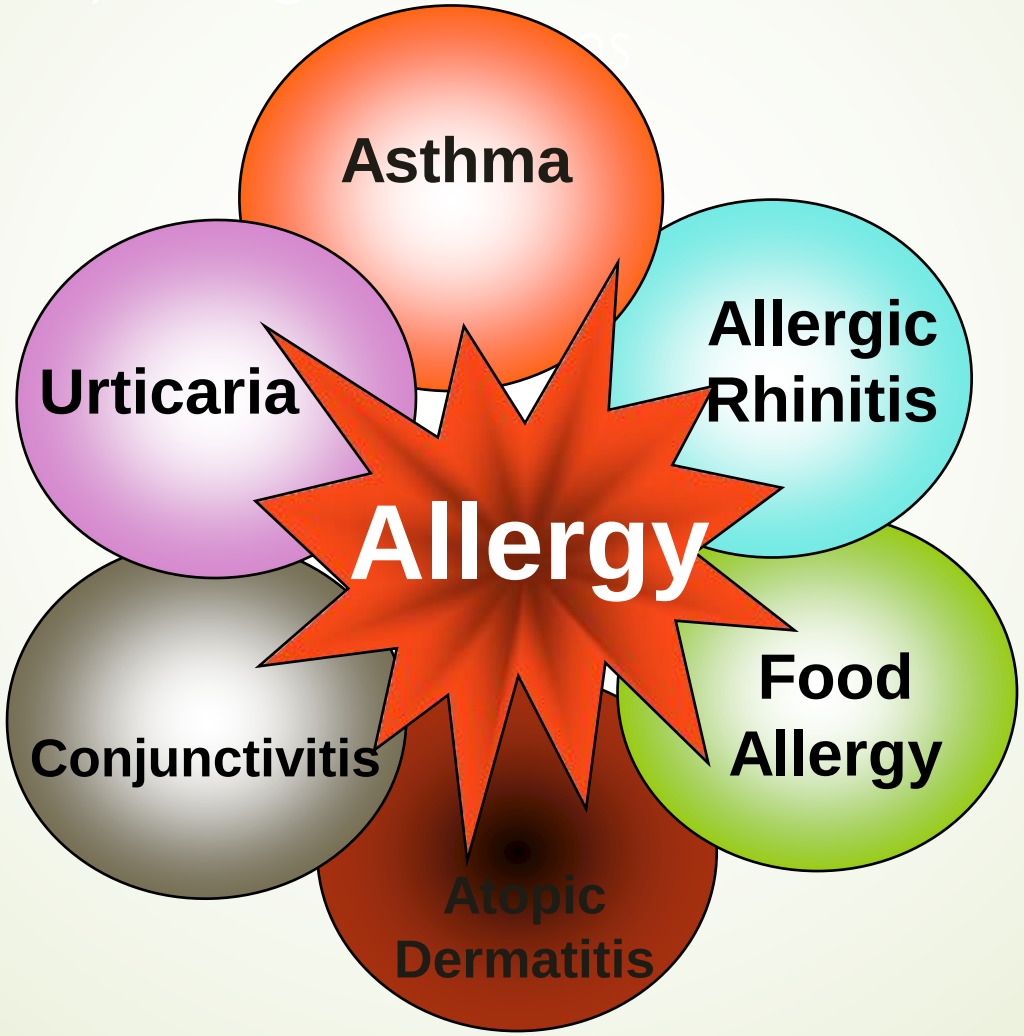
United Airway Disease

dr. Hendrarto S.P.T.H.T.K.L

What is Allergy?

Allergy is an exaggerated immune reaction caused by allergens that can lead to allergy diseases



Tanno LK, et al. World Allergy Organization Journal (2016) 9:24

Allergic Response

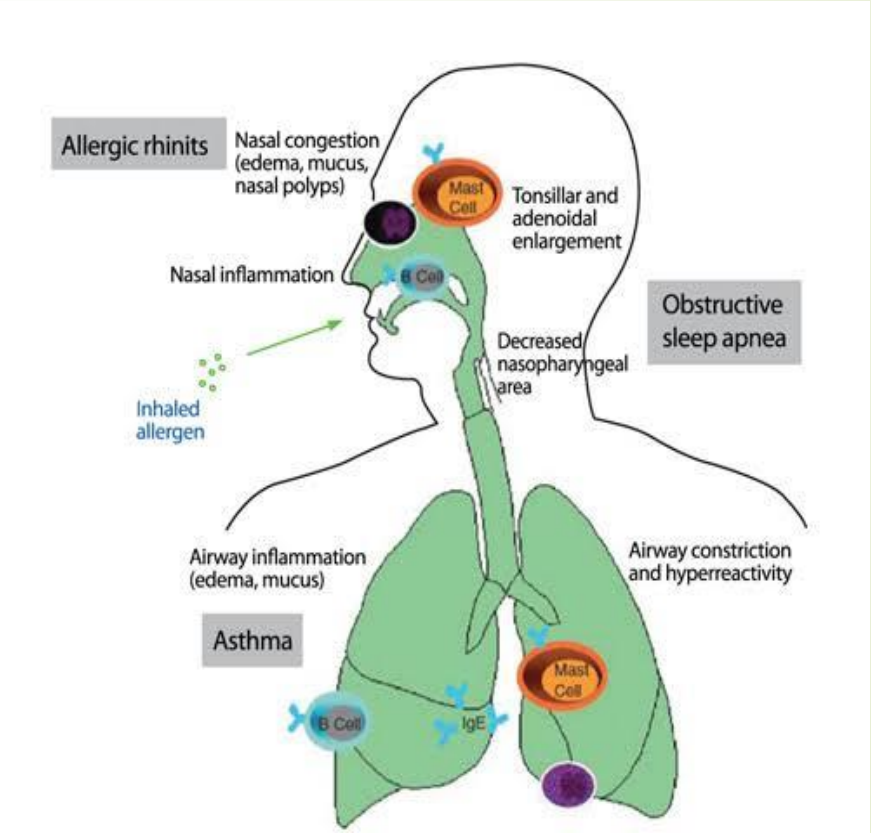
Disease/Reaction	Organ	Sign/Symptoms
Rhinitis	Nose	Sneezing, rhinorrhea, congstion and itching → **Most common**
Asthma	Lower Respiratory Tract	Cough, wheezing, shortness of breath
Dermatitis	Skin	Rach, itching,erythema and oedema
Conjunctivitis	Eyes	itch, redness dan watery eyes
Anaphylaxis	Systemic	Hipotension, shock, death
Gastroenteritis	Digestive tract	Gastrointestinal discomfort, vomitus, diarrhoea dan cramp

Tanno LK, et al. World Allergy Organization Journal (2016) 9:24

Introduction: Allergic Rhinitis, Asthma

- Common diseases that impact a large number of people wide
- 20-30% world wide population
- They have a negative impact on the QoL, sometimes lead to life threatening
- Multiple biological mechanism of allergy

Nevertheless, the disease sometimes undiagnosed or inadequately treated



Respiratory disease is a global burden[1]

- Hundreds of millions of people around the world suffer from preventable chronic respiratory diseases

300 million
people have asthma globally

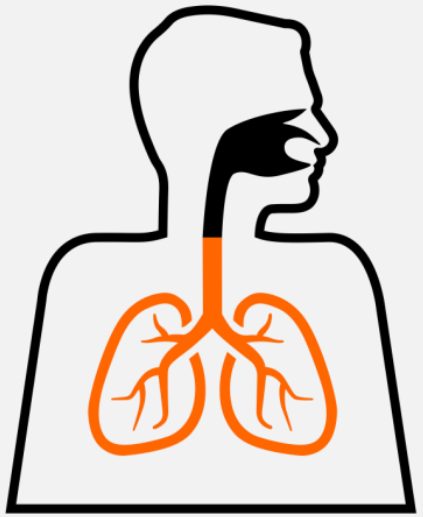
400 million
people have allergic rhinitis globally

- Worldwide, **250,000 people die of asthma every year**; these deaths are related to a lack of proper treatment

1. World Health Organisation, Chronic Respiratory Diseases. Found at: http://www.who.int/gard/publications/chronic_respiratory_diseases.pdf [Accessed October 2016].

Allergic rhinitis and asthma continue to be a significant clinical challenge

Asthma
Definition

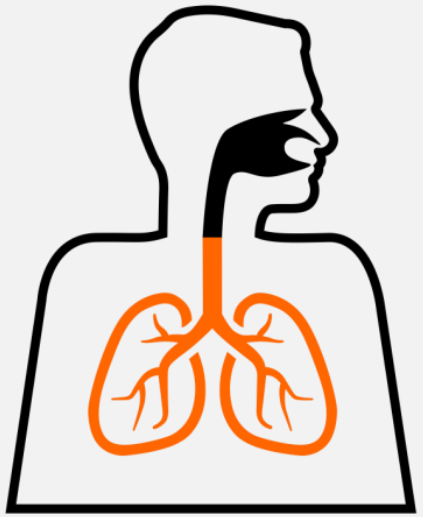


- Asthma is defined as a chronic inflammatory disorder of the lower airways[1,2]
- Characterised by airway hyper-responsiveness and variable airflow obstruction reversible spontaneously or under treatment[2,3]
- Severity is classified as:[4]
  - Mild
  - Moderate
  - Severe

≤18%
of the population in different countries have asthma[5]

1. Kanwa S *et al*. *Ann Otolaryngol Rhinol* 2014; **1**: 1001; 2. World Health Organisation, Chronic Respiratory Diseases. Found at: http://www.who.int/gard/publications/chronic_respiratory_diseases.pdf [Accessed October 2016]; 3. Bateman ED *et al. Eur Respir J* 2008; **31**: 143–78; 4. Rimmer J & Ruhno JW. *Med J Aust* 2006; **185**: 565–71; 5. Global Initiative for Asthma (GINA) Global strategy for asthma management and prevention 2016. Available from: http://ginasthma.org [Accessed October 2016]

Asthma
Characteristics

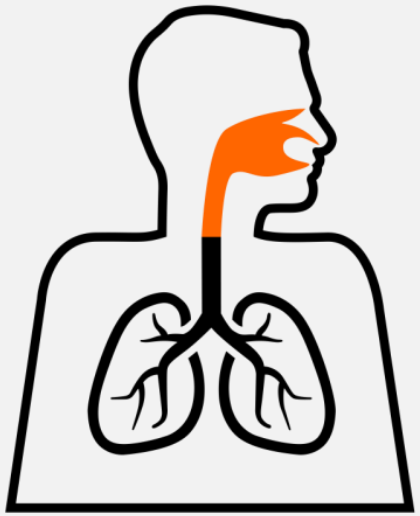


- Asthma is characterised by inflammation causing recurrent episodes of:[1]
  - Wheezing
  - Breathlessness
  - Chest tightness
  - Coughing, especially at night or early morning
  - Variable airflow obstruction that is often reversible, either spontaneously or with treatment
- Asthma exacerbations require unscheduled visits to healthcare providers and changes in treatment management[1]

1. Bourdin A *et al*. *Thorax* 2009; **64**: 999–1004.

Allergic rhinitis (AR)

Definition

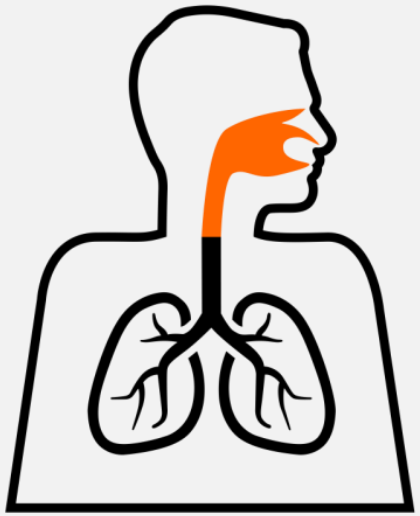


- AR is a condition that affects the upper respiratory tract[1]
- Defined as inflammation of the nasal mucosa and characterised by ≥2 of the following symptoms occurring for more than 1 hour on most days:[1-3]
  - Nasal discharge
  - Nasal blockage
  - Sneezing
  - Itching

10–25%
of western populations have AR[2]

1. Kariya S *et al*. *Ann Otolaryngol Rhinol* 2014; **1**: 1001; 2. Dykewicz MS *et al*. *J Allergy Clin Immunol* 2010; **125**(2 Suppl 2): S103–15. 3. Allergic Rhinitis and its impact on Asthma (ARIA) 2007. Full text ARIA documents and resources at: www.whiar.org

Allergic rhinitis (AR)
Characteristics



- AR can be:[1]
  - **Intermittent** (symptoms occurring less than 4 days a week or for less than 4 consecutive weeks)
  - **Persistent** (symptoms present more than 4 days per week and for more than 4 consecutive weeks)

- AR is driven by a hypersensitive allergic reaction in response to allergens, such as pollen, and is usually immunoglobulin (Ig) E-dependent[1]

- AR can seriously decrease quality of life (QoL), aggravate comorbid conditions, and become a costly medical burden[3]

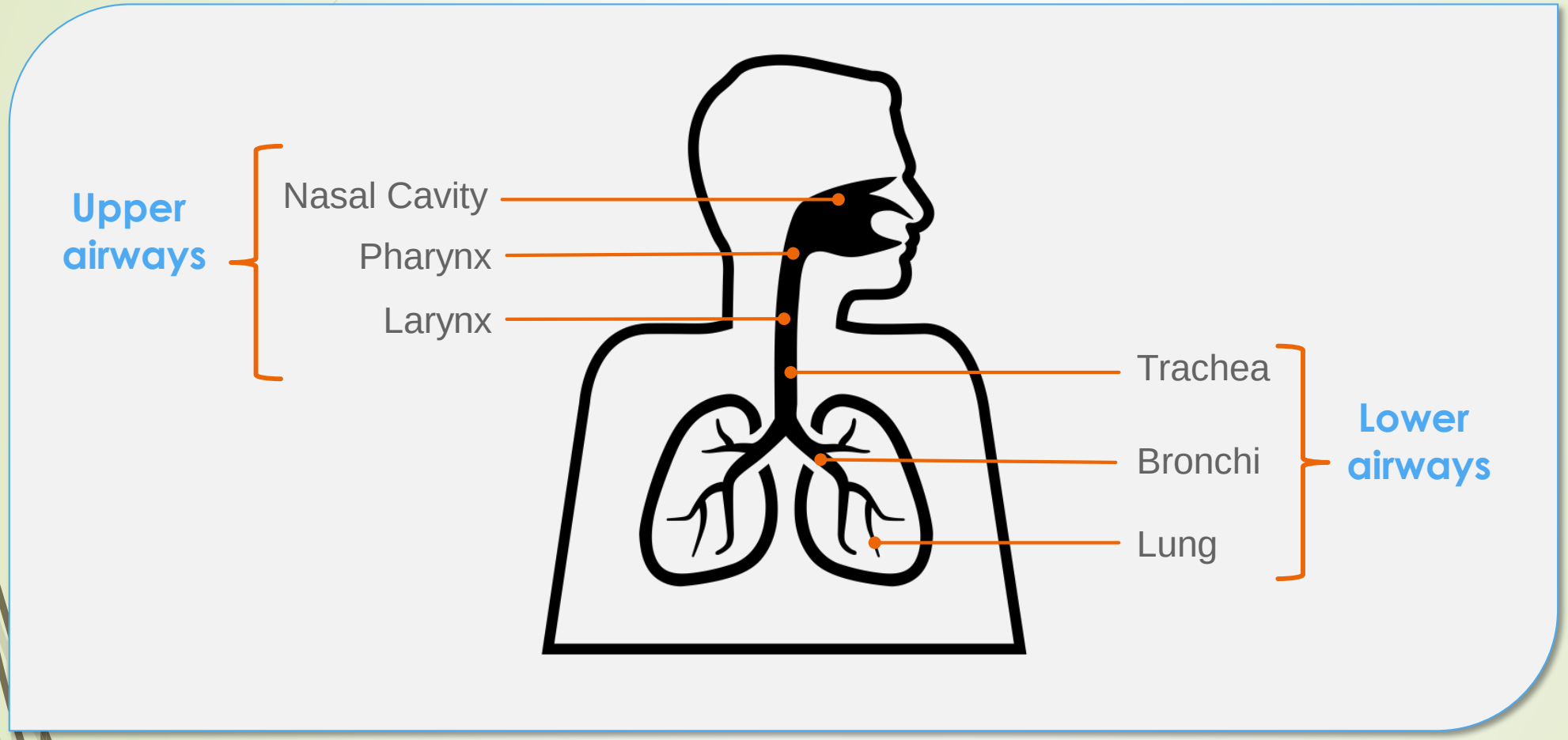
1. Natt F *et al. BMC Ear Nose Throat Disord* 2011; **11**: 3; 2. Dykewicz MS *et al. J Allergy Clin Immunol* 2010; **125**(2 Suppl 2): S103–15; 3. Bourdin A *et al. Thorax* 2009; **64**: 999–1004.

The upper and lower airways are similar

Pendahuluan

- Claudius Galenus : hidung adalah bagian dari "respiratory instrument"
- Sluder (1919) : nasal bronchial reflex (innervasi sama upper – lower airway)
- 10 – 15 tahun : ARIA – WHO , perubahan "localized inflammatory" mencetus systemic respons

The anatomy of the upper and lower airways



1. Rimmer J & Ruhno JW. *Med J Aust* 2006; **185**: 565–71.

The upper and lower airways perform similar roles[1]

1. To support the passage of air into & out of the lungs

2. To defend against inhaled foreign substances

3. To filter out substances in the nose & trap & clear foreign substances in the bronchi

1. Rimmer J & Ruhno JW. *Med J Aust* 2006; **185**: 565–71.

The upper and lower airways are interlinked

- The upper and lower airways are similar in many ways:
  - Anatomically[1]
  - Sensitivity to allergens[2]
  - Inflammatory responses[3]
- Stimulation of the upper airways (e.g. by allergens, infection or environmental pollutants such as smoking) can lead to inflammation of the lower airways and vice versa[4]
- Diseases of the upper airways (e.g. AR) and lower airways (e.g. asthma), are co-morbid conditions
- The upper and lower airways are a continuum, or "unified airway", as opposed to two distinct sections[2,5]

1. Compalati E *et al*. *Expert Rev Clin Immunol* 2010; **6**: 413–23; 2. Ciprandi G *et al. Allergy Asthma Immunol Res* 2012; **4**: 171–7; 3. Bourdin A *et al*. *Thorax* 2009; **64**: 999–1004;
4. Togias A. *J Allergy Clin Immunol* 2003; **111**: 1171–83; 5. Rimmer J & Ruhno JW. *Med J Aust* 2006; **185**: 565–71.

Diseases of the upper and lower airways co-exist

Link between Asthma and Rhinitis

- Upper and lower airways form a continous respiratory tract
- Many inflammatory changes of AR are similar to those of allergic asthma
- The anatomical and immunological link between the lung and nose means that inflammation in one organ influences symptoms in the other.

Expert Rev. Clin. Immunol. 6(3), 413–423 (2010)
Adapted from Phillip G et al. Curr Med Res Opin. 2004;20:1549–1558

Epidemiologic Links between Allergic Rhinitis and Asthma

Many Patients with Asthma Have Allergic Rhinitis

Up to 80%
of all asthmatic patients have allergic rhinitis

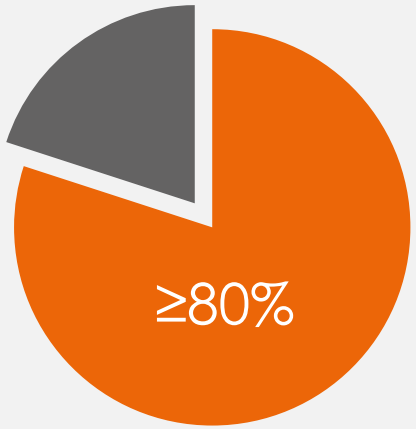
All asthmatic patients

- Relative risk of having Allergic rhinitis and developing asthma **RR = 3.0**
- **Allergic rhinitis** is a significant risk factor for adult-onset asthma

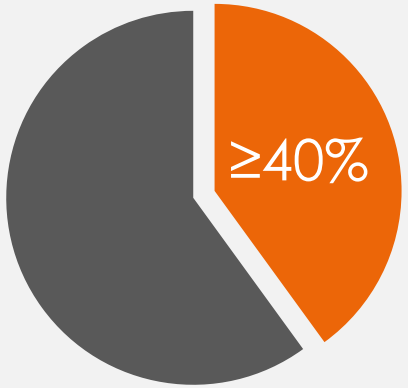
Adapted from Bousquet J et al *J Allergy Clin Immunol* 2001;108(suppl 5):S147–S334; Sibbald B, Rink E *Thorax* 1991;46:895–901; Leynaert B et al *J Allergy Clin Immunol* 1999;104:301–304; Brydon MJ *Asthma J* 1996:29–32.

AR and asthma frequently co-exist with AR being an independent risk factor for asthma[1–3]

Proportion of patients with comorbid AR and asthma



Patients with asthma who also have AR[1,2]

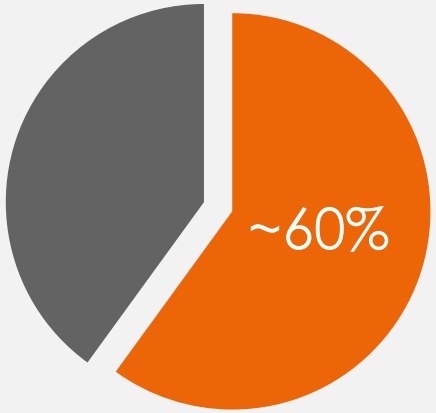


Patients with AR who also have asthma[2]

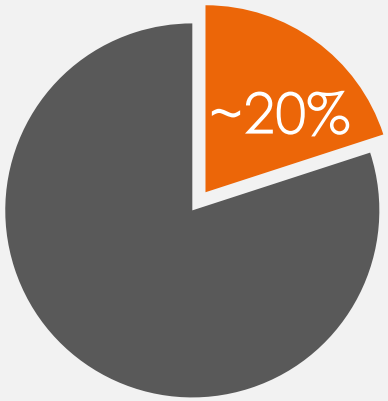
1. Ciprandi G *et al. Respir Med* 2005; **99**: 1606–12; 2. Natt R *et al. BMC Ear Nose Throat Disord* 2011; **11**: 3; 3. Bousquet J *et al. J Allergy Clin Immunol* 2012; **130**: 1049–62.

AR and asthma frequently co-exist in paediatric patients, with allergic rhinitis being an independent risk factor for asthma[1–4]

Proportion of **paediatric patients** with comorbid AR and asthma



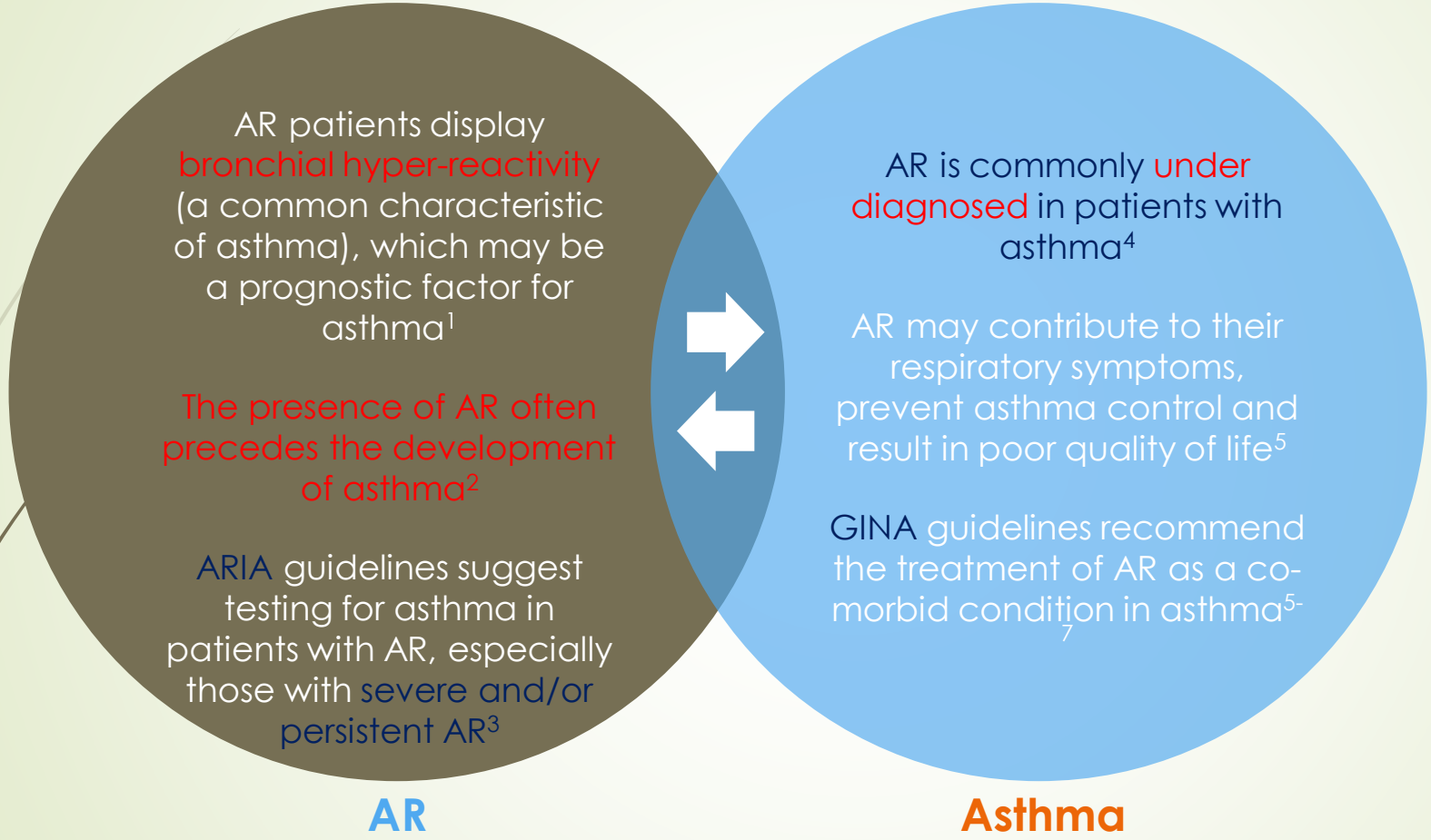
Patients with asthma who also have AR[1,2]



Patients with AR who also have asthma[2]

1. Hanania S, *et al. Clin Exp Allergy*. 2008;**38**:761–6; 2. Kurukulaaratchy KJ, *et al. Respir Med.* 2012;**106**:329–37; 3. Rochat MK, *et al. J Allergy Clin Immunol*. 2010;**126**:1170–5.e2; 4. Bousquet J, *et al. J Allergy Clin Immunol*. 2012;**130**:1049–62.

Asthma and AR frequently co-exist



1. Ciprandi G *et al. Respir Med* 2005; **99**: 1606–12; 2. Leynaert B *et al. J Allergy Clin Immunol* 2004; **113**: 86–93; 3. Bousquet J *et al. J Allergy Clin Immunol* 2012; **130**: 1049–62; 4. Egan M & Bunyavanich S. *Asthma Res Pract* 2015; **1**: 8; 5. Global Initiative for Asthma (GINA) Global strategy for asthma management and prevention 2016. Available from: http://ginasthma.org [Accessed October 2016]; 6. Allergic Rhinitis and its impact on Asthma (ARIA) 2007. Full text ARIA documents and resources at: www.whiar.org [Accessed October 2016]; 7. Bourdin A *et al*. *Thorax* 2009; **64**: 999–1004.

There are many similarities between AR and asthma

The upper and lower airways are anatomically similar

- Both the upper and lower airways are characterised by:[1]
  - Ciliate epithelium
  - Mucinous glands
  - Supported by vascularisation and innervation
- They're both also susceptible to the same exogenous agents:[2]
  - Allergens
  - Infections
  - Environmental pollutants
  - Drugs

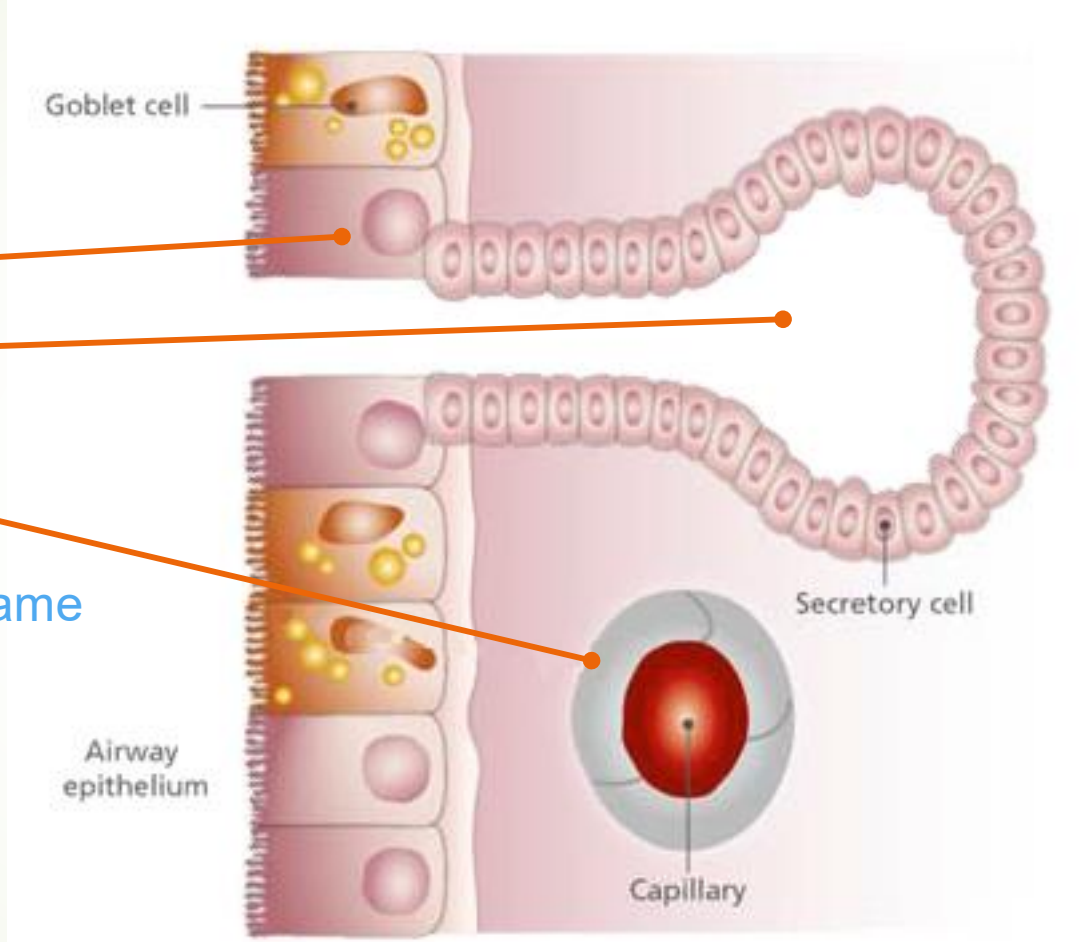
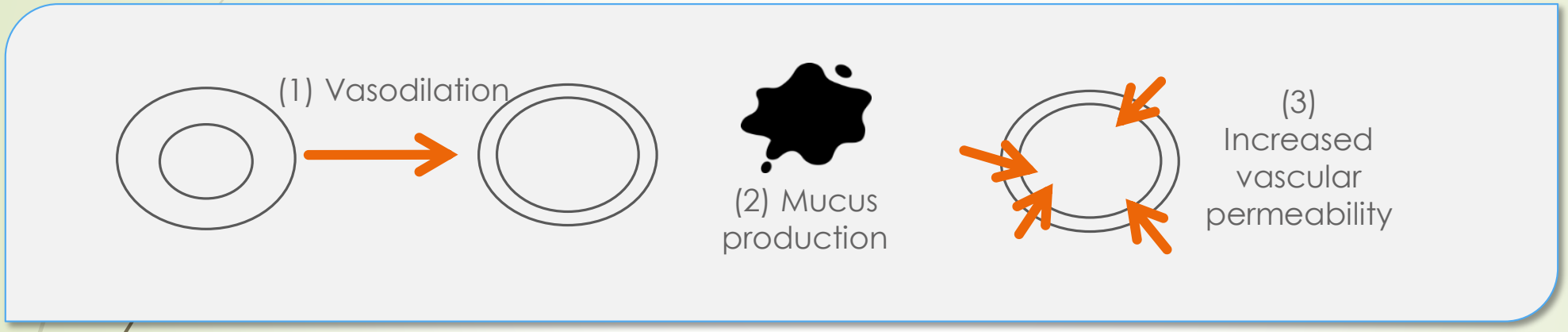


Image adapted from:
King LS, *et al. Nat Rev Mol Cell Biol.* 2004;5:687–98;
Berkebile AR & McCray PB Jr. *Int J Biochem Cell Biol.* 2014;52:124–9.

1. Compalati E *et al. Expert Rev Clin Immunol* 2010; **6**: 413–23; 2. Ciprandi G *et al. Allergy Asthma Immunol Res* 2012; **4**: 171–7; 3. Image adapted from: King LS *et al. Nat Rev Mol Cell Biol* 2014; **5**: 687–98.

AR and asthma have similar pathological features

- AR and asthma both involve a systemic inflammatory response following allergen challenge, characterised by:[1]



- Both nasal and bronchial mucosa respond similarly to external triggers, such as allergens and pollutants
- AR and asthma are both characterised by chronic inflammation of the whole respiratory mucosa and involve similar inflammatory processes[2]

1. Meltzer EO *et al. J Manag Care Pharm* 2004; **10**: 310–7; 2. Sin B & Togias A. *Proc Am Thorac Soc* 2011; **8**: 106–14.

Upper and lower airways show similar inflammatory changes

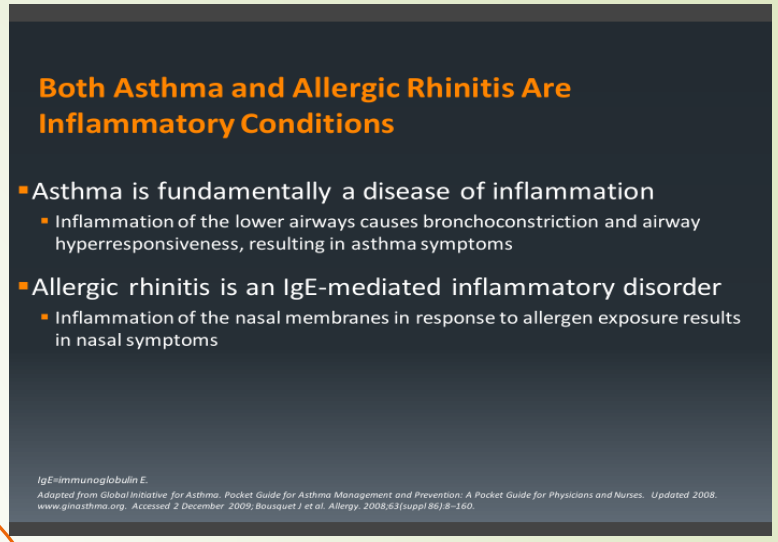
(1) Inflammation in the upper airways can aggravate the lower airways and visa versa[1]

(4) AR patients without bronchial hypersensitivity or other signs of asthma have increased eosinophil levels in their lower airways[4]

Inflammation

(2) Inflammatory mediators released locally subsequently leads to a systemic inflammatory response[1,2]

(3) Asthmatics have increased eosinophil levels in their upper airways even without nasal symptoms[3]



1. Togias A. *J Allergy Clin Immunol* 2003; **111**: 1171–83; 2. Fasano MB. *Curr Opin Otolaryngol Head Neck Surg* 2010; **18**: 15–20; 3. Gaga M *et al. Clin Exp Allergy* 2000; **30**: 663–9;
4. Braunstahl GJ *et al*. *Am J Respir Care Med* 2001; **164**: 858–65.

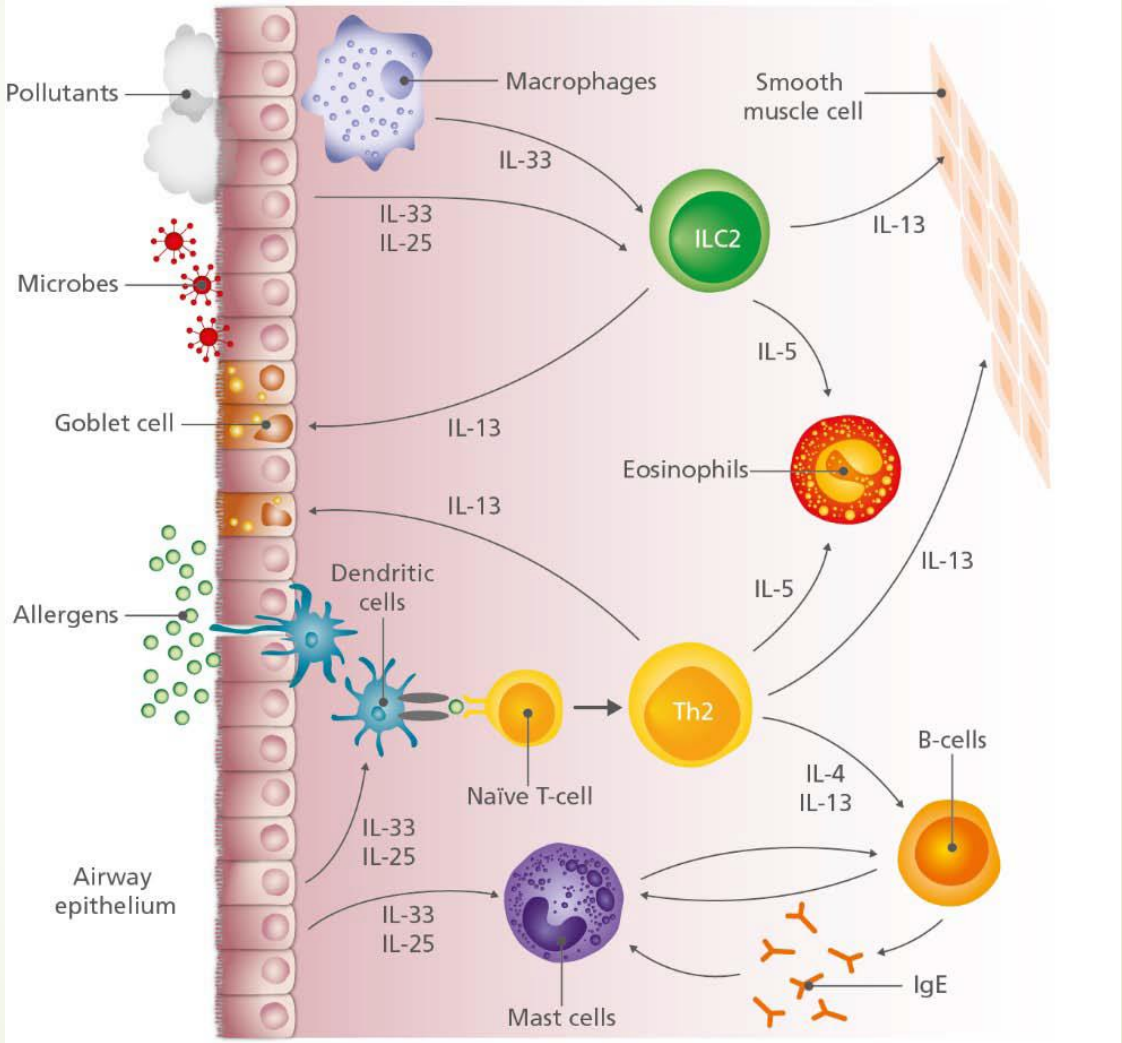
Upper and lower airways show similar inflammatory changes

Characterised by:[1,2]

- Infiltration of leukocytes
- Involving:
  - Eosinophils,
  - Lymphocytes
  - Macrophages
  - Mast cells

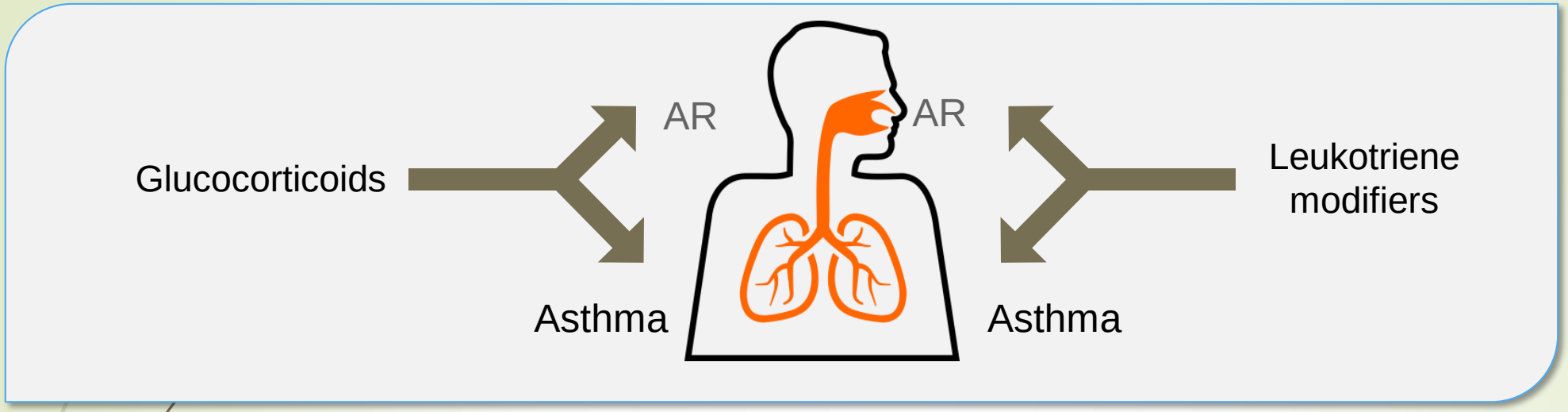
Production of:[2,3]

- Cytokines
- Leukotrienes
- Inflammatory mediators



1. Melzer EO *et al*. *J Manag Care Pharm* 2004; **10**: 310–7; 2. Sin B & Togias A. *Proc Am Thorac Soc* 2011; **8**: 106–14; 3. Bourdin A *et al*. *Thorax* 2009; **64**: 999–1004; 4. Image adapted from: de Groot JC *et al. ERJ Open Res 2015;* **1**: 00024–2015.

The upper are lower airways are responsive to similar therapies



- The effectiveness of similar therapeutic agents in AR and asthma is suggestive of a common pathogenic mechanism:[1]

➨ Treating nasal inflammation in patients with mild allergic asthma has been shown to reduce asthma symptoms and bronchial hyper-responsiveness[2]

➨ The use of nasal steroids was reported to be as equally efficacious in reducing asthmatic symptoms as low doses of bronchial steroids[3]

1. Kariya S *et al. Ann Otolaryngol Rhinol* 2014; **1**: 1001; 2. Lipworth BJ & White PS *Thorax* 2000; **55:** 878-81; 3. Bourdin A *et al. Thorax* 2009; **64**: 999–1004.

Possible mechanisms linking upper and lower airway disease

Respiratory:

- Loss of protective function of the nose
- Neural–vascular interaction between upper and lower airways
- Aspiration of nasal secretions (postnasal drip)
- Aspiration of inflammatory mediators
- Alteration of nasal nitric oxide production
- Altered breathing pattern
- Structural changes related to anatomy or inflammation

Fasano ,Current Opinion in Otolaryngology & Head and Neck Surgery 2010, 18:15–20

Possible mechanisms linking upper and lower airway disease

Systemic

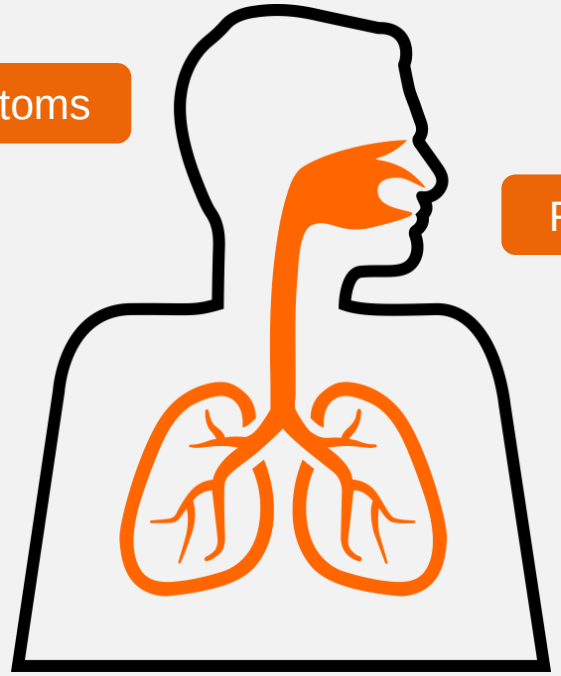
- Activation of inflammatory cell production in bone marrow
- Activation of eosinophils, basophils, mast cells, and lymphocytes following allergen exposure
- Local release of mediators inducing a systemic effect
- Activation of innate stromal and hematopoietic effector cells

Fasano ,Current Opinion in Otolaryngology & Head and Neck Surgery 2010, 18:15–20

The upper and lower airways are therapeutically linked

Treatment of AR in asthma patients has been shown to:[1]

- Improve asthma symptoms
- Reduce asthma exacerbation induced by exercise
- Improve pulmonary functions tests



- Reduce treatment costs
- Reduce the risk of emergency room treatment or hospitalisations

1. Bourdin A *et al*. *Thorax* 2009; **64**: 999–1004.

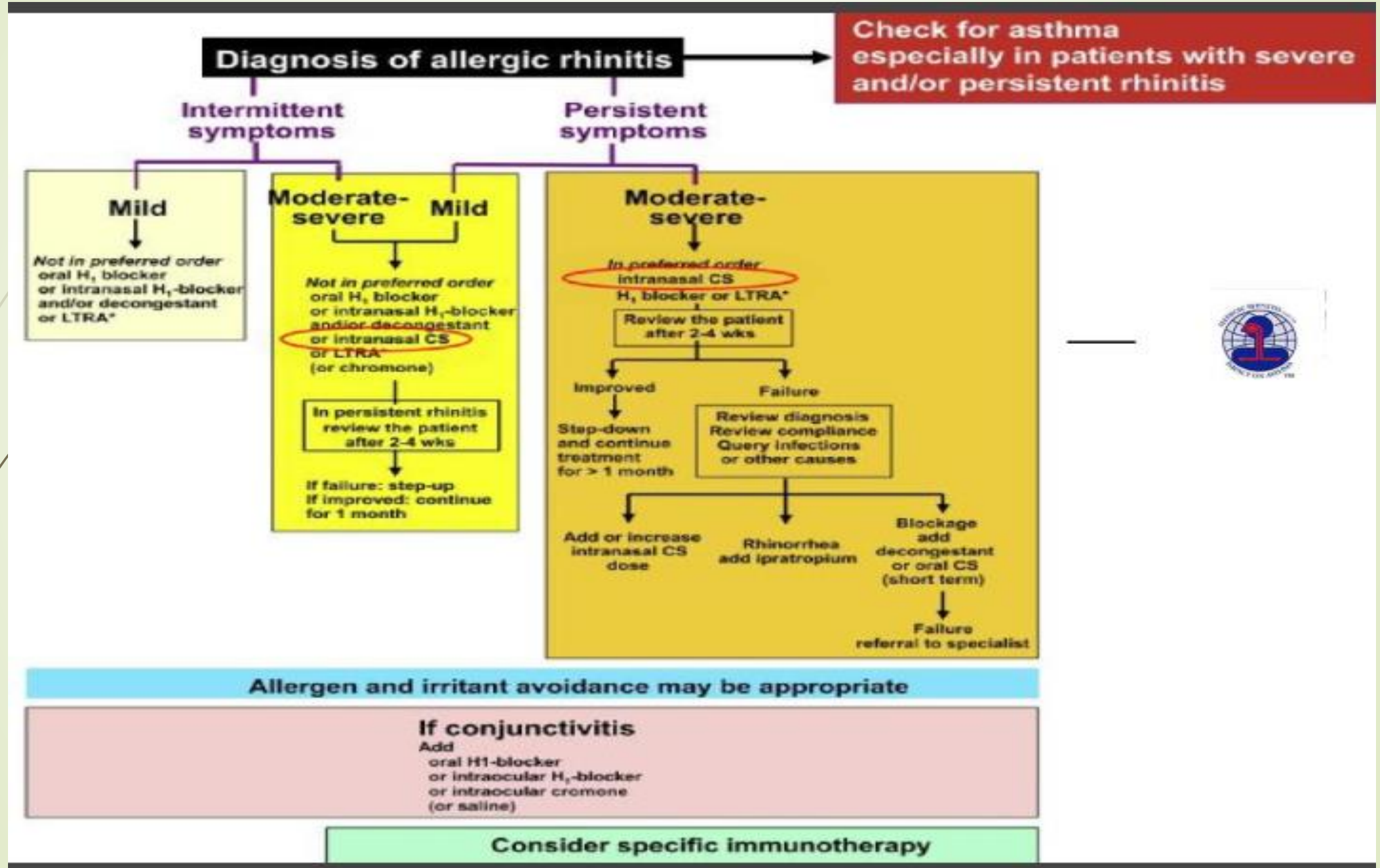
Treatment of Allergic Rhinitis (2010 ARIA)

Non-Sedating Anti-histamine & LTRA in ARIA GUIDELINE

Mild intermittent	Moderate severe intermittent	Mild persistent	Moderate severe persistent
	Intra-nasal steroid		
	Local Cromone		
Oral or local non-sedating antihistamine			
Intra-nasal decongestant (<5days) or oral decongestant →			
LTRA* *In particular for patients with asthma			
Allergen and irritant avoidance			
Immunotherapy			

Bousquet J, Van Cauwenberge P, Khaltaev N. ARIA Workshop Group, World Health Organization. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001;108:S147-334.
Adapted from the ARIA official slide kit, slide 32 - Used with permission

llergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 Revision
Allergy Clin Immunol 2010;126:466-76.)


Diagnosis of allergic rhinitis
Check for asthma especially in patients with severe and/or persistent rhinitis
Intermittent symptoms
Persistent symptoms
Mild
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or LTRA*
Moderate-severe
Mild
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or intranasal CS
or LTRA*
(or chromone)
In persistent rhinitis review the patient after 2-4 wks
If failure: step-up
If improved: continue for 1 month
Moderate-severe
In preferred order
intranasal CS
H1 blocker or LTRA*
Review the patient after 2-4 wks
Improved
Step-down and continue treatment for > 1 month
Failure
Review diagnosis
Review compliance
Query infections
or other causes
Add or increase intranasal CS dose
Rhinorrhea add ipratropium
Blockage add decongestant or oral CS (short term)
Failure referral to specialist
Allergen and irritant avoidance may be appropriate
If conjunctivitis
Add
oral H1-blocker
or intraocular H1-blocker
or intraocular cromone
(or saline)
Consider specific immunotherapy

Treatment of allergic rhinitis

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

Bousquet et al. Allergy 2003

Treating Rhinitis May Help Asthma

- The key to successful therapy for rhinitis and asthma is the prevention or suppression of inflammation
- Treatment of rhinitis has been shown to be beneficial to the lower airways
- Treating inflammation in the upper airways indirectly improves asthma symptoms and decreases bronchial hyperreactivity

One Airway, One Disease

ARIA and IPAG Guidelines Recommend a Combined Approach to Managing Asthma and Allergic Rhinitis

- Patients with allergic rhinitis should be evaluated for asthma
- Patients with asthma should be evaluated for allergic rhinitis
- A strategy should combine the treatment of upper and lower airways in terms of efficacy and tolerability

ARIA=Allergic Rhinitis and its Impact on Asthma; IPAG=International Primary Care Airways Groups

Adapted from Bousquet J et al *J Allergy Clin Immunol* 2001;108(suppl 5):S147–S334; International Primary Care Airways Group, Los Angeles, California, USA, MCR Vision, 2005.

TERIMAKASIH dan SEMOGA BERMANFAAT

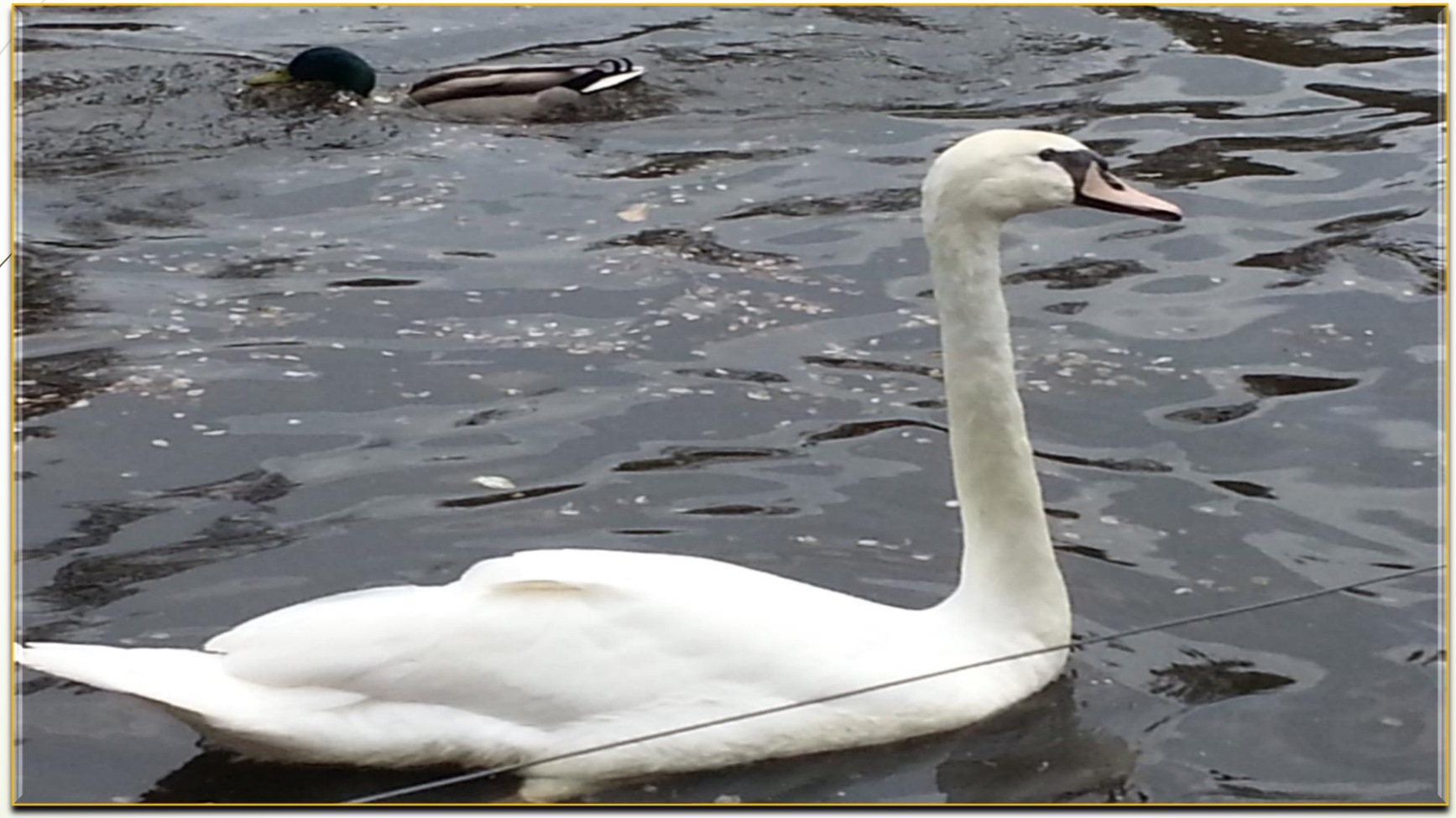
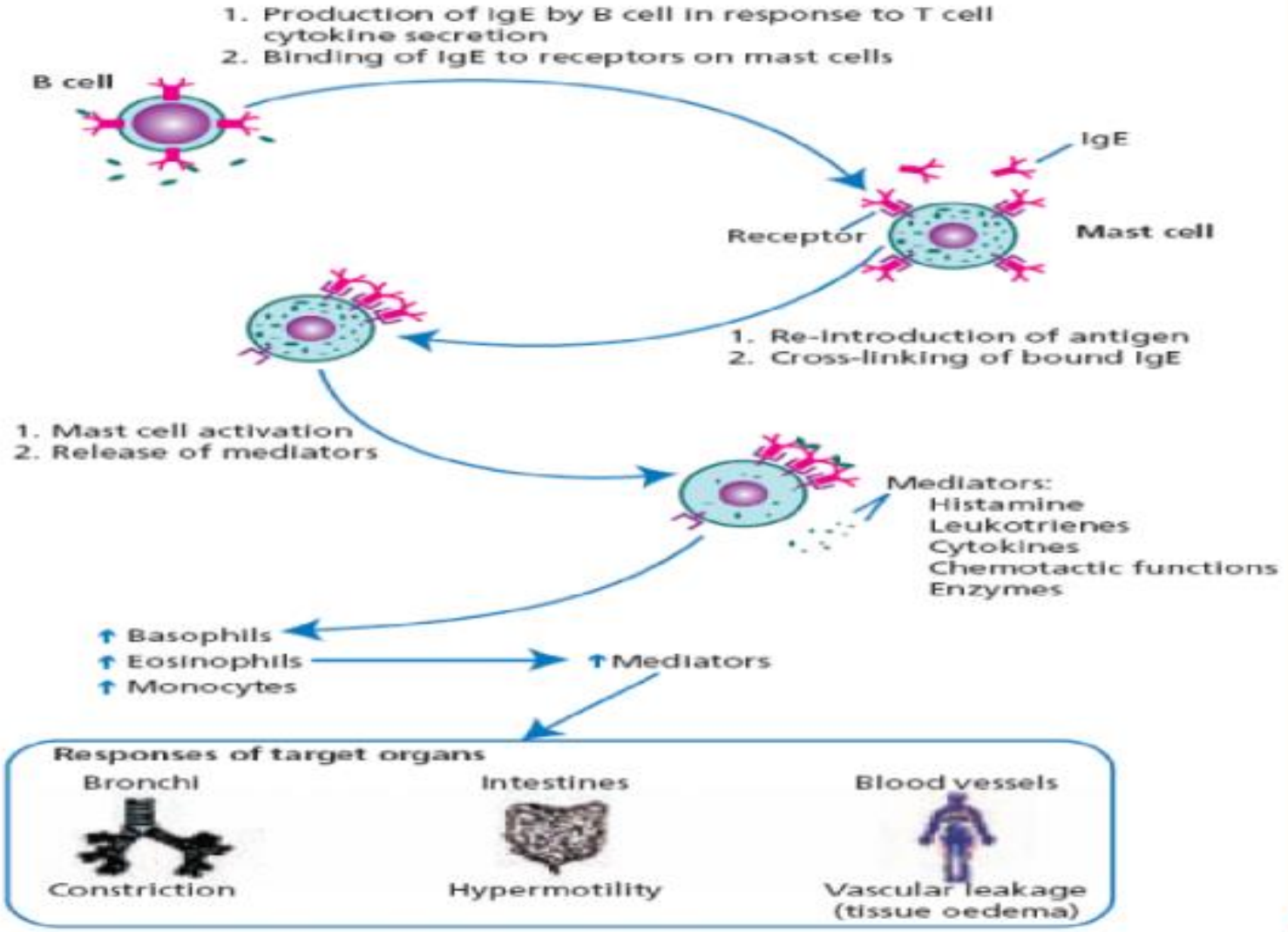
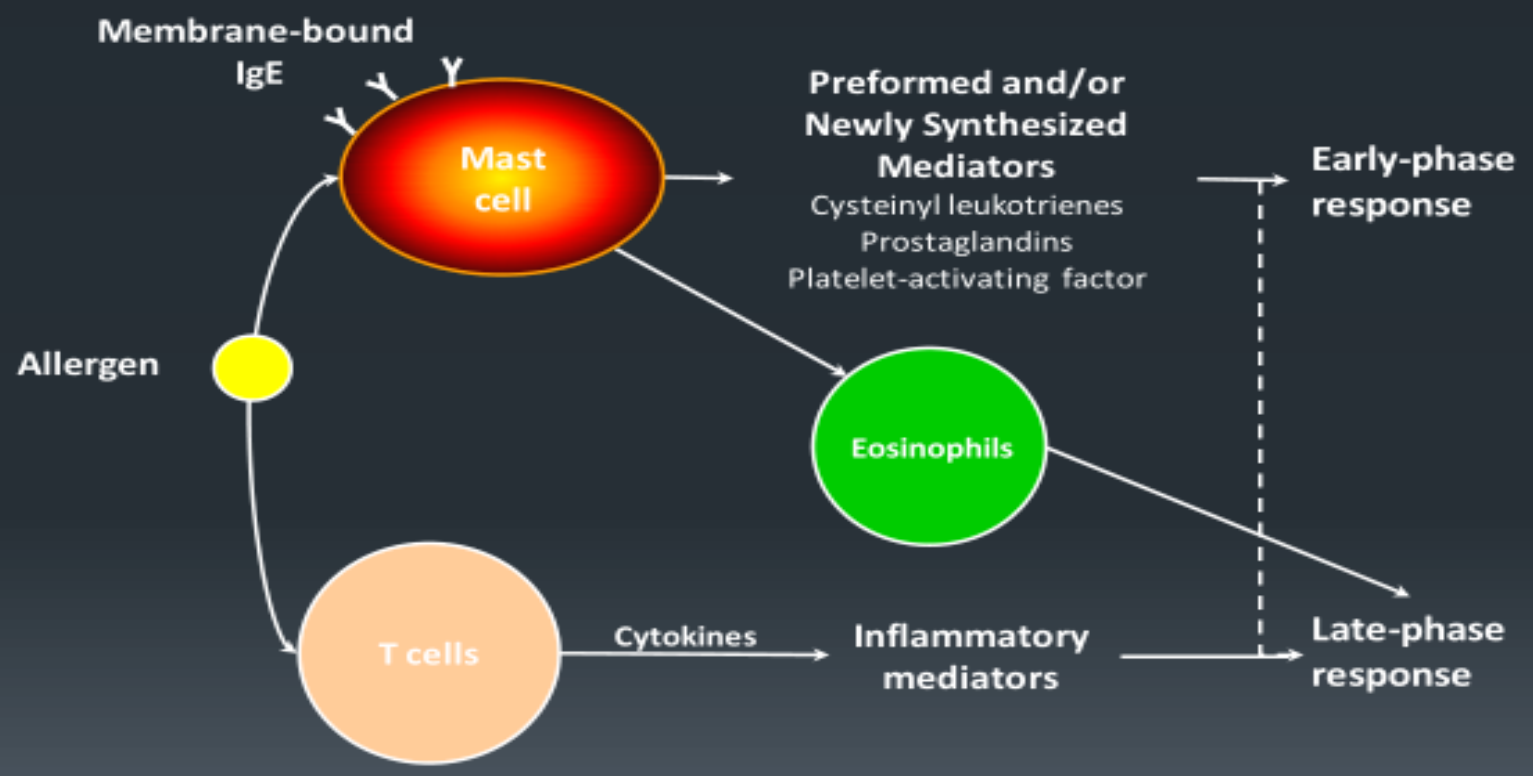


Figure 6. The early and late phase responses of the allergic cascade, including the inflammatory cells involved, mediators released and resulting symptoms

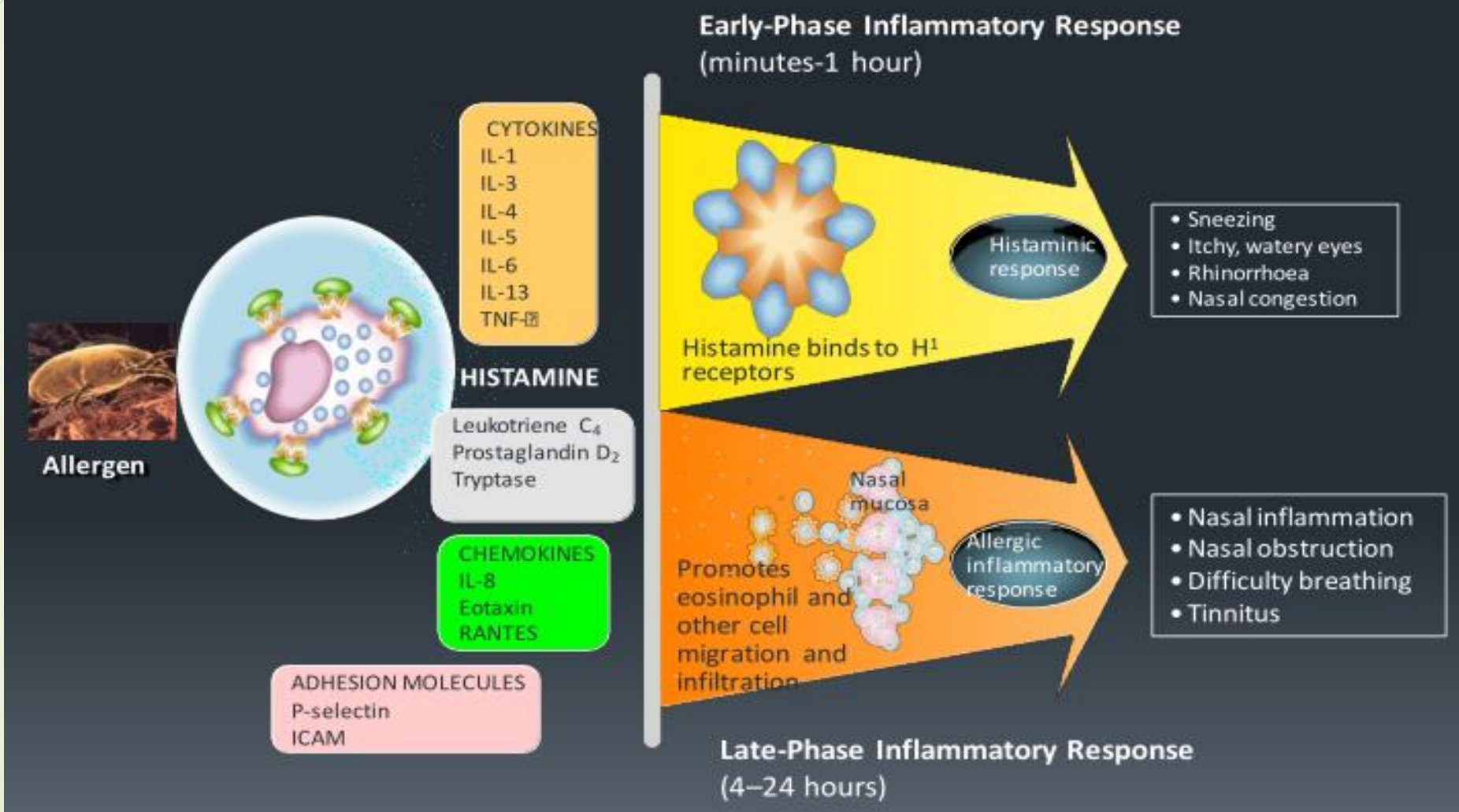


Asthma and Allergic Rhinitis Share Common Inflammatory Cells and Mediators



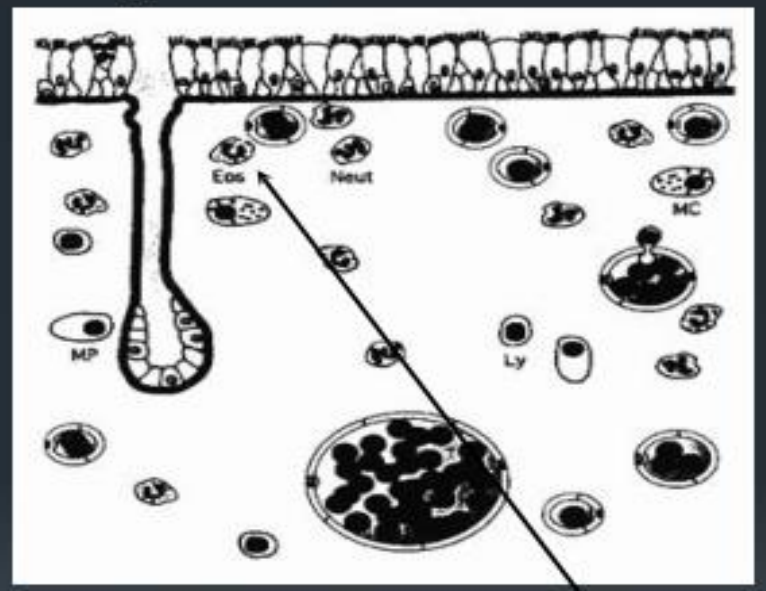
Adapted from Casale TB et al. *Clin Rev Allergy Immunol.* 2001;21:27–49; Kay AB. *N Engl J Med.* 2001;344:30–37.

Allergic Rhinitis



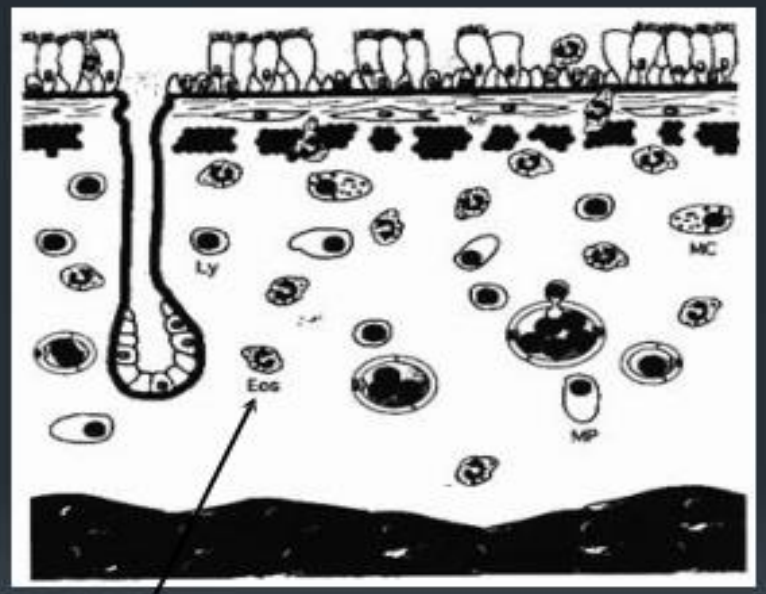
Allergic Rhinitis and Asthma Share a Similar Inflammatory Process and Occur in the Mucosa

Allergic rhinitis



Nasal mucosa

Asthma



Bronchial mucosa

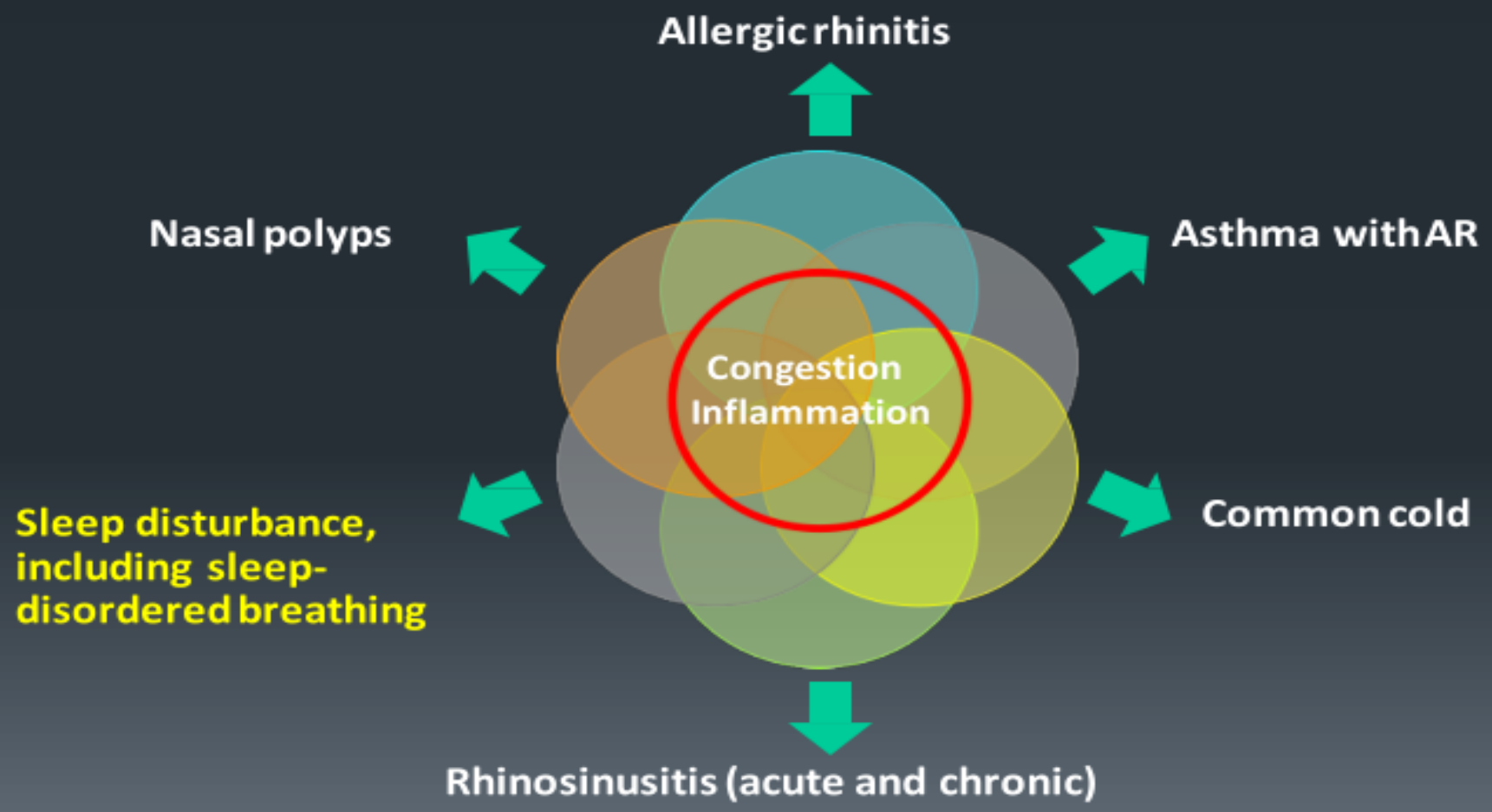
Eosinophil infiltration

Eos=eosinophils; neut=neutrophils; MC=mast cells; Ly=lymphocytes; MP=macrophages

Adapted from Bousquet J et al *J Allergy Clin Immunol* 2001;108(suppl 5):S148–S149.

Congestion and Inflammation:

Adverse Clinical Impact in Upper Respiratory Disease



Impact of allergic rhinitis on lung function

- Both AR and asthma have airflow limitation as the main functional consequence
- The forced expiratory volume in 1 second (FEV_1), a measurement of exhaled volume during the first second of a forced expiratory maneuver, may be impaired in approximately 5% of patients with AR who report only nasal symptoms.

How Allergic rhinitis affects asthma

Allergic rhinitis may promote or exacerbate asthma through several physiologic mechanisms that link the disorders.

These include :

1. The vagal (rhinobronchial) reflex, which causes nasal stimulation to induce bronchoconstriction.
2. Systemic release of mediators and cytokines.
3. Postnasal drip and resulting irritation.
4. The need for oral respiration caused by nasal obstruction, which causes dry, cold air to penetrate into the bronchi and promote bronchial hyperreactivity

Other Proposed pathophysiologic mechanisms of asthma exacerbated by sinusitis

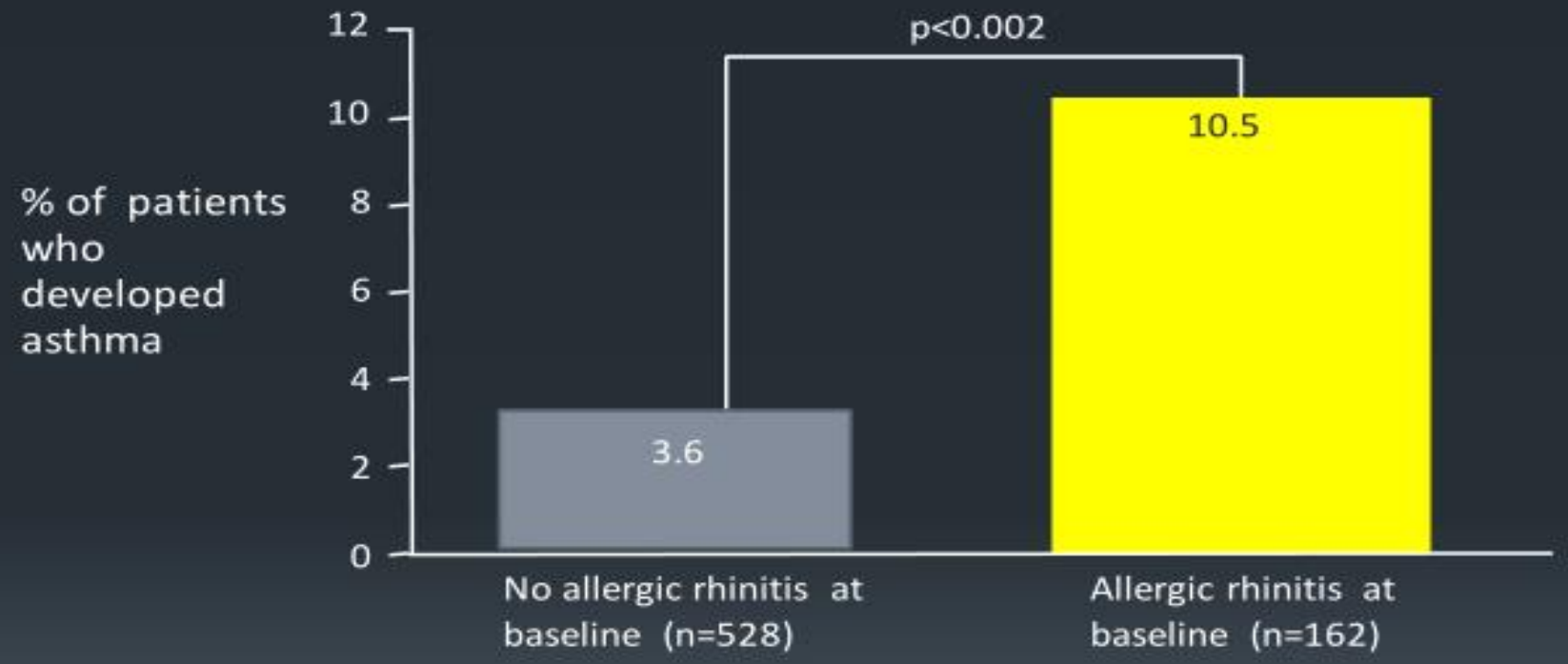
- Spread of inflammatory mediators and chemotactic factors to lower airways triggers sinobronchial reflex mechanism.
- Stimulation of autonomic nervous system causes acute bronchial hyperresponsiveness.

Slavin RG, Asthma and Sinusitis. J allergy Clin Immunol 1992;90:534-7

Epidemiologic Links between Allergic Rhinitis and Asthma

Allergic Rhinitis Is a Risk Factor for Asthma

Allergic rhinitis increased the risk of asthma about threefold [1]

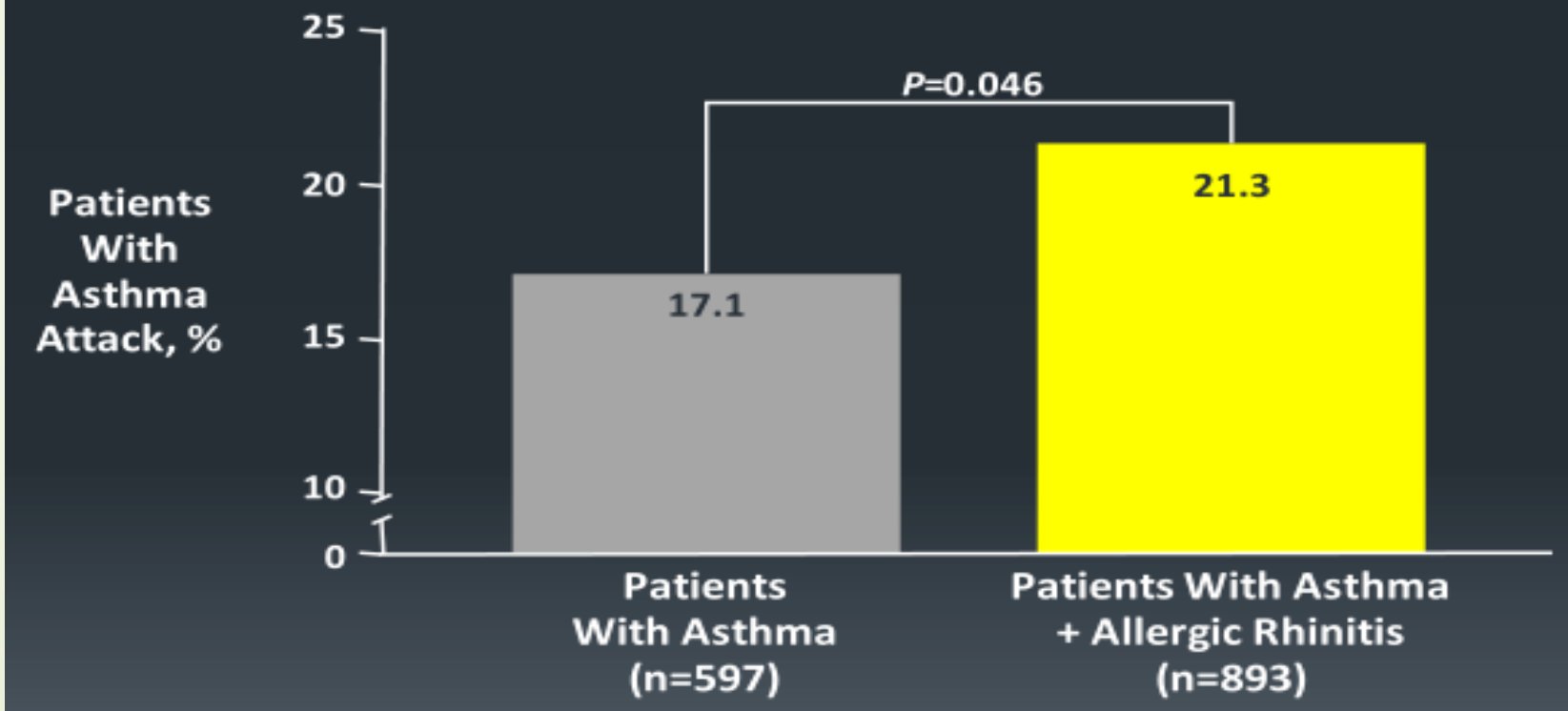


23-year follow-up of first-year college students undergoing allergy testing; data based on 738 individuals (69% male) with average age of 40 years

1. Celine Bergeron and Qutayba Hamid. **Relationship between Asthma and Rhinitis: Epidemiologic, Pathophysiologic, and Therapeutic Aspects Allergy Asthma Clinical Immunol.2005**

Adapted from Settipane RJ et al *Allergy Proc* 1994;15:21–25.

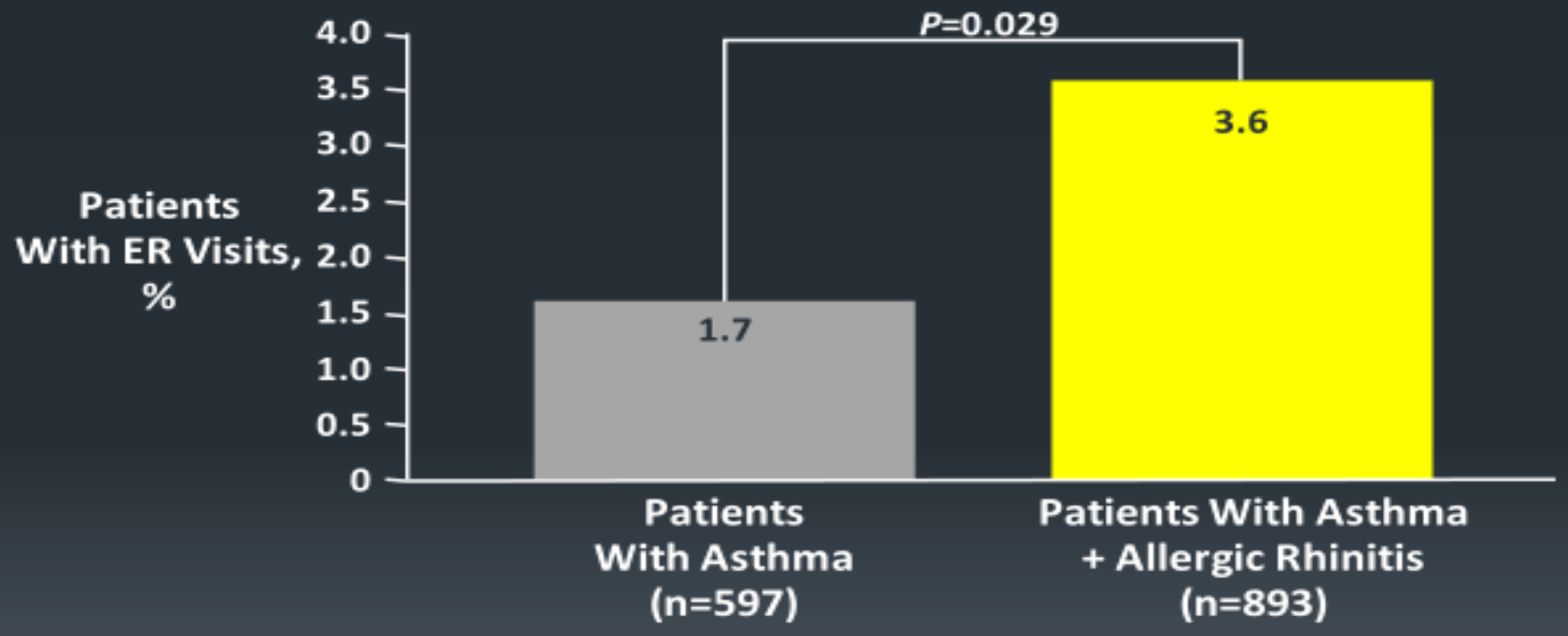
Allergic Rhinitis Increased the Risk of Asthma Attacks



Post hoc analysis of medical resource use/asthma attacks in asthmatic patients with and without concomitant allergic rhinitis over 52 weeks

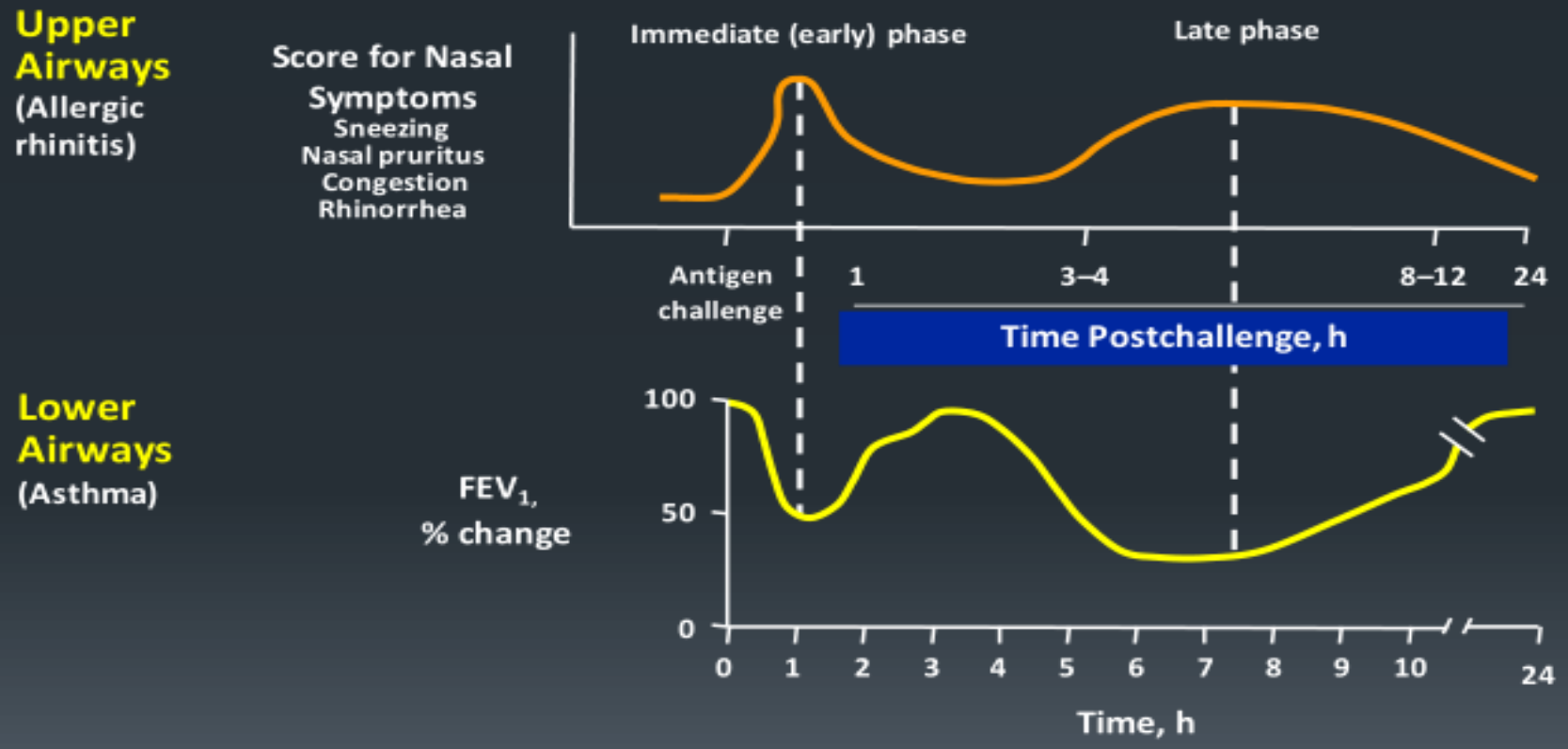
Adapted from Bousquet J et al. *Clin Exp Allergy.* 2005;35:723–727.

Allergic Rhinitis Doubled the Risk of ER Visits in Patients With Asthma



Post hoc analysis of medical resource use/asthma attacks in asthmatic patients with and without concomitant allergic rhinitis over 52 weeks
ER=emergency room.
Adapted from Bousquet J et al. *Clin Exp Allergy*. 2005;35:723–727.

Symptoms Correlate With the Early- and Late-Phase Responses in Allergic Rhinitis and Asthma



FEV_1=forced expiratory volume in 1 second.

Adapted from; Togias A. *J Allergy Clin Immunol.* 2000;105(6 pt 2):S599–S604.

omis dan histologis	Bukti epidemiologis	Bukti patofisiologis	Perkembangan biomarker	Bukti klinis dan pengobatan
nasal dan bronkial terdiri dari epitel ng berada diatas membran basalis. membran basalis terdapat lamina elenjar dan sel goblet.	19-38% pasien dengan rhintis alergi (AR) memiliki asthma yang bersamaan dan 30-80% pasien asthma memiliki AR.	Komunikasi antara jalan napas atas dan bawah diusulkan melalui respon inflamatorik sistemik yang berasal dari sumsum tulang.	Peran microbiome: anak yang dibesarkan pada perkebunan tradisional memiliki prevalensi penyakit alergi yang lebih rendah daripada anak yang tumbuh dewasa di area perkotaan.	Terapi AR dapat memperbaiki gejala asthma
a bertindak sebagai sistem transpor hkan udara keluar dan masuk ke		Adanya penebalan membran basement epitel, penanda tipikal dari remodelling jalan napas bawah, tidak hanya pada pasien asthma tetapi juga pada pasien atopik tanpa asthma dan juga pasien dengan AR	Peran microRNA (miRNA); adanya miRNA yang sama dalam mekanisme patogenik yang berbeda baik pada AR dan sthma, seperti jaras IL-13, protein pengikat GATA 3, dan sekret mucin.	Penurunan pada gejala asthma dan AR setelah pemberian terapi steroid intranasal untuk rhinitis
a memberikan perlindungan terhadap ing yang terhirup, dengan sebagian tikel 5-10 µm diameter tersaring keluar idung, gas iritan dan solubel secara dihilangkan melalui disolusi pada sal. Fungsi saluran napas bawah juga lengan partikel inhalasi yang lebih perangkap dan dibersihkan oleh mukosilier.		Pada pasien asthma non-alergi telah disorot mengenai peran dari keberadaan IgE pada mukosa bronkial, serupa dengan mukosa nasal pada rhinitis alergi lokal.		Leukotriene receptor antagonis telah diketahui berguna untuk penanganan pasien asthma yang dipersulit oleh AR
				Antibodi anti-IgE monoklonal rekombinan manusia Omalizumab mengurangi gejala bronkial dan nasal serta mengurangi kunjungan tak terjadwal karena asthma Imunoterapi alergen efektif untuk terapi asthma dan rhinitis

Bukti Anatomis

- Keduanya memberikan perlindungan terhadap benda asing yang terhirup, dengan sebagian besar partikel 5-10 μm diameter tersaring keluar melalui hidung, gas iritan dan solubel secara ekstensif dihilangkan melalui disolusi pada sekresi nasal. Fungsi saluran napas bawah juga serupa, dengan partikel inhalasi yang lebih kecil diperangkap dan dibersihkan oleh eskalator mukosilier.

Bukti Epidemiologi

- 19-38% pasien dengan rhintis alergi (AR) memiliki asthma yang bersamaan dan 30-80% pasien asthma memiliki AR.

Bukti Patofisologis

- Komunikasi antara jalan napas atas dan bawah diusulkan melalui respon inflamatorik sistemik yang berasal dari sumsum tulang.
- Adanya penebalan membran basement epitel, penanda tipikal dari remodelling jalan napas bawah, tidak hanya pada pasien asthma tetapi juga pada pasien atopik tanpa asthma dan juga pasien dengan AR.
- Pada pasien asthma non-alergi telah disorot mengenai peran dari keberadaan IgE pada mukosa bronkial, serupa dengan mukosa nasal pada rhinitis alergi lokal.

Perkembangan Biomarker

- Peran microbiome: anak yang dibesarkan pada perkebunan tradisional memiliki prevalensi penyakit alergi yang lebih rendah daripada anak yang tumbuh dewasa di area perkotaan.
- Peran microRNA (miRNA); adanya miRNA yang sama dalam mekanisme patogenik yang berbeda baik pada AR dan asthma, seperti jaras IL-13, protein pengikat GATA 3, dan sekret mucin.

Bukti Klinis Dan Pengobatan

- Terapi AR dapat memperbaiki gejala asthma
- Penurunan pada gejala asthma dan AR setelah pemberian terapi steroid intranasal untuk rhinitis
- Leukotriene receptor antagonis telah diketahui berguna untuk penanganan pasien asthma yang dipersulit oleh AR
- Antibodi anti-IgE monoklonal rekombinan manusia (Omalizumab) mengurangi gejala bronkial dan nasal serta mengurangi kunjungan tak terjadwal karena asthma
- Imunoterapi alergen efektif untuk terapi asthma dan rhinitis

Kesimpulan

Hubungan antara saluran udara bagian atas dan bawah, yang disebut **United Airway Disease**, telah diungkapkan oleh beberapa bukti epidemiologis, patofisiologis, dan klinis, mengubah pandangan patogen secaara umum tentang alergi pernapasan.

AR dan asma merupakan manifestasi dari **proses inflamasi** tunggal dan membutuhkan pendekatan diagnostik dan terapeutik yang terintegrasi untuk mendapatkan kontrol penyakit secara menyeluruh.