

Asthma



Definition

- .Chronic inflammatory disease with inflammation due to complex interaction between inflammatory cells, mediators and airways cells
- .The chronic inflammation is associated with hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning
- .These episodes are usually associated with widespread but variable airflow obstruction within the lung, that is often reversible either spontaneously or with treatment

Risk factors for development of asthma

- Genetic risk factors - atopy
 - and
- Perinatal factors- smoking, age
- Environmental interactions
 - - air : tobacco, smog, allergens, work exposure
 - - life style , nutrition, obesity ,hygiēna,GORD
 - - infection (viral)
- Drugs - aspirin,antibiotics - allergy
 - - beta blockers

Patophysiology

- is complex

- involves following components:

- airway inflammation
- intermittent airflow obstruction
- bronchial hyperresponsiveness
-

Phenotypes of asthma – divide on:

- .Age

- .Sex

- .Type of inflammatory reaction

- . Clinical picture of disease - refractory asthma

- - severe asthma

- - exercise

- .Occupational

- .Special situation: asthma in pregnancy

-

Type of inflammation

•Eosinophilic : atopic -

• non atopic -

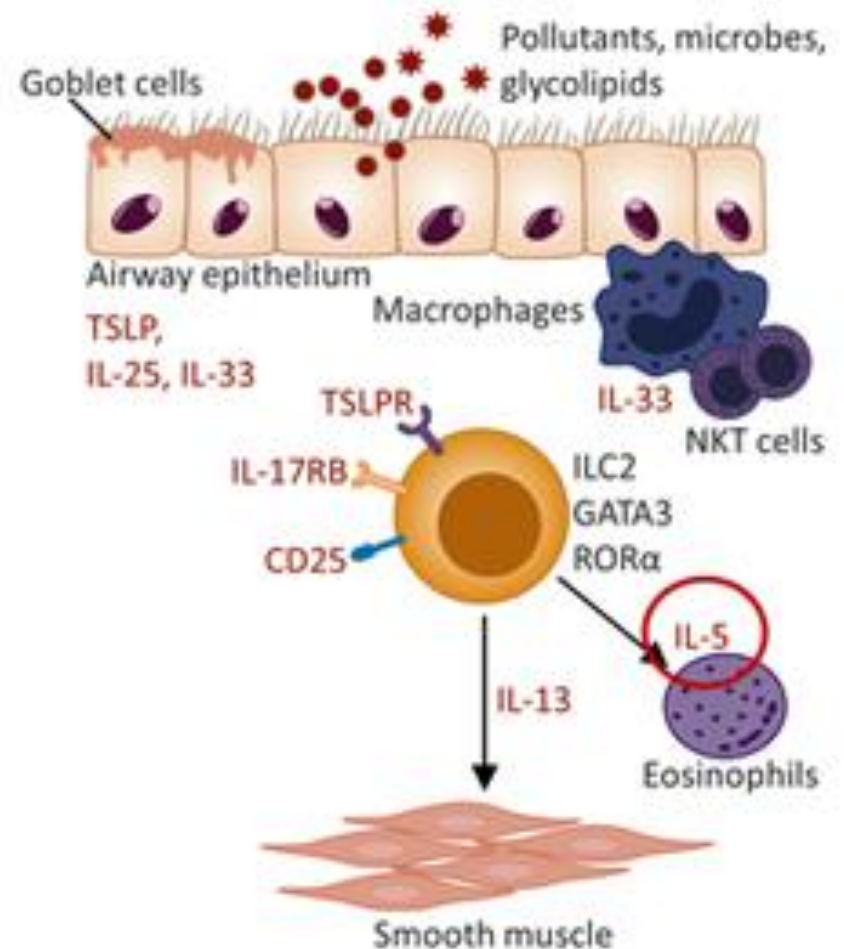
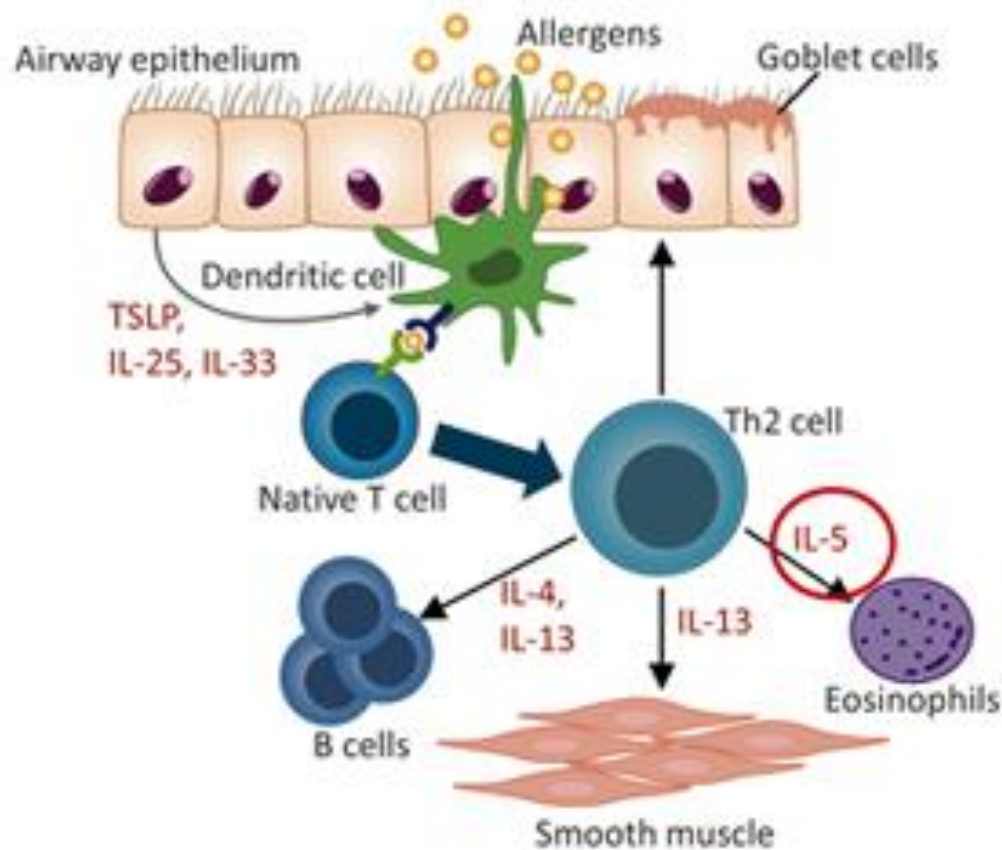
•Non eosinophilic : neutrophilic

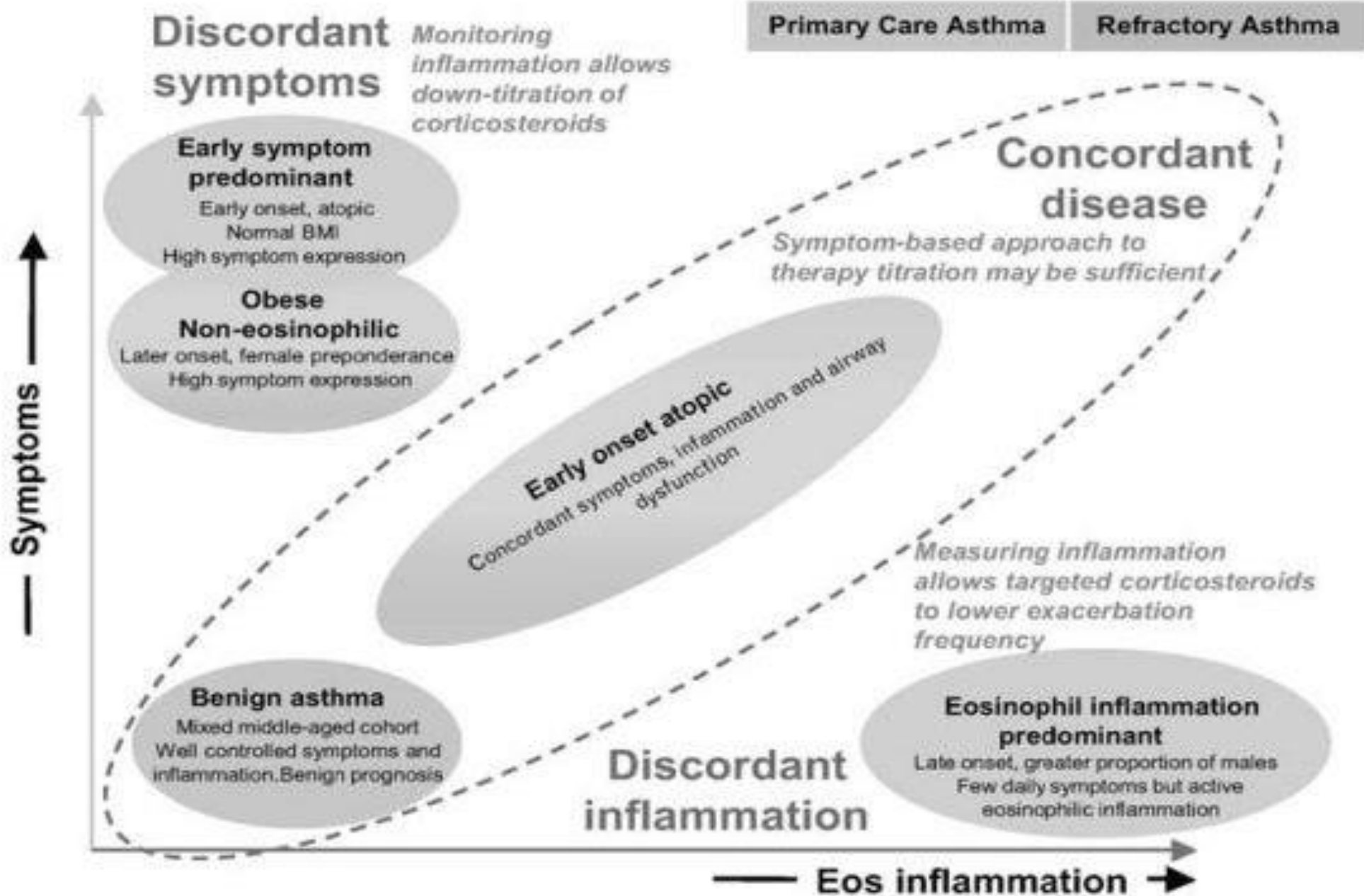
• without population of
inflammatory cells

Mechanisms of Eosinophilic Asthma

Allergic Eosinophilic Airway Inflammation

Nonallergic Eosinophilic Airway Inflammation





Clinical features

- .May be normal
- .Cough – dry
- .Shortness of breath
- .Wheeze, classically expiratory
- .Chest tightness
- .Chest deformity / hyperinflation -long standing or poor controlled asthma

Severe -life threatening asthma may have no wheeze and a silent chest , tachypnoea, tachycardia or bradycardia, cyanosis, use of accessory muscles of respiration, features of anxiety, general distress, pulsus paradoxus , exhaustion, confusion or coma.

PO₂ low to 8kPa, pCO₂ up to 5-6 kPa!!!

Main differential diagnosis in asthma

.CHOPN

.Tumors

.Upper airway obstruction

.Thromboembolic disease, PPH, Vasculitis

.Vocal cord dysfunction

.Foreign body aspiration

.Infection, CCF, ILD

.Left heart insufficiency

.Gastroesophageal reflux disease

Dg and assessment of asthma

- .History taking – family, occupation, drugs, hobbies, diseases
- .Physical examination
- .Pulmonary function tests
- .Sputum analysis

Dg and assesment of asthma

- Laboratory : blood tests, IgE, ECP, ABG,..
- FeNO
- X-ray , CT
- Examination of upper airways diseases
- Alergic screnning
- Examination of expiratory air or sputum:
leukotriens (B4,D4,C4...)

Spirometry

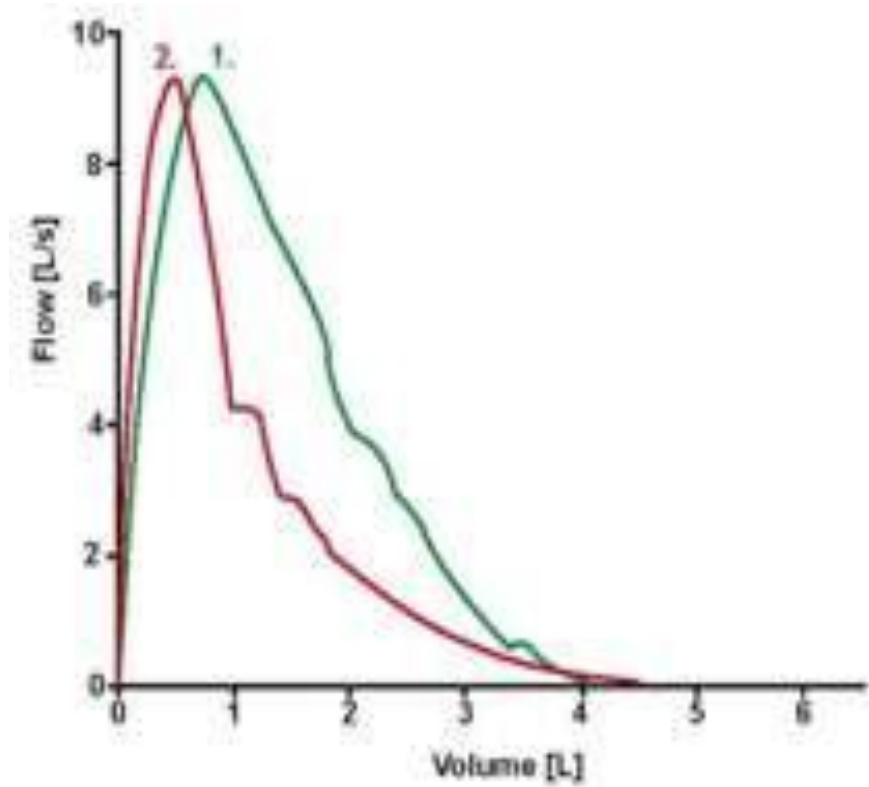
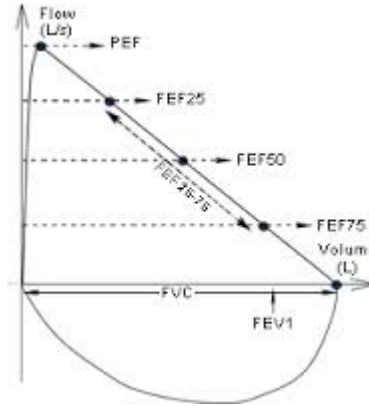


Figure 2-5. Levels of Asthma Control

Characteristic	Controlled (All of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV ₁) [‡]	Normal	< 80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	One in any week [†]

* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡ Lung function is not a reliable test for children 5 years and younger.

Table 4 – Classification of asthma severity

Severity level	Symptom frequency		FEV ₁ or PEF (% predicted)	PEF variability (%)
	Daytime	Nighttime		
Intermittent	≤ 2/week	≤ 2/month	≥ 80	< 20
Mild persistent	> 2/week but < 1/day	> 2/month	≥ 80	20 - 30
Moderate persistent	Daily	> 1/week	> 60 - < 80	> 30
Severe persistent	Continuous	Frequent	≤ 60	> 30

FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow.

From National Asthma Education and Prevention Program. 1997.¹⁷

SEVERITY COMPONENTS	INTERMITTENT	PERSISTENT ASTHMA: daily medication		
		MILD	MODERATE	SEVERE
Symptoms	Less than once a week	More than twice per week but not daily	Daily	Throughout the day
Nocturnal Symptoms	Less than twice a day per month	Three-four times per month	More than once a week but not every night	Often every night per week
Interference with activity	Brief exacerbations	Exacerbations may cause minor limitation of activity and sleep	Exacerbations more than twice a week and may cause some limitation of activity and sleep	Frequent exacerbations with marked limitation of physical activity
SABA use	≤ 2 days per week	>2 days per week, but not daily and not more than once on any day	Daily	Several times per day
Pulmonary Function Test	<ul style="list-style-type: none"> • Normal FEV₁ between exacerbations • FEV₁: >80% predicted • FEV₂/FVC: normal 	<ul style="list-style-type: none"> • FEV₁: >80% predicted • FEV₂/FVC: normal 	<ul style="list-style-type: none"> • FEV₁: >60% but <80% predicted • FEV₂/FVC: reduced 5% 	<ul style="list-style-type: none"> • FEV₁: <60% predicted • FEV₂/FVC: reduced 5%
Recommended Treatment Strategy	STEP- 1 <i>Preferred:</i> SABA PRN	STEP- 2 <i>Preferred:</i> Low-dose ICS <i>Alternative:</i> Cromolyn, LTRA, Nedocromil, or Theophylline	STEP- 3 <i>Preferred:</i> Low-dose ICS + LABA OR Medium-dose ICS <i>Alternative:</i> Low-dose ICS + either LTRA, Theophylline, or Zileuton	STEP- 4 or 5 STEP- 4 : <i>Preferred:</i> Medium-dose ICS + LABA <i>Alternative:</i> Medium-dose ICS + either LTRA, Theophylline, or Zileuton STEP- 5 : <i>Preferred:</i> High-dose ICS + LABA AND Consider Omalizumab for patients who have allergies
			Consider Oral Steroids	Consider Oral Steroids



Each Step: patient education, environmental control, and management of comorbidities.
 Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.

Quick-relief medication for all patients:

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIA) generally indicates inadequate control and the need to step up therapy.

Adapted from National Heart, Blood, and Lung Institute Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma. NIH Publication no. 08-4051,2007.

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.Tromboembolic disease

.Vasculitis

.Vocal cord dysfunction

.Foreign body aspiration

.Infection,CCF

.Left heart insuficiency , ILD

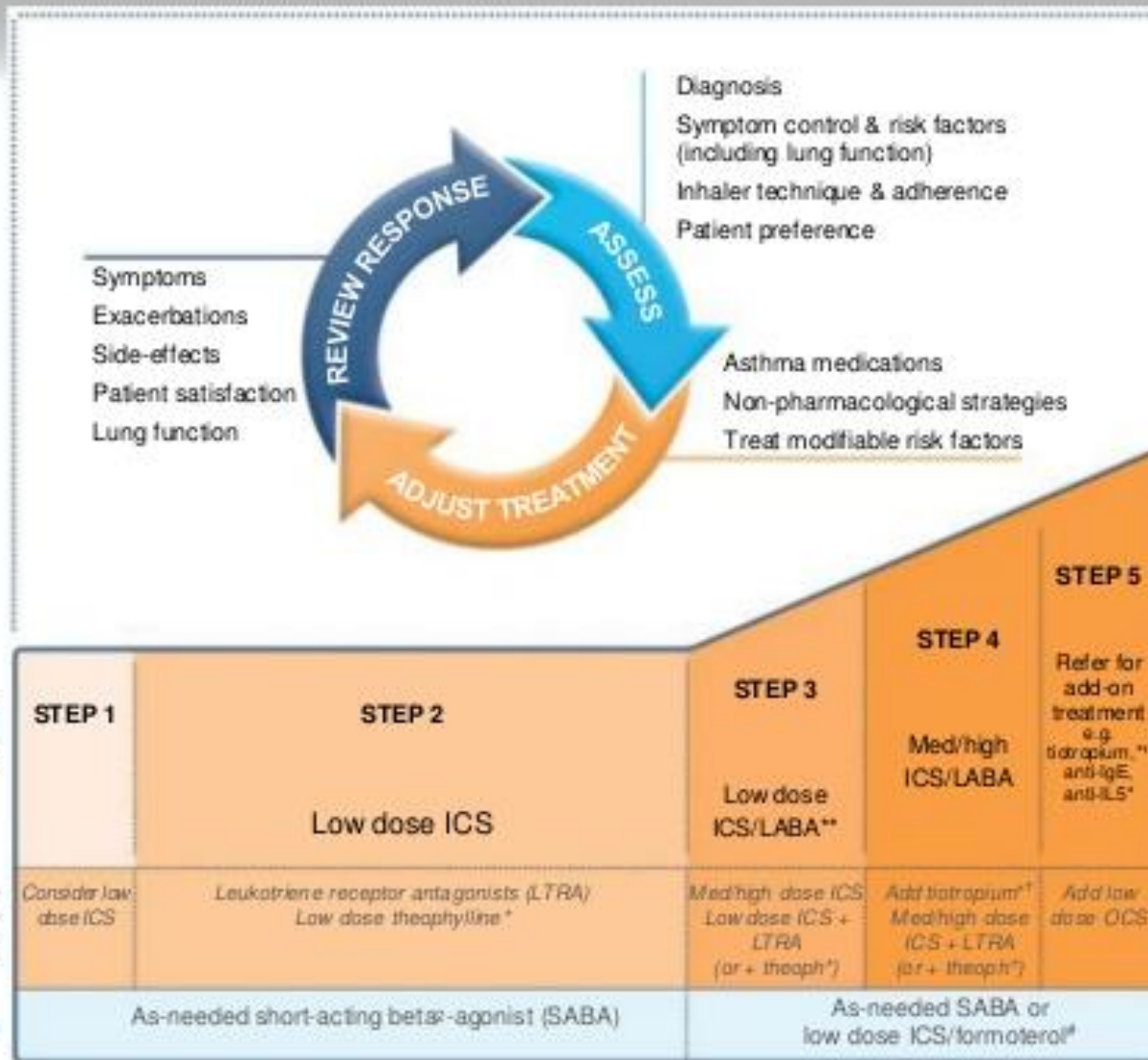
.Gastroesophageal reflux disease

therapy



- Preventive - corticosteroids
- - antileukotriens
- - anti IgE, anti IL-5,4,13
- - specific immunotherapy
- Control agents – LABA, LAMA
- -long acting theophylline
- Relievers - SABA, SAMA, short acting theophylline
-

Stepwise management - pharmacotherapy



*Not for children <12 years
 **For children 6-11 years, the preferred Step 3 treatment is medium dose ICS
 †For patients prescribed BDP/formoterol or BUD/formoterol maintenance and reliever therapy
 ‡ Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations

Pharmacologic management

•Control agent :inhaled or systematic steroids

- leucotriens modifiers
- inhaled cromones
- long acting bronchodilatators
- theophylline-long acting
- anti IgE
- specific immunoterapy

•Relief agent: short acting bronchodilatators

- systemic steroids

Oropharyngeal candidiasis

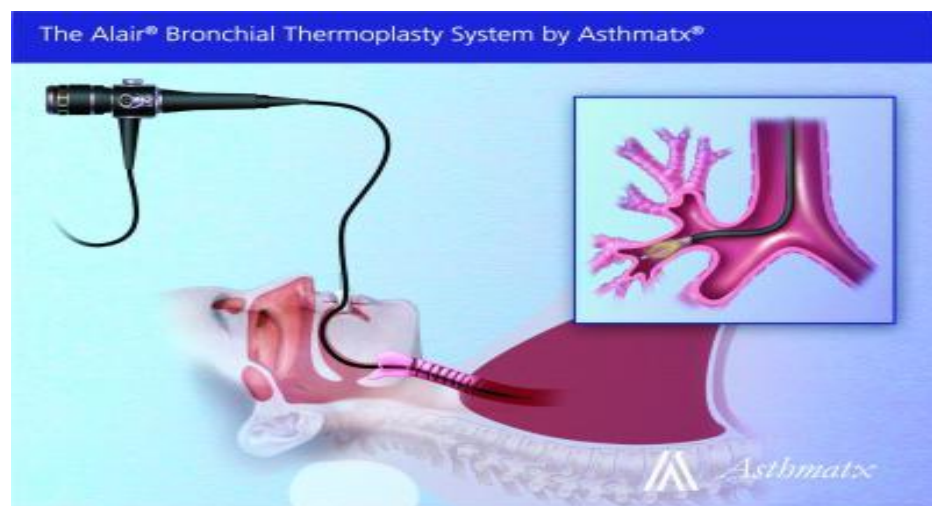
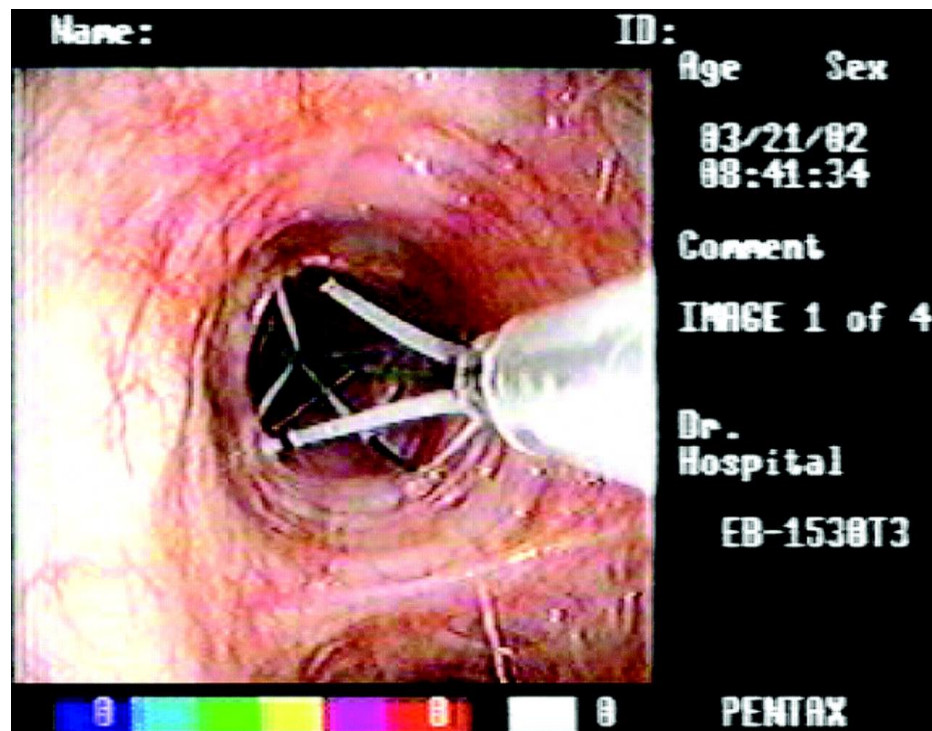
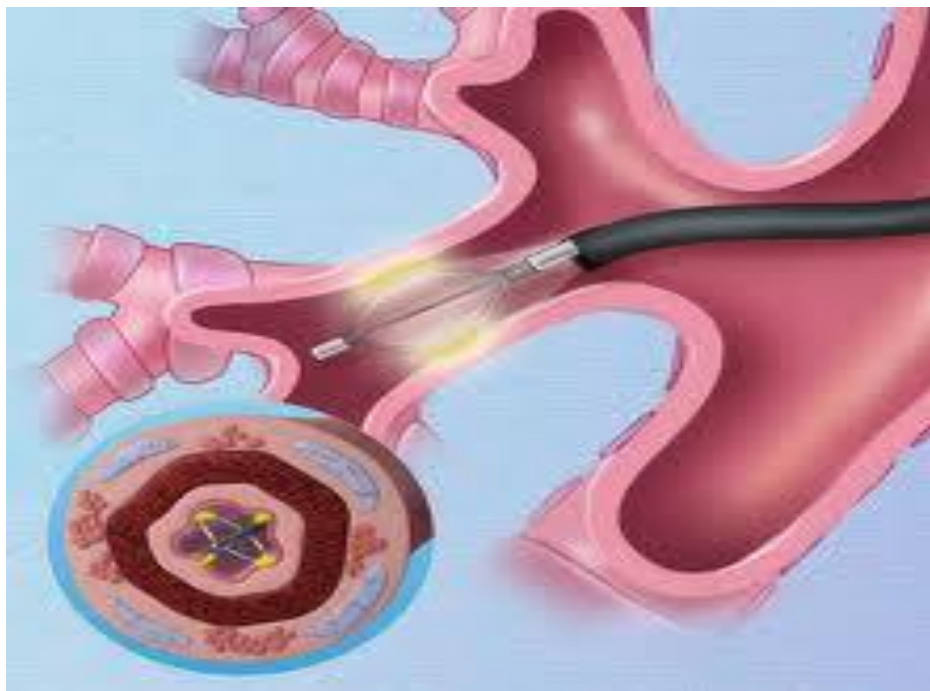


Non pharmacologic management

- .Allergen avoidance
- .No smoke !
- .Dietary
- .Weight reduction
- .Exercise -breathing exercise
- .Patient education
- .Bronchial termoplasty

Bronchiální termoplastika

FEV1 nad 60%, příprava kortikoidy



In hospital treatment of acute asthma

- B2 agonists - nebulised 5-10 mg/h
- Anticholinergic drug- nebulised
- Steroid IV or oral
- MgSO₄
- Theophylline -IV aminophyllin 5mg/kg
- Antibiotics -if infection
- Rehydration
- Oxygen

Intubation-decision

- .Progressive exhaustion
- .Respiratory arrest
- .Decreased level of consciousness
- .Persistent respiratory acidosis (pH low7,2)
- .Hypoxemia (SATS low 90%)
- .Hypercapnia is not indication for intubation ?- studies shows improvment of aggresive use of bronchodilatators

Why we are not successful in treatment ?

Tabulka 7: Airesmog [11]

Airesmog		
A	Allergy + Adherence to the therapy	Adherence
I	Infection + Inflammation	Infekce
R	Rhinitis + Rhinosinusitis	Rhinosinusitida a polypy
E	Exercise + Error in diagnosis	Event. jiné diagnózy
S	Smoking + pSychogenic factors	pSyché a kouření
M	Medications	Medikace (NSAID, ACE-I, betablokátory)
O	Occupational exposures, Obezity + OSA	Obezita, OSA a profese
G	GER	GER

Posouzení přítomnosti alergie a typu zánětu je základem navrhované klasifikace, proto zde v české verzi AIRESMOGu neuváděno.

Charcot-Robin-Leyden Crystals (Lysophospholipase From Eosinophils)



von Leyden EV. *Tagbl Vers Deutsche Naturl Arzte*. 1871;22:24.

Curschmann's Spirals

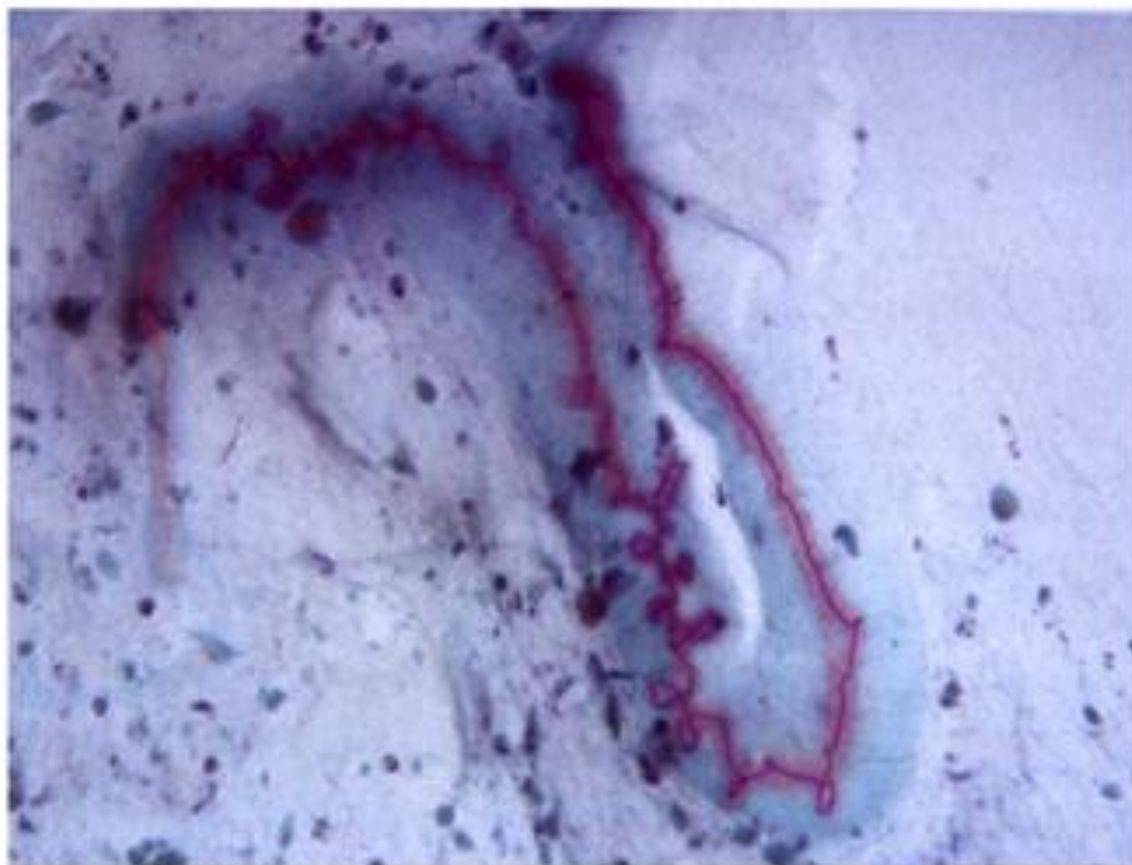


Image courtesy of Christian Virchow, FRCP, FCCP, FRCR.



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Sputum Eosinophils

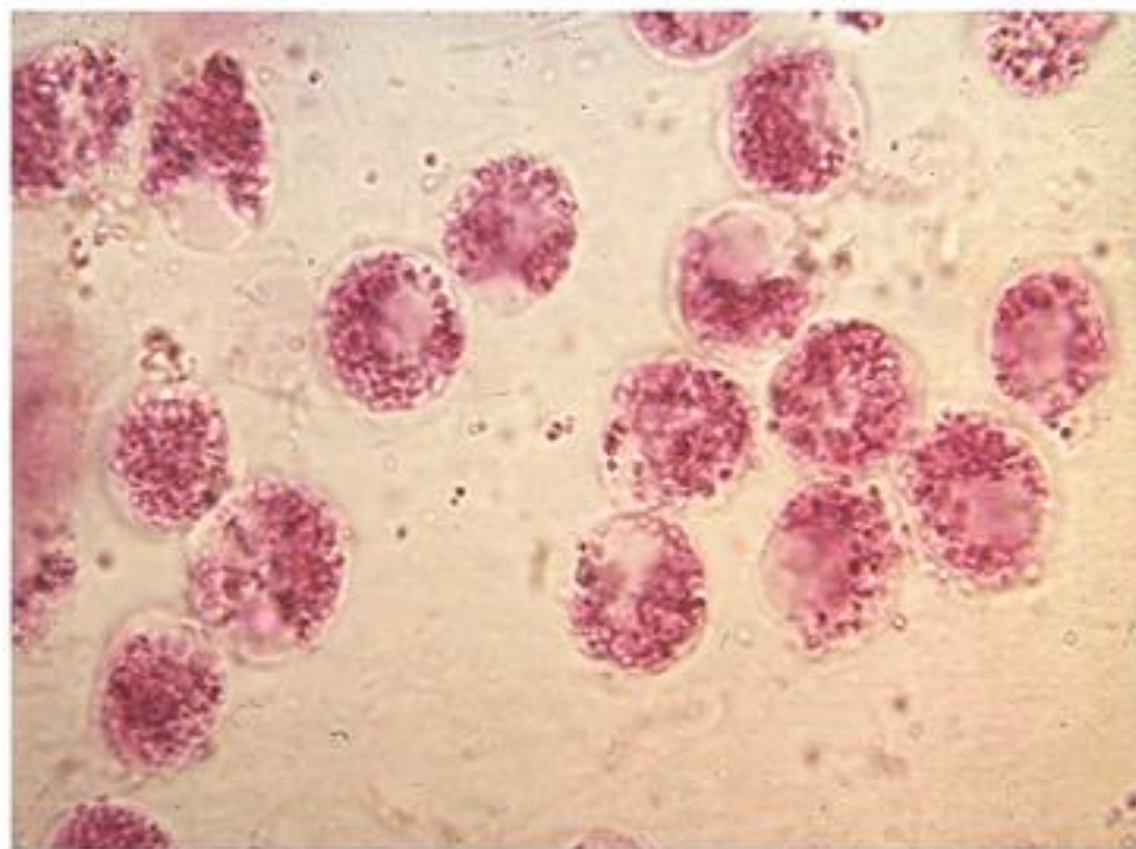


Image courtesy of Christian Virchow, FRCP, FCCP, FAAAAI.

Add-On Treatment to Discuss in Step 5

Therapies that may be proposed include:

- Add-on tiotropium for patients ≥ 12 years of age with history of exacerbations
- Add-on anti-IgE (omalizumab) for patients with severe allergic asthma
- Add-on anti-IL-5 (mepolizumab [SC] or reslizumab [IV]) for severe eosinophilic asthma in patients ≥ 12 years of age

Other add-on treatment options at step 5 include:

- Sputum-guided treatment
- Add-on low-dose OCS (≤ 7.5 mg/day prednisone equivalent)

Anticytokines Against IL-5

3 anticytokines against IL-5 are currently being developed, and 2 are licensed in some countries:

Reslizumab ^(a)	Mepolizumab ^(b)	Benralizumab ^(c)
Ligand blockade	Ligand blockade	Receptor blockade
Anti-IL-5 mAb	Anti-IL-5 mAb	Anti-IL-5R α mAb
Humanized IgG	Humanized IgG	Humanized IgG

a. Castro M, et al. *Lancet Respir Med*. 2015;3:355-366.

b. Abonia JP, et al. *Expert Rev Clin Immunol*. 2011;7:411-417.

c. Ghazi A, et al. *Expert Opin Biol Ther*. 2012;12:113-118.

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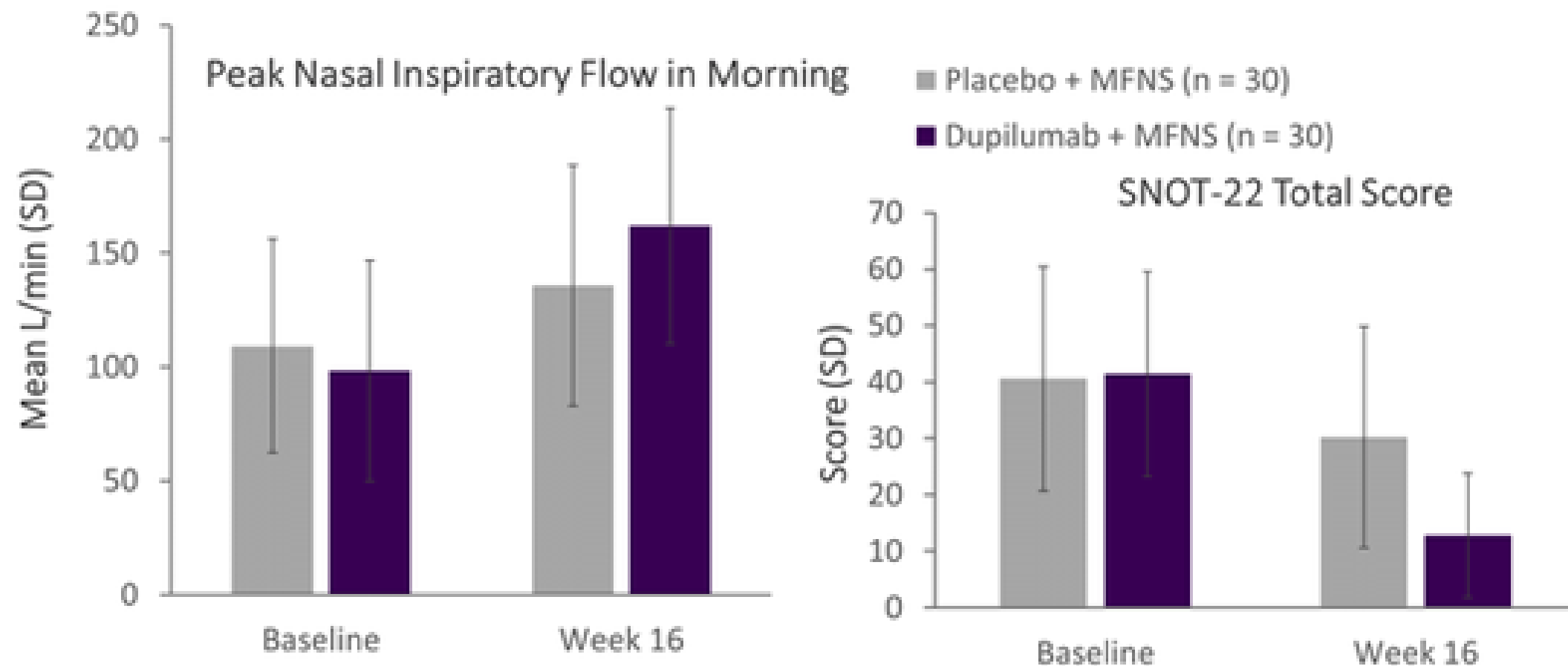
Reslizumab ^[a]	Mepolizumab ^[b]	Benralizumab ^[c]
3 mg/kg BW every 4 weeks	100 mg every 4 weeks	30 mg every 8 weeks
IV	SC	SC
≥ 400 EOS/mL	≥ 150 EOS/mL	≥ 300 EOS/mL

a. Castro M, et al. *Lancet Respir Med*. 2015; 3:355-366.

b. Abonia JP, et al. *Expert Rev Clin Immunol*. 2011;7:411-417.

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Effect of SC Dupilumab on Nasal Polyp Burden in Patients With Chronic Sinusitis and Nasal Polyposis



Clinical Trials: Persistence of Response to Omalizumab Can Be Predicted at 16 Weeks

N=272

Persistence rates:
Response:
91.4%
Nonresponse:
62.0%



*Response = excellent improvement of asthma; nonresponse = moderate, poor, or worsening asthma
Bousquet J, et al. *Allergy*. 2011;66:671-678.