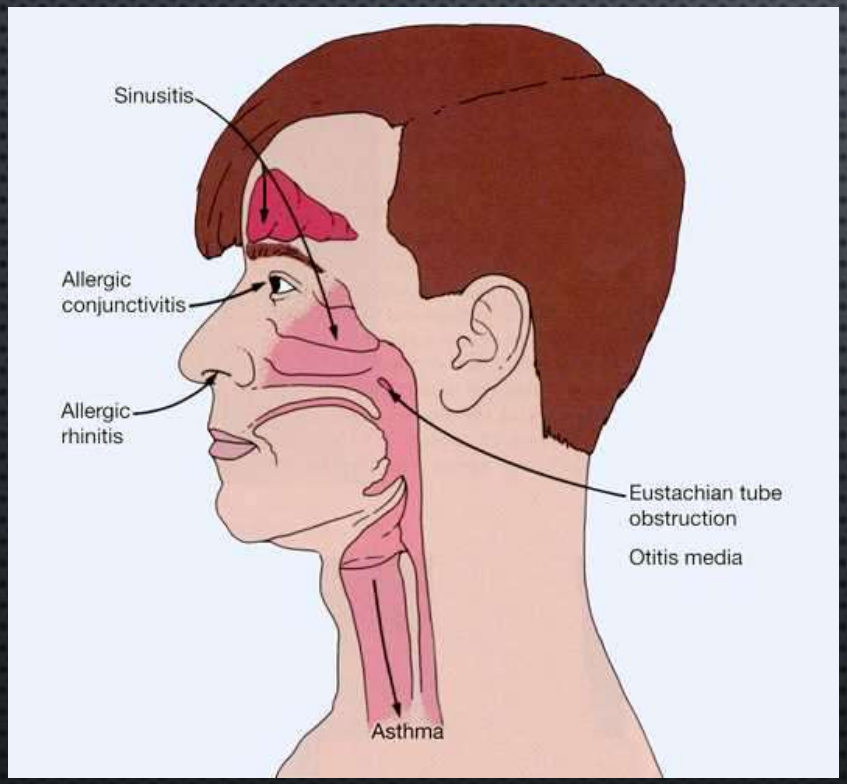
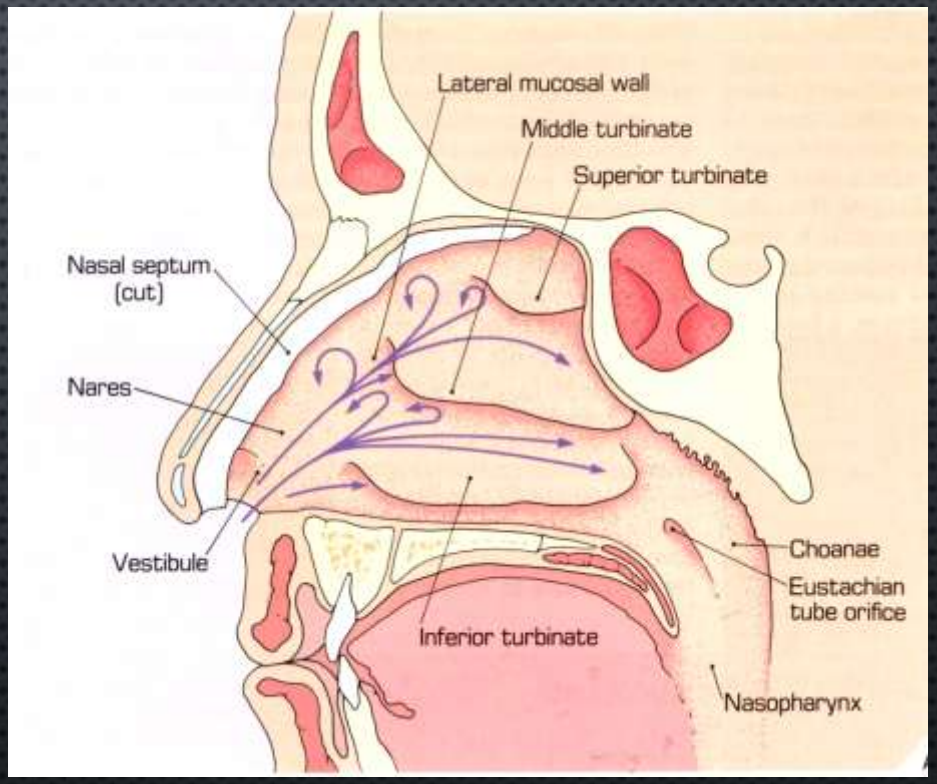
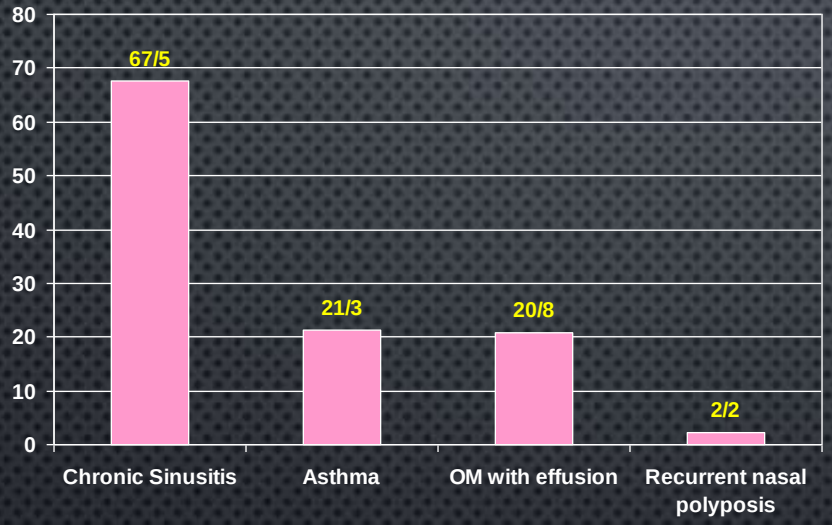
Allergic Rhinitis and Co-morbidities





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

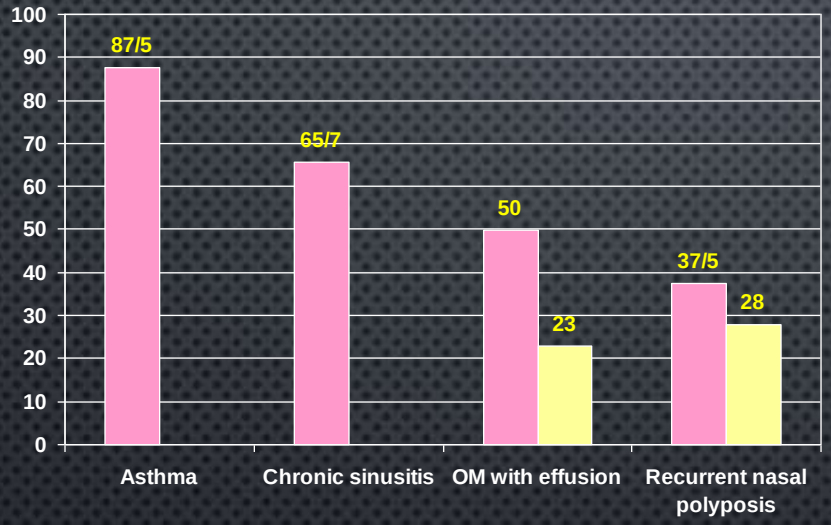
Allergic Rhinitis and Co-morbidities
How Common are the co-morbidities?



Proportion of Allergic Rhinitis patients who also have selected co-morbid disorders

Curr Med Res Opin 2004. 20:305-307

Co-morbidities and Allergic Rhinitis How Common is the association?



Proportion of co-morbidities patients who also have Allergic Rhinitis

Curr Med Res Opin 2004. 20:305-307

AR and Sinusitis in children

- AR and Sinusitis frequently co-exist and are definitely linked
- Sinusitis is one of the most underreported diagnoses in young children
- Pediatric sinus disease is characterized histologically by marked tissue eosinophilia, with mast cells expressing the activation marker
- There has been an ↑ in association between AR, positive skin tests, and sinusitis

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AR and Sinusitis: Pathophysiology

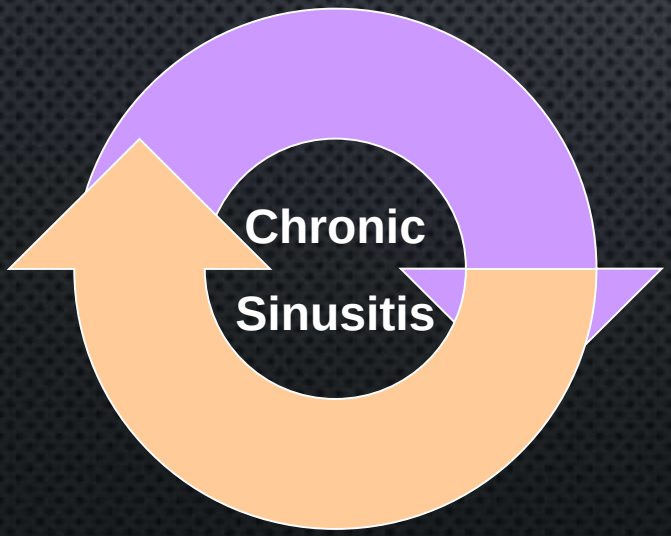
- Swelling of the mucous membranes, whether due to allergy, infection or other causes, may obstruct the drainage and aeration of the sinuses and one might therefore expect allergy to increase the risk of developing acute and chronic sinusitis.**

- During acute sinusitis there is swelling of mucous membranes, infiltration of eosinophils, and resulting ciliostasis and pooling of secretions that probably contribute to the subsequent infection

- Chronic rhino-sinusitis may be associated with a similar inflammatory process to that observed in AR

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

- Adolescent subjects with AR: 3-fold greater risk of developing de novo asthma as compared with subjects without AR
- Exposure to allergens and sensitization are important risk factors for childhood asthma
- AR and Asthma frequently co-exist and are considered as twin expressions of the same disease

- Possible relations exist between AR and asthma:
  - AR may confound the diagnosis of asthma
  - AR may be statistical associated with asthma
  - AR may exacerbate coexisting asthma
  - AR may have a causal role in the pathogenesis of asthma

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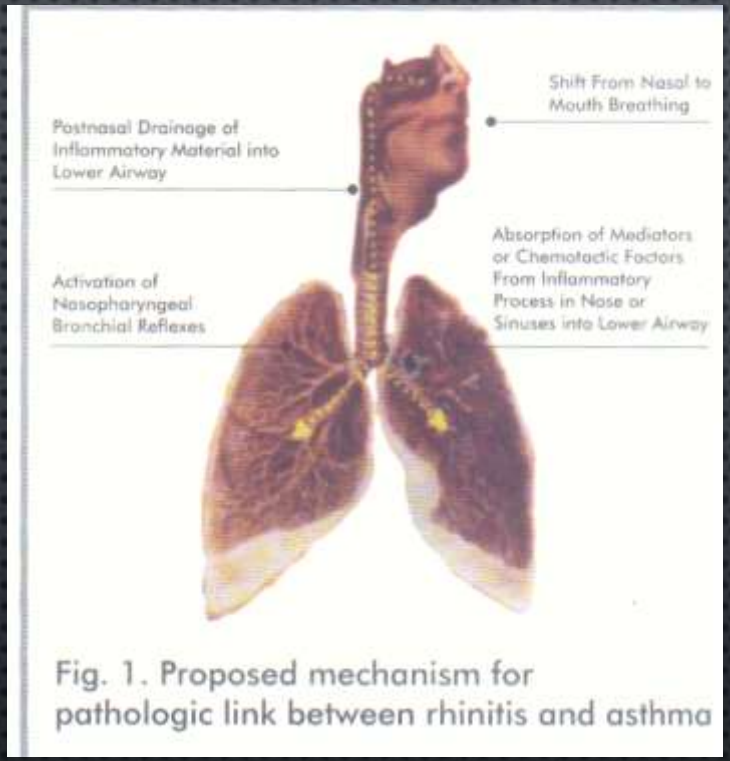

Fig. 1. Proposed mechanism for pathologic link between rhinitis and asthma

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, β2 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**

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AR with Asthma: Pathophysiology

Inflammation in the nose → lower airway hyperresponsive.

Possible mechanisms include

- **Nasobronchial reflex:** Nasal allergic response altering bronchial responsiveness through.
- **Rhinovirus adhesion theory:** Allergen induced ICAM-1 serves as receptor for rhinovirus infection leading to infection and asthma exacerbation.
- **Mouth breathing** caused by nasal obstruction resulting in bronchospasm to cool dry air.
- **Pulmonary aspiration** of nasal contents transferring mediators

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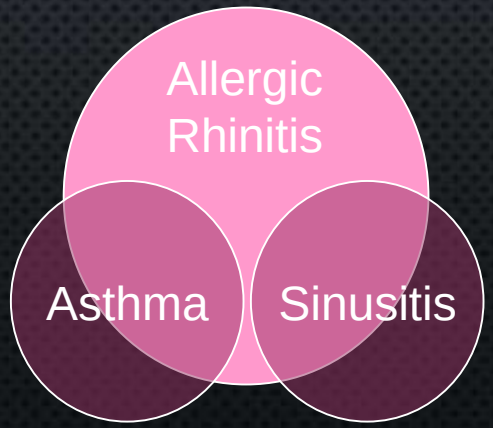
AR, Sinusitis, Asthma: The link

Common Triggers and Pathophysiology

Anatomy/ Physiology
- Upper and lower airways are contiguous
- Functional linkage – nose vs mouth breathing
- Similar histology(epithelial, neural, vascular)

Same triggers
- HDM, pollen, pet dander, moulds, fungi

Same cells
- Mast cells
- Eosinophils



Same mediators
- IgE
- Histamine
- Cytokines
- Leukotrienes

Same drugs
- Anti IgE ?
- Steroids(ICS/ INS)
- Antihistamines ?
- Antileukotrienes ?

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AR and Otitis media in children

- OME refers to a non infectious condition of the middle ear, usually accompanied by Eustachian tube dysfunction with accumulation of serous fluid

- Allergy as a risk factor for OM*

- Atopic children more susceptible to both symptomatic AOM & asymptomatic OME*

- 40-50 % of children > 3 years with chronic OM have confirmed AR**

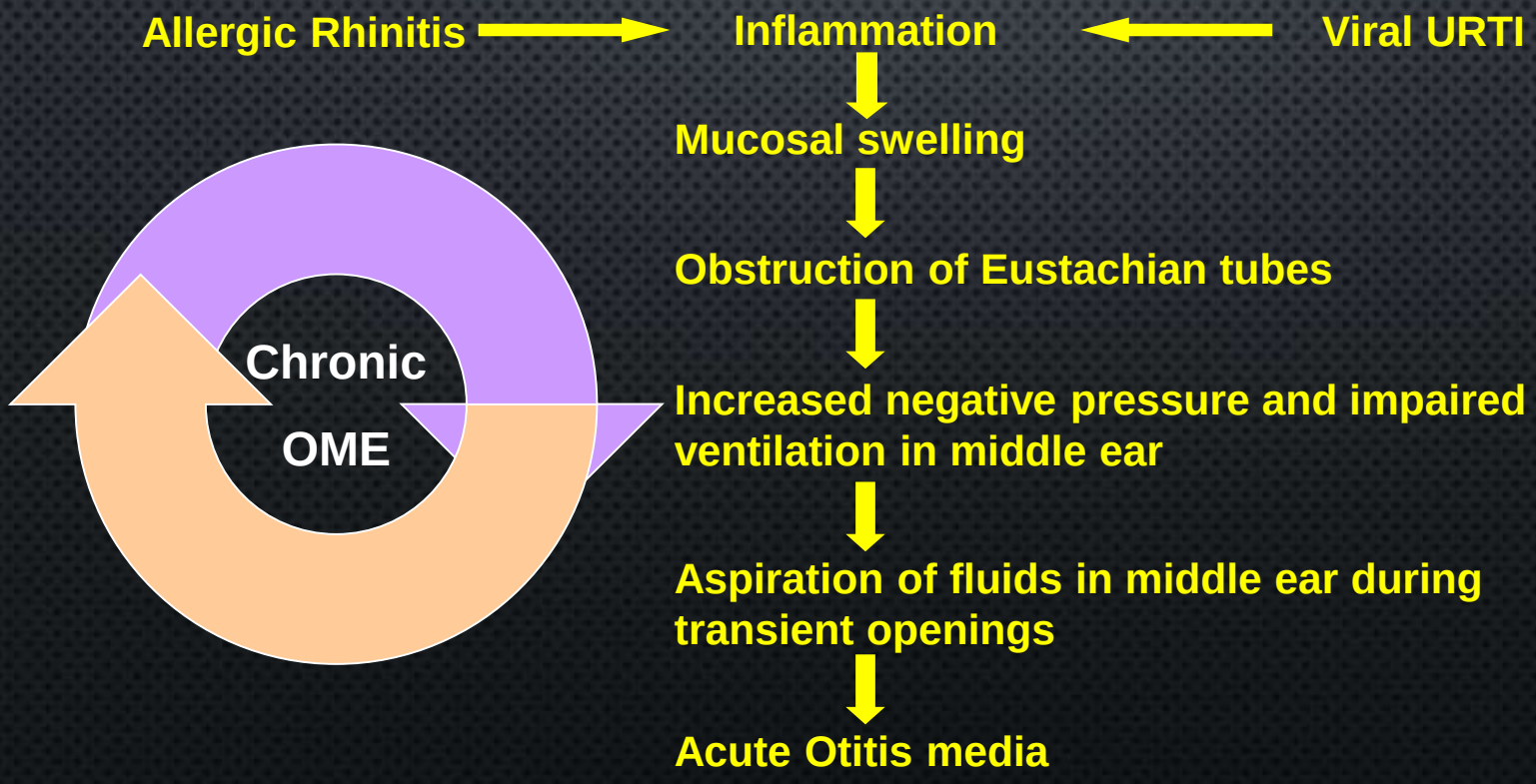
- Presence of higher levels of IgE or ECP in the middle ear of allergic children than levels found in the serum at the same time***

*Doyle et al. Curr Opin All Clin Immunol 2002
**Fireman et a., JACI 1997
***Bernstein et al. Otolaryngol Head Neck Surg 1985

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



Complications of AR with Chronic OME

- Chronic middle ear effusions may lead to hearing deficit and speech impairment in children
- 519 children with Chronic MEE attending a pediatric allergy clinic reported that 98% 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
- Children with AR, in addition to having MEE and hearing impairment may have a characteristic hypernasal quality to their voice and has potential to affect speech development.

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AR & obstructive sleep apnea

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

- One study from an otolaryngology department found an association between tonsillar hypertrophy and AR. Only 8% of children in 6th grade without tonsillar hypertrophy had AR, whereas AR was apparent in 29.7% of children with tonsillar hypertrophy

- 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

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ARIA workshop and children

- The prevalence of seasonal allergic rhinitis is higher in children and adolescents than in adults
- Varied prevalence of rhinitis across the world 0.8% to 14.9% (6-7 years) & from 1.4% to 39.7% (13-14 years)
- Significant correlation between asthma & rhinitis in school going children
- During the ragweed pollen season, 60% of children developed Eustachian tube obstruction
- Gastro esophageal reflux can be associated with rhinitis, especially in children

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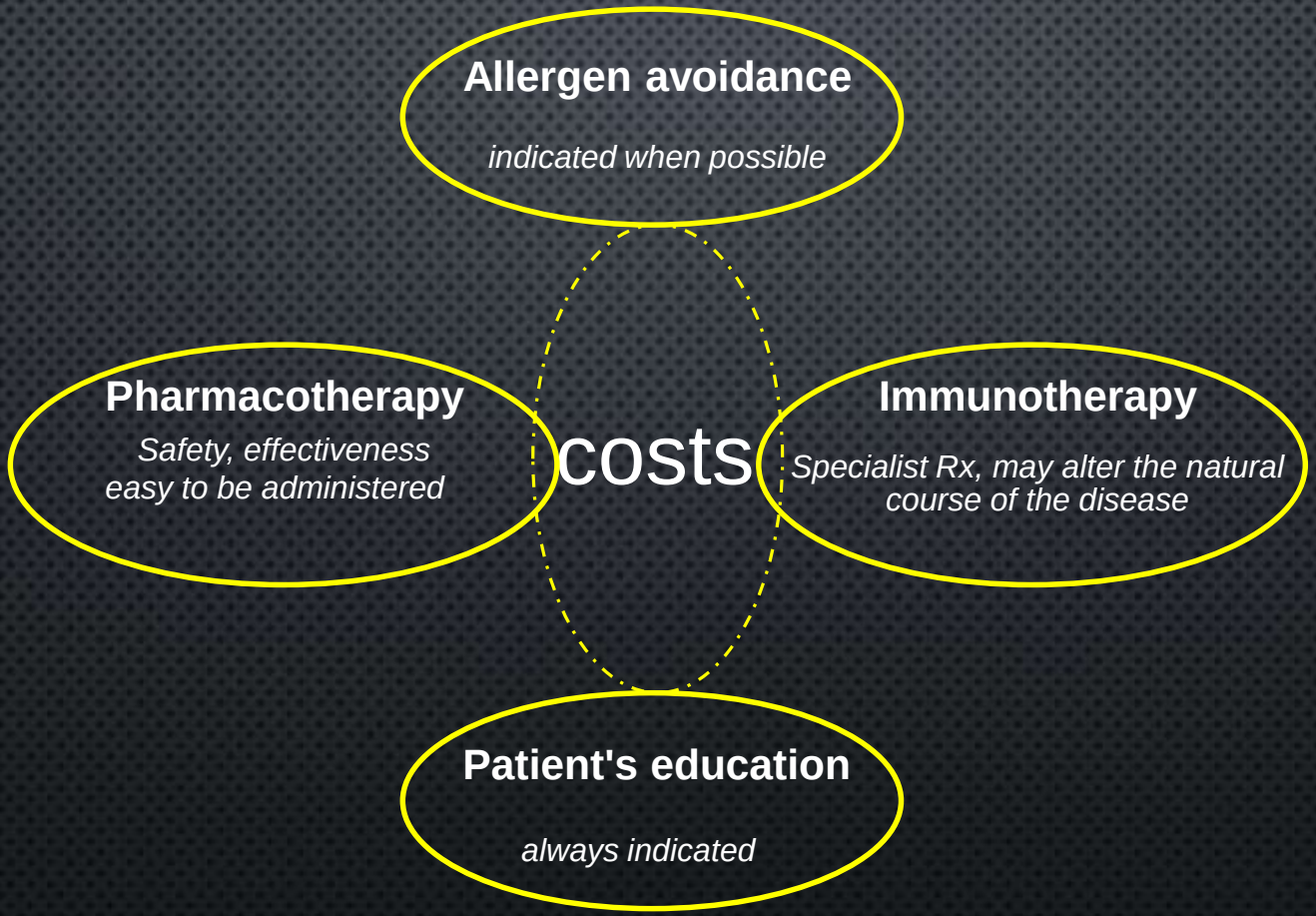
ARIA workshop: Recommendations

- 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

ARIA workshop: Therapeutic options

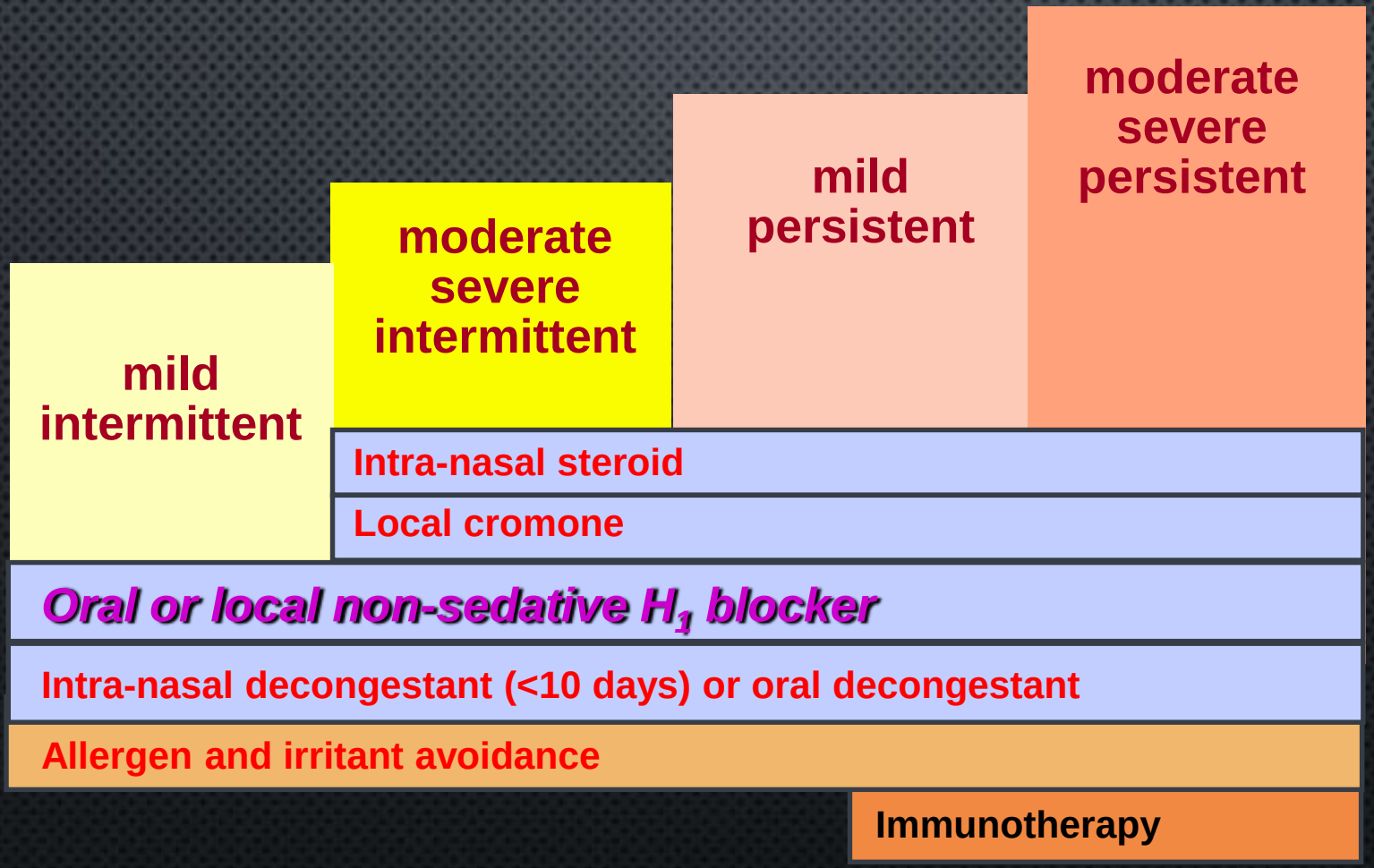


Therapeutic options for AR

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. 1999;83:13-25. 16. Busse WW. Clin Exp Allergy. 1996;26:868-879.

Step ladder treatment of AR: ARIA



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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	++

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

- Seasonal allergic rhinitis per se may affect learning ability and concentration.

- 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

Impact of AR on socio-economic costs

Direct Medical Costs

Physician Visits

Procedures

Hospitalization

Medication

Indirect Medical Costs

Lost days of work

Decreased productivity

School days missed

Intangible Medical Costs

Quality Of Life Issues

Psycho-social aspect of the disease

Impairment at work / school

Side effects of OTC

Fergussan B. OCNA Suppl. Feb 1998

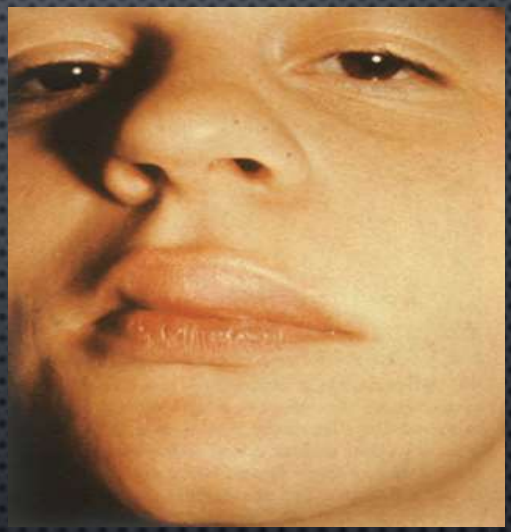
Effect of AR on pediatric QOL

- School absences & poor performance due to distraction, fatigue & irritability
- Poor interaction & labeling by peers and embarrassment, isolation and low self esteem

- Adverse effects of most of antihistamines and decongestants
- Adverse impact on parents QOL
- Anxious, overprotective, work absences, family social life, etc.


Thank You
For Your
Attention

Urticarial rash & Angio-oedema



Urticaria

A transient erythematous skin eruptions due to oedema of the dermis, associated with itching. (Wheal & Flare rashes) or Hive

Angioedema

Transient swellings of deeper dermal, subcutaneous and submucosal tissues.

Angioedema accompanies urticaria in approximately 50% of adults and 80% or more of children