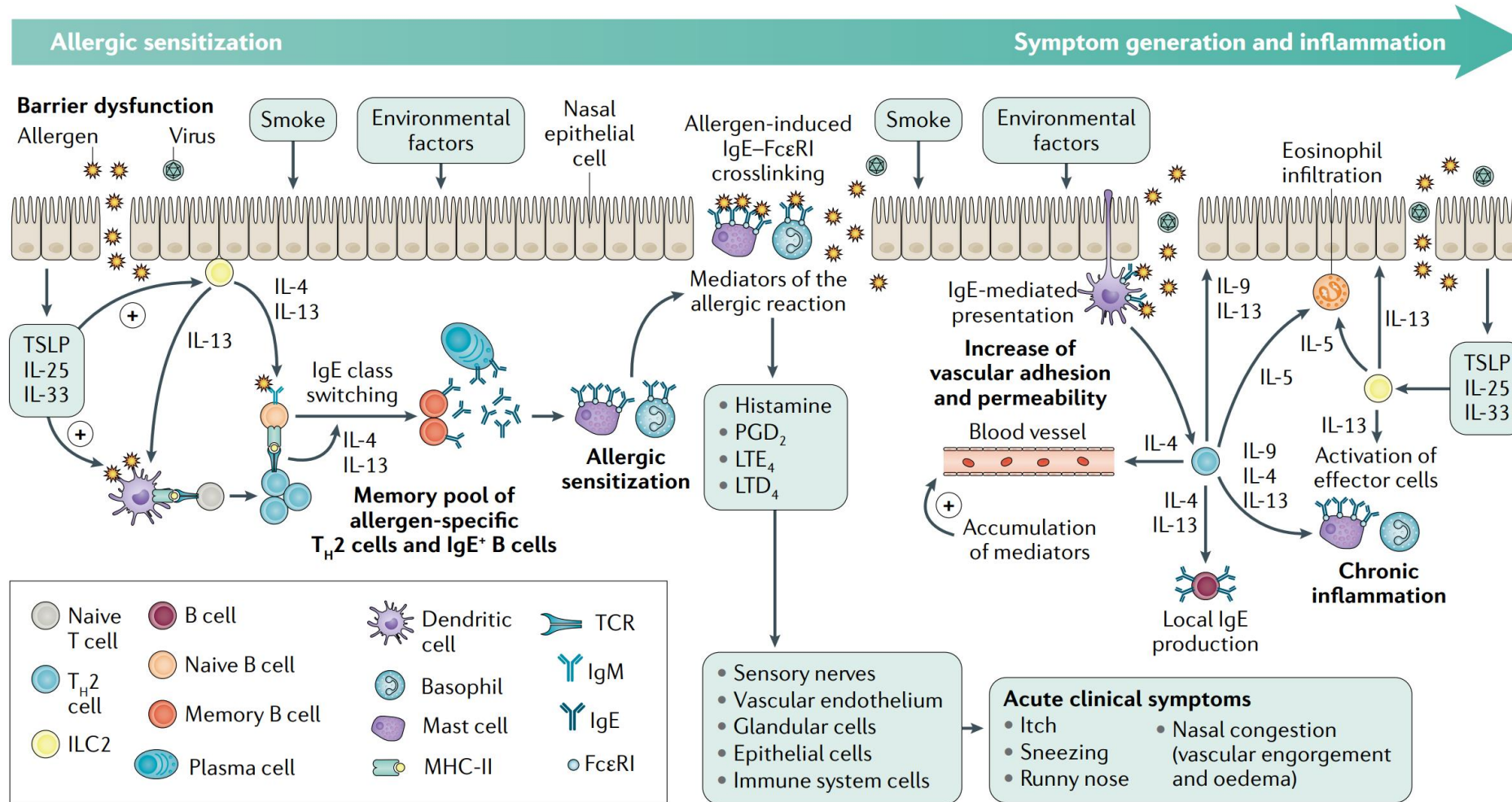


Allergic Rhinitis and Its Impact on Asthma (ARIA)

Nima Parvaneh, MD

Children's Medical Center
Tehran University of Medical Sciences

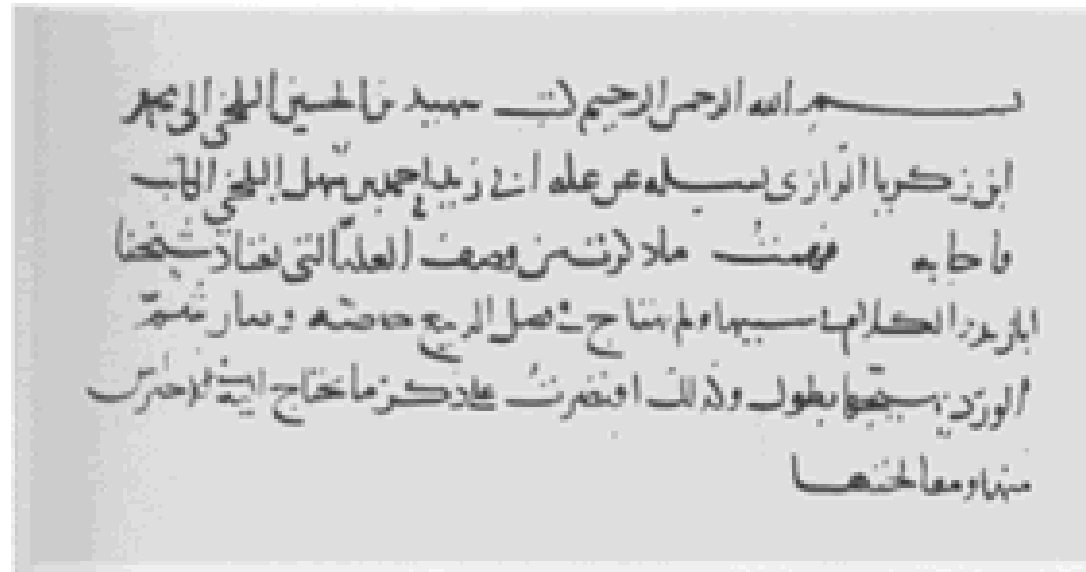
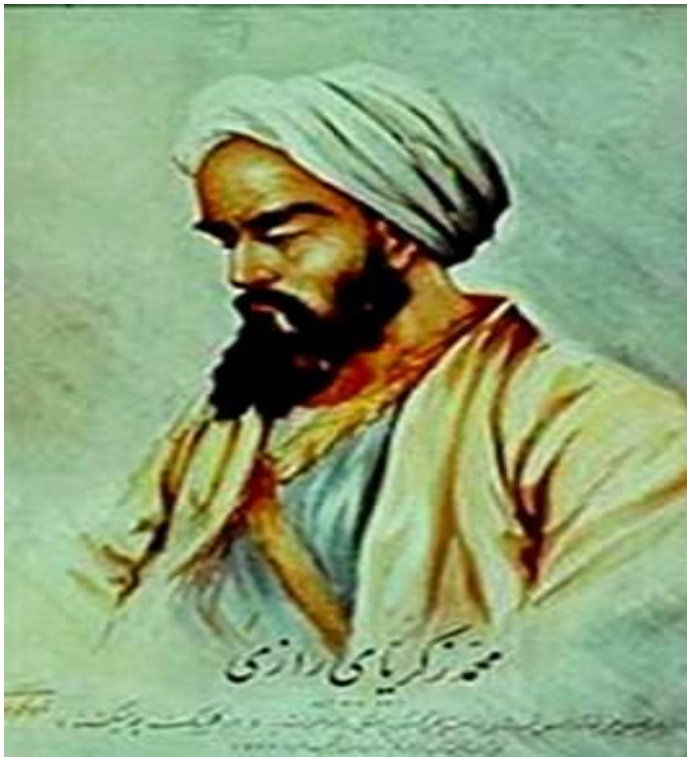
Pathophysiology of Allergic Rhinitis



Razi's report about seasonal allergic rhinitis (hay fever) from the 10th century AD

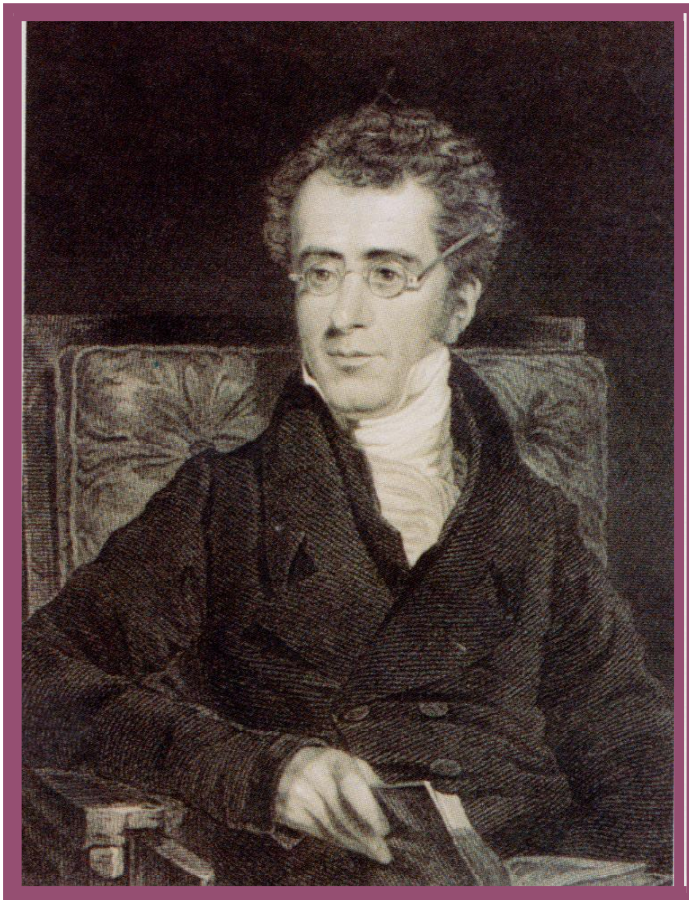
Authors: [G A Bungy](#), [J Mossawi](#), [S A Nojourni](#), [J Brostoff](#)

International archives of allergy and immunology. 07/1996; 110(3):219-24



First description of hay fever

John Bostock, Med Chir Trans, 1819; 10: 161



"About the beginning or middle of June in every year

.... A sensation of heat and fulness is experienced in the eyes

.... To this succeeds irritation of the nose producing sneezing

.... To the sneezings are added a further sensation of tightness of the chest, and a difficulty of breathing"

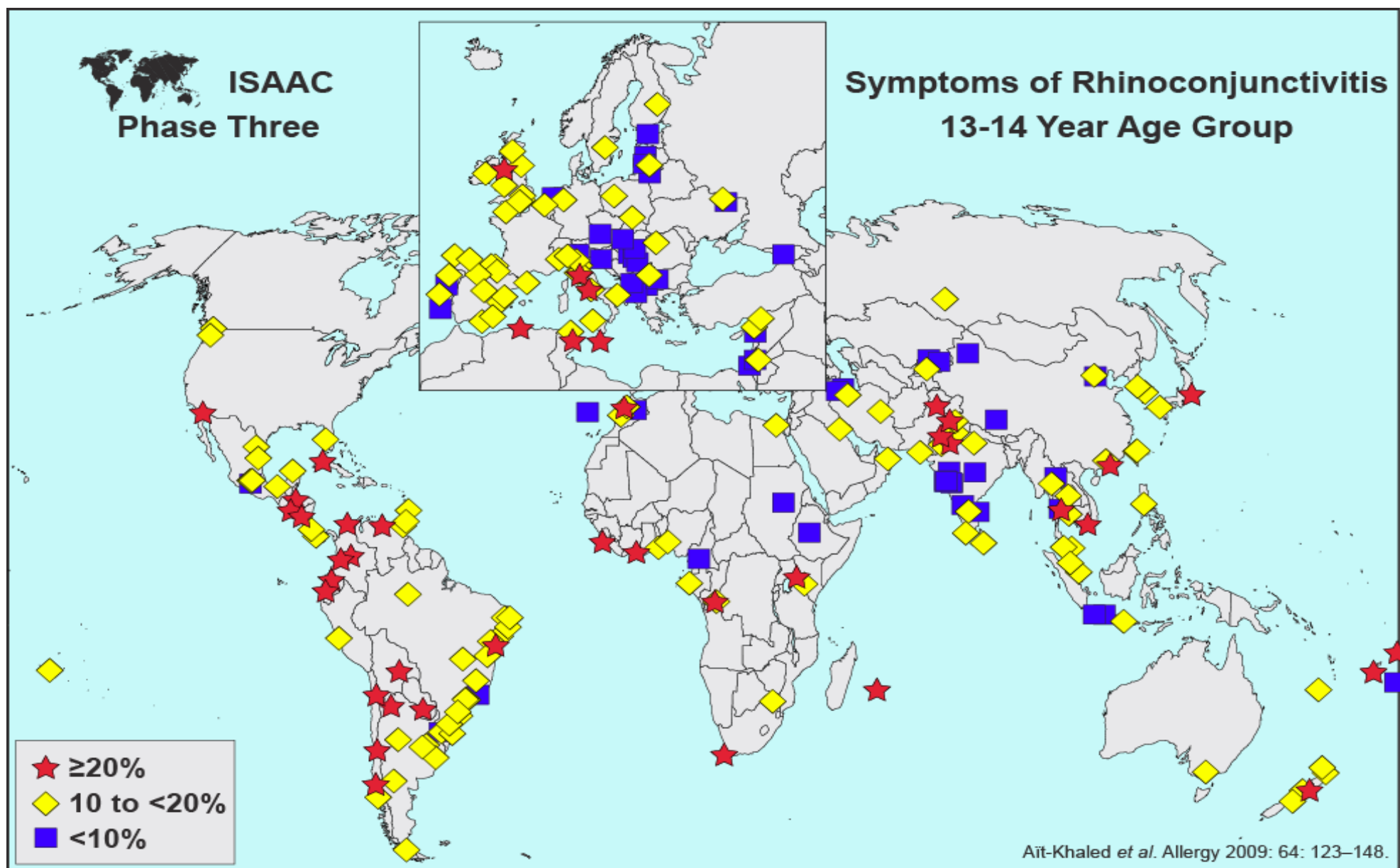
Allergic Rhinitis (AR) burden

- a **global health problem** (5 to 50 % of the population)
- Its **prevalence is increasing**
- AR alters **social life** and affects **school performance** and **work productivity**
- **Costs** are substantial



ISAAC Phase Three

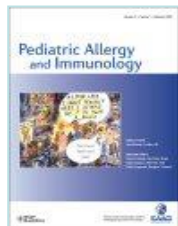
Symptoms of Rhinoconjunctivitis 13-14 Year Age Group



ISAAC Phase III in IRAN

Centre	N	R ever %	R last year %	HF ever %	RC last year %	RC Severe %
Rasht	3004	27.6	20.2	5.5	7.2	0.3
Tehran	3119	33.4	25.1	10.5	12.3	0.3
Total	6123	30.5	22.7	8.1	9.8	0.3

R, rhinitis
HF, hay fever
RC, rhinoconjunctivitis



Björstén B et al.2007

Allergic Rhinitis and Its Impact on Asthma (ARIA)

- Development of evidence-based guidelines during **a workshop held at WHO in December 1999** (J Allergy Clin Immunol, suppl, Nov 2001).
- The document has been endorsed by several allergy, respiratory, ENT and Pediatric associations
- The last guideline published at 2010
- Revisions made at 2014, and 2016





The ARIA initiative goals

- **update knowledge** of physicians
- highlight the **impact of allergic rhinitis on asthma**
- evidence-based **diagnosis**
- evidence-based **treatments**
- a **stepwise approach** to the management
- to **assess the magnitude of the problem** in developing countries and to implement guidelines

United Airways Disease = One Way, One Disease

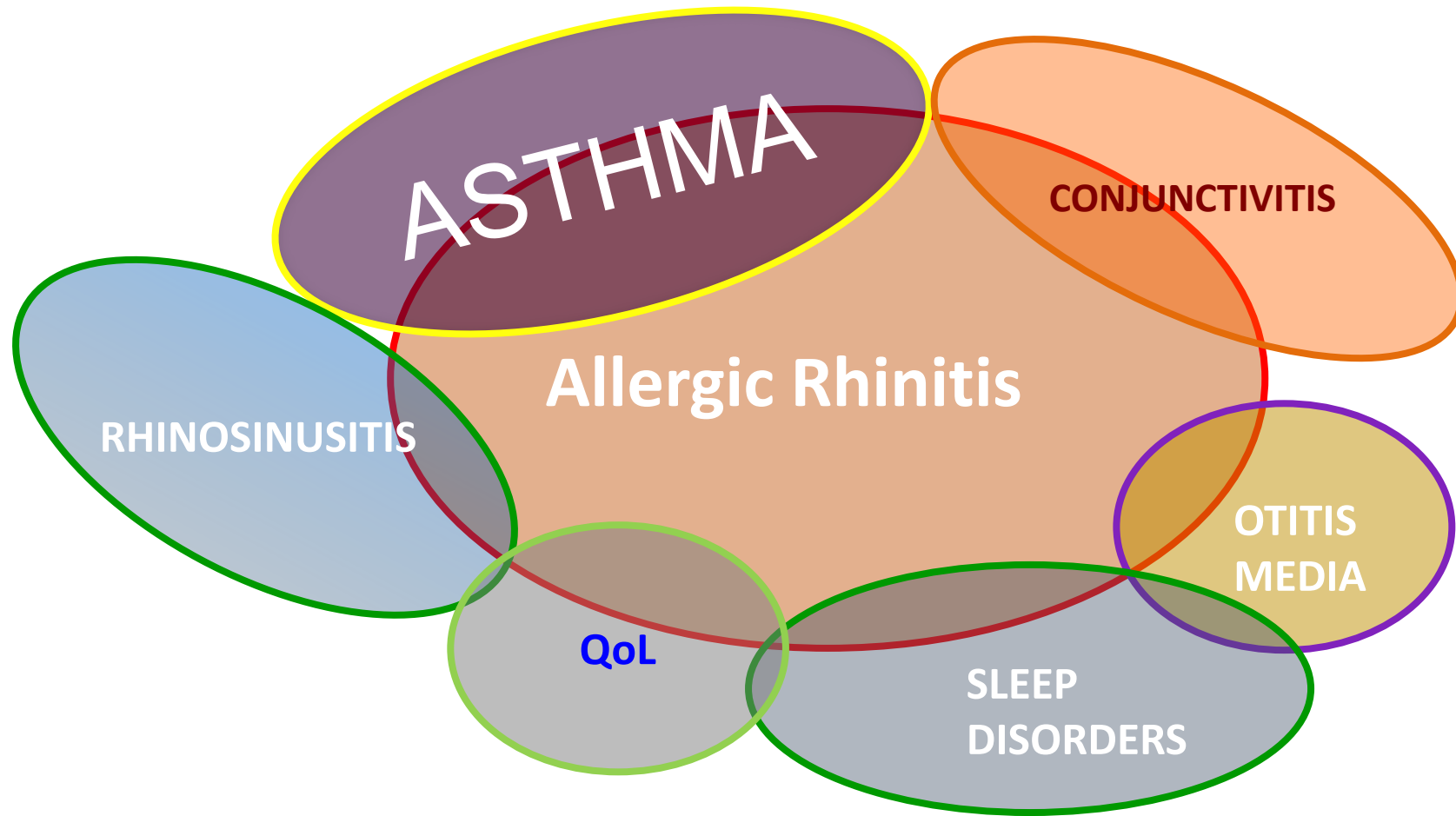
Allergic Rhinitis

- Occurs in up to 20% of the general population
- Occurs in approximately 85% of asthmatics
- AR patients have a 3-fold risk of developing asthma

Asthma

- Occurs in 5-10% of the general population
- Occurs in up to 50% of AR patients

Rhinitis and its co-morbidities





Links between rhinitis and asthma: Epidemiologic evidence

- 1- Asthma prevalence is increased in allergic and non-allergic rhinitis**
- 2- Rhinitis is almost always present in asthma**
- 3- Rhinitis may be a risk factor for asthma**
- 4- Non-specific bronchial hyperreactivity is increased in persistent rhinitis**

Rhinitis / Asthma : Similarities

- Frequently coexist
- Respiratory pseudostratified epithelium
- IgE-dependent mechanisms
- Th2 lymphocyte activation
- Eosinophil recruitment
- Mast cell / basophil activation and transepithelial migration

Rhinitis / Asthma: Differences

Rhinitis

- Epithelium intact
- Basement membrane normal
- No airway smooth muscle
- Venous sinusoids
- Submucosal glands prominent
- Remodeling absent
- Antihistamines effective
- β_2 -agonists ineffective

Asthma

- Epithelium disrupted
- Basement membrane abnormal
- Bronchial smooth muscle
- No venous sinusoids
- Submucosal glands few
- Remodeling present
- Antihistamines ineffective (?)
- β_2 -agonists effective



ARIA

The classification "**seasonal**" and "**perennial**" allergic rhinitis

has been changed to

"**intermittent**" and "**persistent**"
allergic rhinitis

ARIA Classification



Intermittent

- . < 4 days per week
- . or < 4 weeks

Persistent

- . ≥ 4 days per week
- . and ≥ 4 weeks



Mild

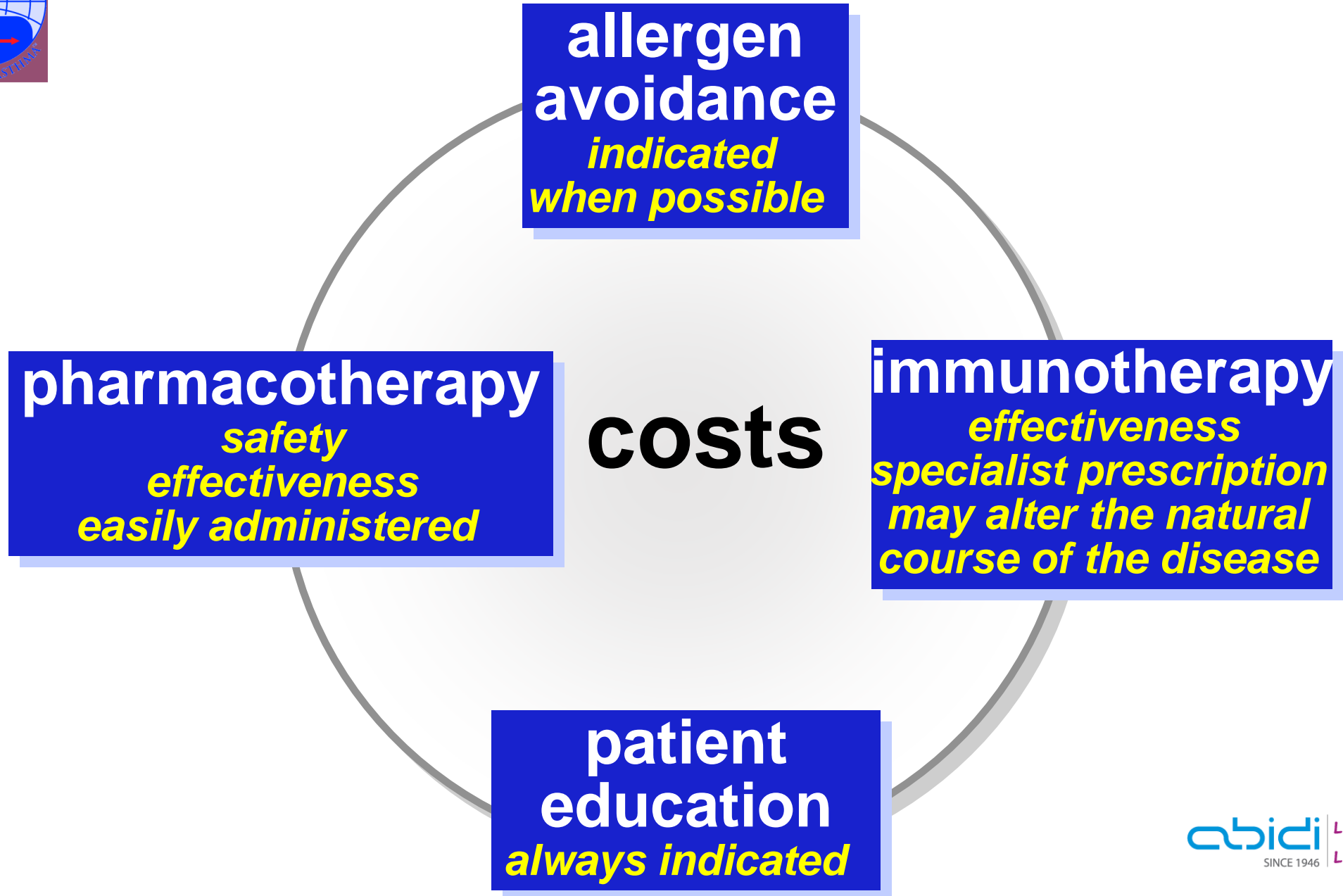
normal sleep
& no impairment of daily
activities, sport, leisure
& normal work and
school
& no troublesome
symptoms

Moderate-severe

one or more items

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

in untreated patients



Allergen avoidance

House dust mite

- Use bed-encasing for mattress and duvet/pillows (pore diameter $<10\text{ }\mu\text{m}$)
- Wash bedding weekly in hot water and dry in a heated drier
- Remove dust mite reservoirs (i.e., toys and stuffed animals, carpets)
- Reduce indoor humidity (less than 50%)
- Vacuum with a HEPA filter bag
- Remind that chemicals to kill mites or denature proteins have a modest effect

Pets

- Remove pet from bedrooms and everywhere the child spends a lot of time
- Clean accurately upholstered furniture, walls, and carpet
- Remove upholstered furniture and carpet if possible
- Encase the mattress and pillows with bed encasing (pore diameter $<6\text{ }\mu\text{m}$)
- Keep the pet clean with frequent washes
- Use a HEPA air filter

Cockroach and pests

- Inspect to detect hiding places debris (grease, kitchen) and identify food sources
- Store food in sealed containers
- Exterminate with pesticides or bait traps
- Remove clutter and seal holes or cracks in the home

Indoor molds^a

- Reduce indoor humidity (less than 50%)
- Remove contaminated carpets, wallpaper, and woodwork
- Treat washable surfaces with detergent and water and then dry completely
- Repair water leaks

Pollens

- Keep windows closed
- Bath to remove allergens from hair and body
- Consider to use HEPA air filtration
- Consider same principles for outdoor mold avoidance

Treatment options for Allergic Rhinitis

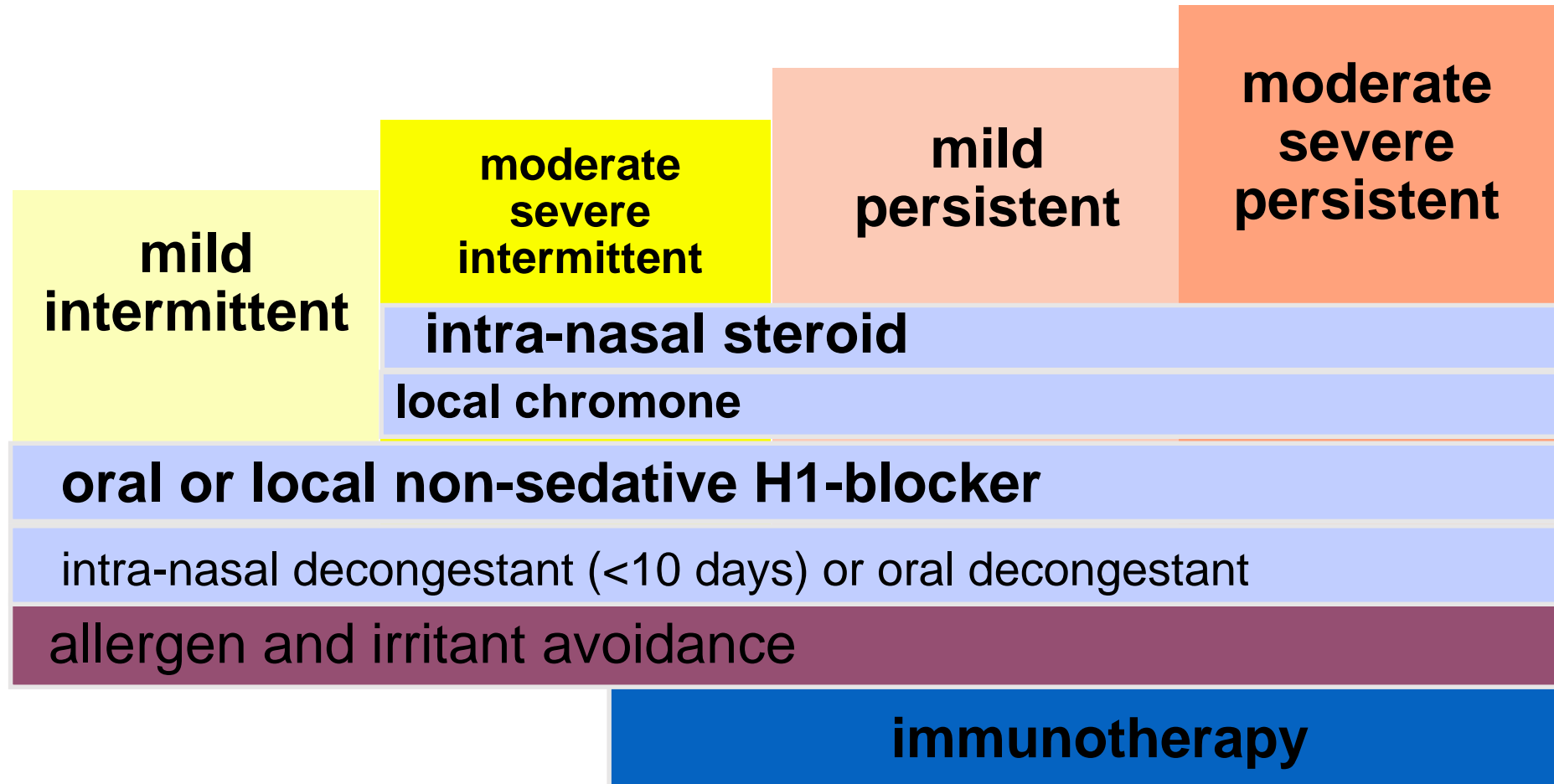
Treatment	Rhinorrhoea	Sneezing	Nasal itch	Nasal obstruction	Ocular symptoms	Onset of action
Oral H ₁ -antihistamine	++	++	+	+	+	1–3 hours
Intranasal H ₁ -antihistamine	++	++	+	+	0	<30 minutes
Ocular H ₁ antihistamine	0	0	0	0	+++	15 minutes
Intranasal corticosteroid	+++	+++	+++	+++	+ to ++	6–48 hours
Intranasal corticosteroid plus intranasal H ₁ -antihistamine	++++	++++	++++	++++	+++	10–60 minutes
Nasal decongestant	0	0	0	+++	0	15 minutes
Intranasal chromone	+	+	+	+	0	15 minutes
Ocular chromone	0	0	0	0	++	15 minutes
Leukotriene receptor antagonist	+	+	+	+	0	1 hour
Intranasal anti-cholinergic agent	++	0	0	0	0	1 hour

0, no evidence of efficacy;+ to +++++, increasing levels of evidence of efficacy.



Treatment of allergic rhinitis (ARIA)

Allergic Rhinitis and its Impact on Asthma



ARIA 2016²¹

1. In patients with SAR, we suggest either a combination of INCS + OAH or INCS alone, but the potential net benefit might not justify spending additional resources.
2. In patients with PAR, INCSs alone are recommended rather than a combination of an INCS + an OAH.
3. In patients with SAR, we suggest either a combination of an INCS + an INAH or an INCS alone, but the choice of treatment depends on patient preferences. At initiation of treatment (first 2 weeks), a combination of an INCS + an INAH might act faster than an INCS alone and might therefore be preferred by some patients. In settings in which the additional cost of combination therapy is not large, a combination therapy might be a reasonable choice.
4. In patients with PAR, we suggest either a combination of an INCS + an INAH or an INCS alone.

For all of these recommendations, the level of evidence was low^{2,3} or very low.^{1,4}

US practice parameters 2017²²

For initial treatment of nasal symptoms of SAR in patients ≥ 12 years of age, clinicians:

- should routinely prescribe monotherapy with an INCS rather than a combination of an INCS and an oral H₁-antihistamine or
- should recommend an INCS over an LTRA (for ≥ 15 years of age).
- For moderate-to-severe symptoms, clinicians can recommend the combination of an INCS and an INAH.



Mild intermittent rhinitis

ARIA

Options (not in preferred order)

- oral or intranasal anti-H1
- intranasal decongestants
- oral decongestants (not in children)



Moderate-severe intermittent rhinitis

Mild persistent rhinitis

ARIA

Options (not in preferred order)

- oral or intranasal anti-H1
- oral anti-H1 + decongestant
- intranasal CS
- (chromones)

Patient should be re-assessed after 2-4 wks



Moderate-severe persistent rhinitis

ARIA

Step-wise approach

- intranasal CS as a first line treatment
- if major blockage: add short course of oral CS or decongestant

Re-assess after 2-4 weeks

- if symptoms present add:
 - oral anti-H1 (\pm decongestants)
 - ipratropium

Drugs	Ages	Dose
Beclomethasone	> 6 years	6-12y: 1 spray q12h, >12y: 1-2 spray q12h
Fluticasone propionate	> 4 years	6-12y: 1 spray qd, >12y: 2 sprays qd
Mometasone	> 2 years	2-12 y: 1 spray qd, >12y: 2 sprays qd
Budesonide	> 6 years	6-12y: 2 sprays qd, >12y: upto 4 sprays qd
Azelastine	> 6 years	6-12y: 1 spray bid, >12y: 1-2 spray bid
Olopatadine	> 6 years	6-12y: 1 spray bid, >12y: 2 sprays bid
Cromolyn sodium	> 2 years	1 spray every 4-6 hr
Ipratropium bromide	> 5 years	5-12y: 2 spray q8h, >12y: 2 spray q-6-8h
Oxymetazoline	> 6 years	2-3 sprays in each nostril q12h
Phenylephrine drop	> 2 years	< 6 y: 0.125% q2-4h > 6 y: 0.25% q4h
Cetirizine	> 6 months	< 6 y: 2.5 mg > 6 y: 5 mg
Desloratadine	> 6 months	< 1y: 1mg, 1-5y: 1.25mg, 6-11y: 2.5mg, >12y: 5mg
Loratadine	> 2 years	2-5 y: 5mg/d, >6y: 10mg/d
Fexofenadine (Allegra)	>2 years	2-11y: 30 mg/d, 120-180mg/d
Montelukast	> 6 months	6 mo-5y: 4mg, 6-14y: 5mg, >14y: 10mg

When to Consider Referral

- Question as to **etiology** of the rhinitis
- Symptoms **not adequately** managed
- Multiple **complications** or **co-morbidities**
- Allergen **avoidance** & patient **education**
- Allergy **specialized tests & challenges**
- Management of **immunotherapy**



ARIA Recommendations

- 1- Patients with persistent rhinitis should be evaluated for asthma**
- 2- Patients with persistent asthma should be evaluated for rhinitis**
- 3- A strategy should combine the treatment of upper and lower airways in terms of efficacy and safety**

پسر دوازده ساله ای با آبریزش و احتقان بینی از 3 ماه قبل مراجعه کرده است. بیمار تقریباً هر شب دچار گرفتگی بینی می شود و خواب نامناسب دارد. اخیراً دچار افت عملکرد تحصیلی در مدرسه هم شده است. شدت بیماری وی در چه مرحله ای است؟

- Mild intermittent
- Mild persistent
- Moderate-Severe intermittent
- Moderate-Severe persistent

ARIA 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 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

in untreated patients

مناسب ترین درمان برای وی کدام یک از داروهای زیر است؟

- Oral Loratadin
- Intranasal Mometasone
- Oral Montelukast
- Intranasal Cromolyn



Moderate-severe persistent rhinitis

ARIA

Step-wise approach

- intranasal CS as a first line treatment
- if major blockage: add short course of oral CS or decongestant

Re-assess after 2-4 weeks

- if symptoms present add:
 - oral anti-H1 (\pm decongestants)
 - ipratropium

نحوه درست استفاده از اسپری استروئید بینی چگونه است؟

Priming	<p>Before you use the spray for the first time, you will need to prime it by spraying several times into the air – follow the manufacturer’s instructions.</p> <p>You will need to prime your spray again if you have not used it for more than a few days.</p>
Getting ready	<ol style="list-style-type: none"> 1. Shake the bottle before each use. 2. If your nose is blocked by mucus, blow your nose gently (or use a saline spray or rinse, then wait 10 minutes before using the spray medication).
Before spraying	<ol style="list-style-type: none"> 3. Tilt your head slightly forward. 4. Gently put the nozzle into one nostril, using your opposite hand. Avoid pushing it in hard to avoid damaging the barrier that divides your two nostrils (the septum). 5. Aim the nozzle towards the hole inside your nose: <ul style="list-style-type: none"> • slightly to the outside, not towards the septum • inwards towards the middle of your head (parallel to the roof of your mouth), not towards the top of your nose.
Spraying	<ol style="list-style-type: none"> 6. Breathe in gently and press to spray at the same time. Avoid sniffing hard during or after spraying. Sniffing could force the spray into the back of the throat instead of inside the nose where it needs to work. 7. Repeat for the other nostril.
After spraying	<ol style="list-style-type: none"> 8. Wipe the tip of the spray device with a dry handkerchief or tissue, and put the cap back on. <p>If you have been advised to use two different nasal sprays, use one, wait 10 minutes, then use the other.</p>



در صورتی که علایم بیمار پس از دوهفته بهبودی نسبی داشته است. کدام یک از اقدامات درمانی زیر به عنوان تشدید درمان دارویی توصیه می شود؟

- اضافه کردن لوراتادین خوراکی به اسپری مومتازون
- تغییر اسپری مومتازون به اسپری بودزوناید
- اضافه کردن اسپری اولانتین به اسپری مومتازون
- شروع استروئید خوراکی

ARIA 2016²¹

1. In patients with SAR, we suggest either a combination of INCS + OAH or INCS alone, but the potential net benefit might not justify spending additional resources.
2. In patients with PAR, INCSs alone are recommended rather than a combination of an INCS + an OAH.
3. In patients with SAR, we suggest either a combination of an INCS + an INAH or an INCS alone, but the choice of treatment depends on patient preferences. At initiation of treatment (first 2 weeks), a combination of an INCS + an INAH might act faster than an INCS alone and might therefore be preferred by some patients. In settings in which the additional cost of combination therapy is not large, a combination therapy might be a reasonable choice.
4. In patients with PAR, we suggest either a combination of an INCS + an INAH or an INCS alone.

For all of these recommendations, the level of evidence was low^{2,3} or very low.^{1,4}

US practice parameters 2017²²

For initial treatment of nasal symptoms of SAR in patients ≥ 12 years of age, clinicians:

- should routinely prescribe monotherapy with an INCS rather than a combination of an INCS and an oral H₁-antihistamine or
- should recommend an INCS over an LTRA (for ≥ 15 years of age).
- For moderate-to-severe symptoms, clinicians can recommend the combination of an INCS and an INAH.

کودک برای بررسی عوامل آلرژی زا به آلرژیست ارجاع شده است. تست پوستی پریک برای آلرژن
ماییت مثبت است. برای کنترل این آلرژن در محیط خانه، چه توصیه هایی میکنید؟

Allergen avoidance

House dust mite

Use bed-encasing for mattress and duvet/pillows (pore diameter $<10\text{ }\mu\text{m}$)

Wash bedding weekly in hot water and dry in a heated drier

Remove dust mite reservoirs (i.e., toys and stuffed animals, carpets)

Reduce indoor humidity (less than 50%)

Vacuum with a HEPA filter bag

Remind that chemicals to kill mites or denature proteins have a modest effect

والدین کودک نگران اپیدمی COVID-19 هستند و در مورد خطر استفاده از استروئید استنشاقی بینی
نظر شما را جویا می شوند.

With the current knowledge, in patients with COVID-19 infection, **intra-nasal corticosteroid can be continued** in allergic rhinitis at the recommended dose

Intranasal corticosteroids in allergic rhinitis in COVID-19 infected patients: An ARIA-EAACI statement. Allergy. 2020 Mar 31. doi: 10.1111/all.14302.