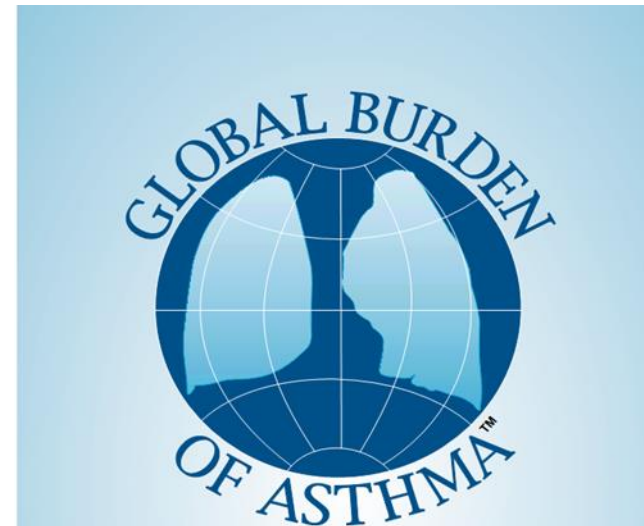


BRONCHIAL ASTHMA IN CHILDREN

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university professor



LESSON PLAN

1. Background
2. Definition
3. Epidemiology
4. Risk factors, triggers, pathogenesis
5. Clinical signs
6. Diagnosis. Asthma Predictive index
7. Differential diagnosis
8. Asthma classification
9. Asthma therapy
 - 9.1. The “reliever” therapy, according to child age
 - 9.2. The “controller” therapy, according to child age
 - 9.3. Allergen immunotherapy
10. Prognosis
11. Prevention
12. Asthma education
13. References

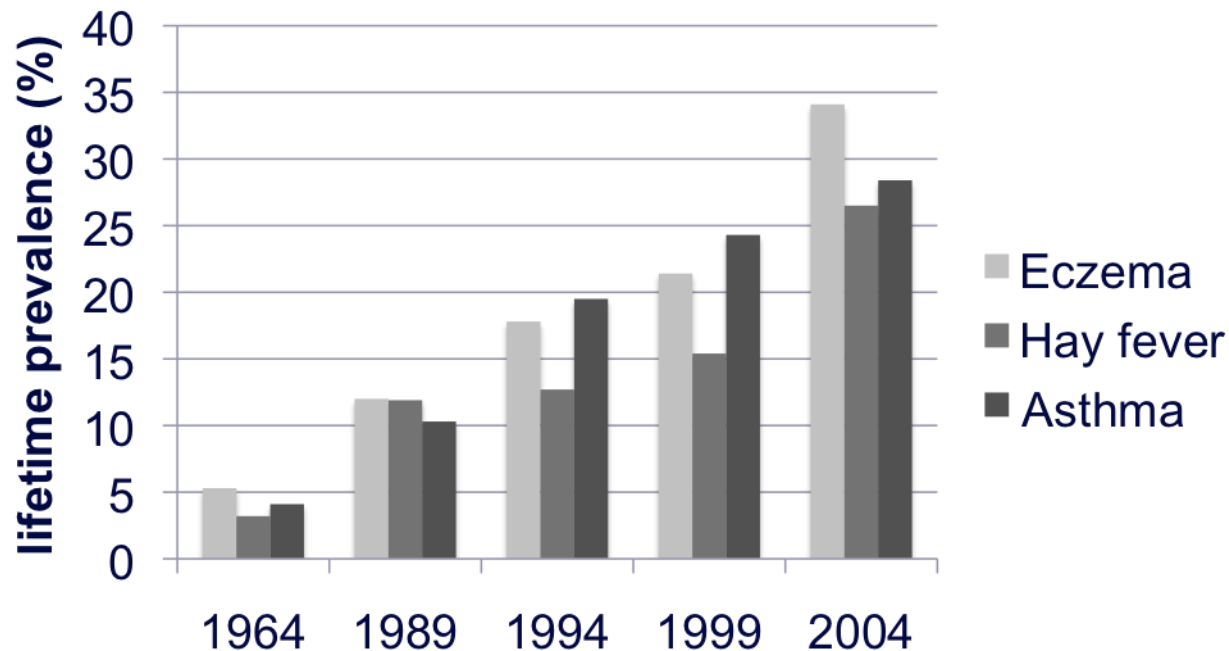
1. BACKGROUND

- Asthma is one of the most common chronic diseases worldwide with an estimated 300 million affected individuals
- Expected by 2025: 100 m. additional
- Prevalence is increasing in many countries, especially in children
- Considerable economic costs
- The prevalence is 8-10 times higher in developed countries than in developing countries.



Increasing continuously of the patients with allergic disease in developed countries

Period 1964 – 2004 children 9-12 y.o. (Aberdin)



from **McNeill et al.**, Pediatric and Perinatal Epidemiology 2009;**23**: 506-512

Burden of asthma

- Health care expenditure on asthma is very high
 - Developed economies might expect to spend 1-2 % of total health care expenditures on asthma.
 - Developing economies likely to face increased demand due to increasing prevalence of asthma
 - Poorly controlled asthma is expensive
 - However, investment in prevention medication is likely to yield cost savings in emergency care

2. DEFINITION

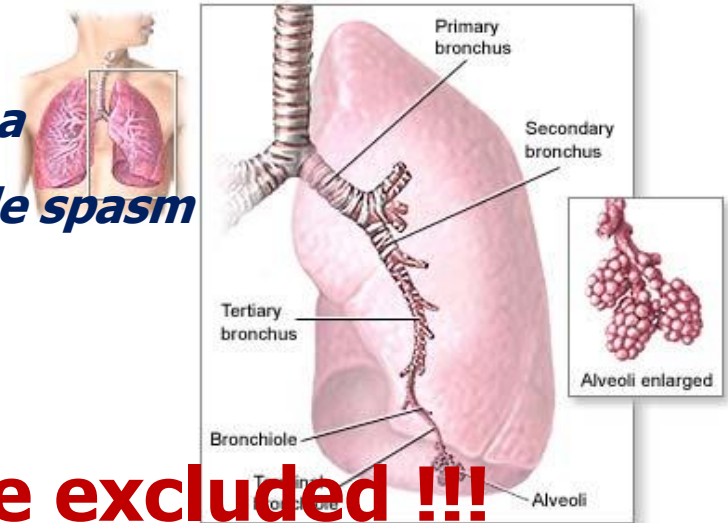
Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation

with intermittent lower-airway obstruction, that is reversible either spontaneously or as the result of treatment

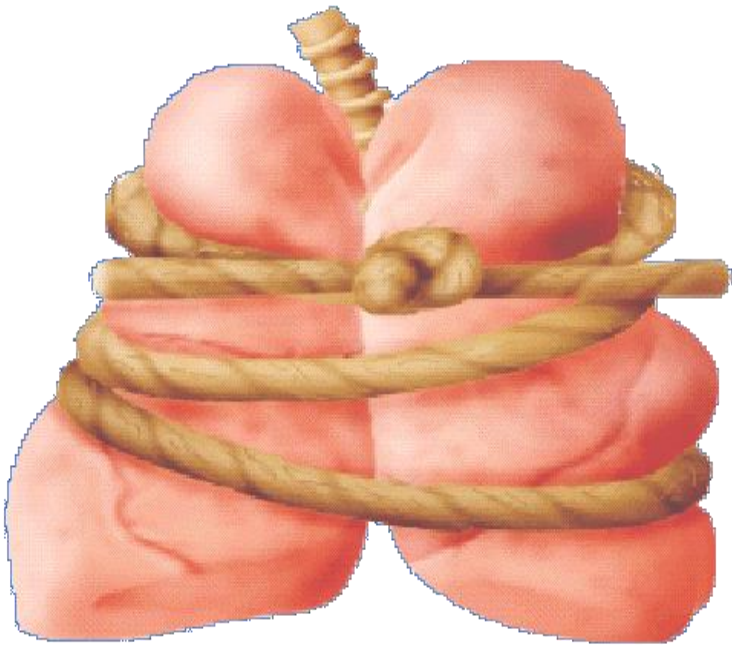
- *Inflammation and edema*
- *Bronchial smooth-muscle spasm*
- *Mucous plugging*

AND

Alternative diagnoses are excluded !!!

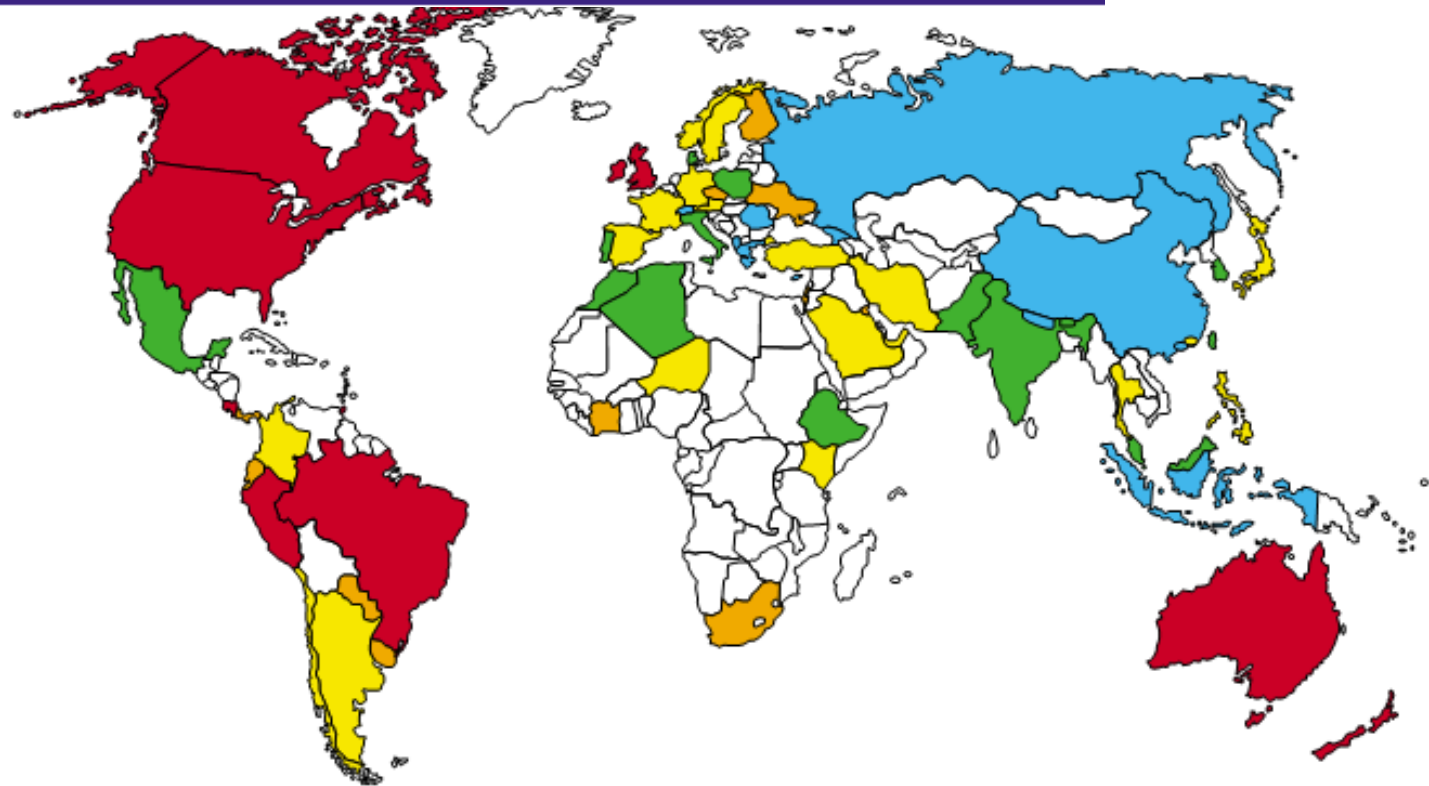


3. EPIDEMIOLOGY

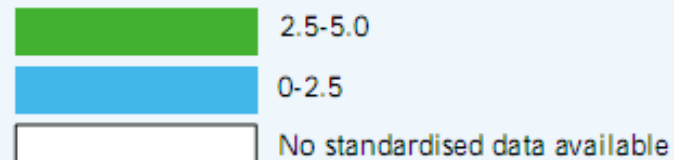
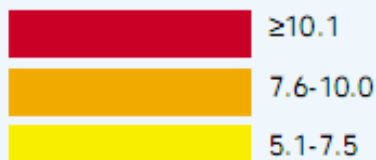


Asthma is a major cause of school and work absence. Annually, the World Health Organization (WHO) has estimated that 15 million disability-adjusted life-years are lost and 250,000 asthma deaths are reported worldwide.¹ (2008).

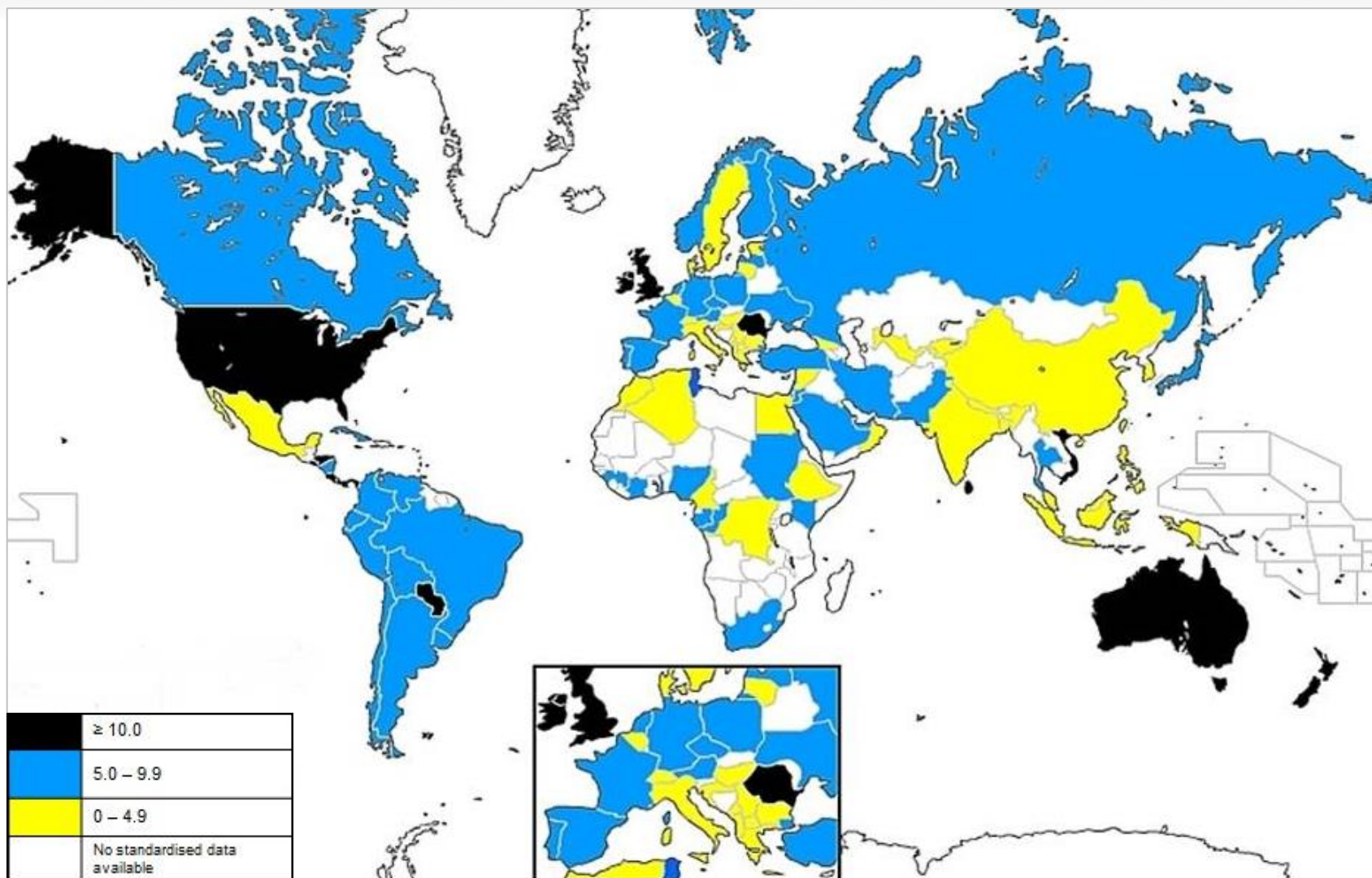
World Map of the Prevalence of Clinical Asthma



Proportion of population (%)*

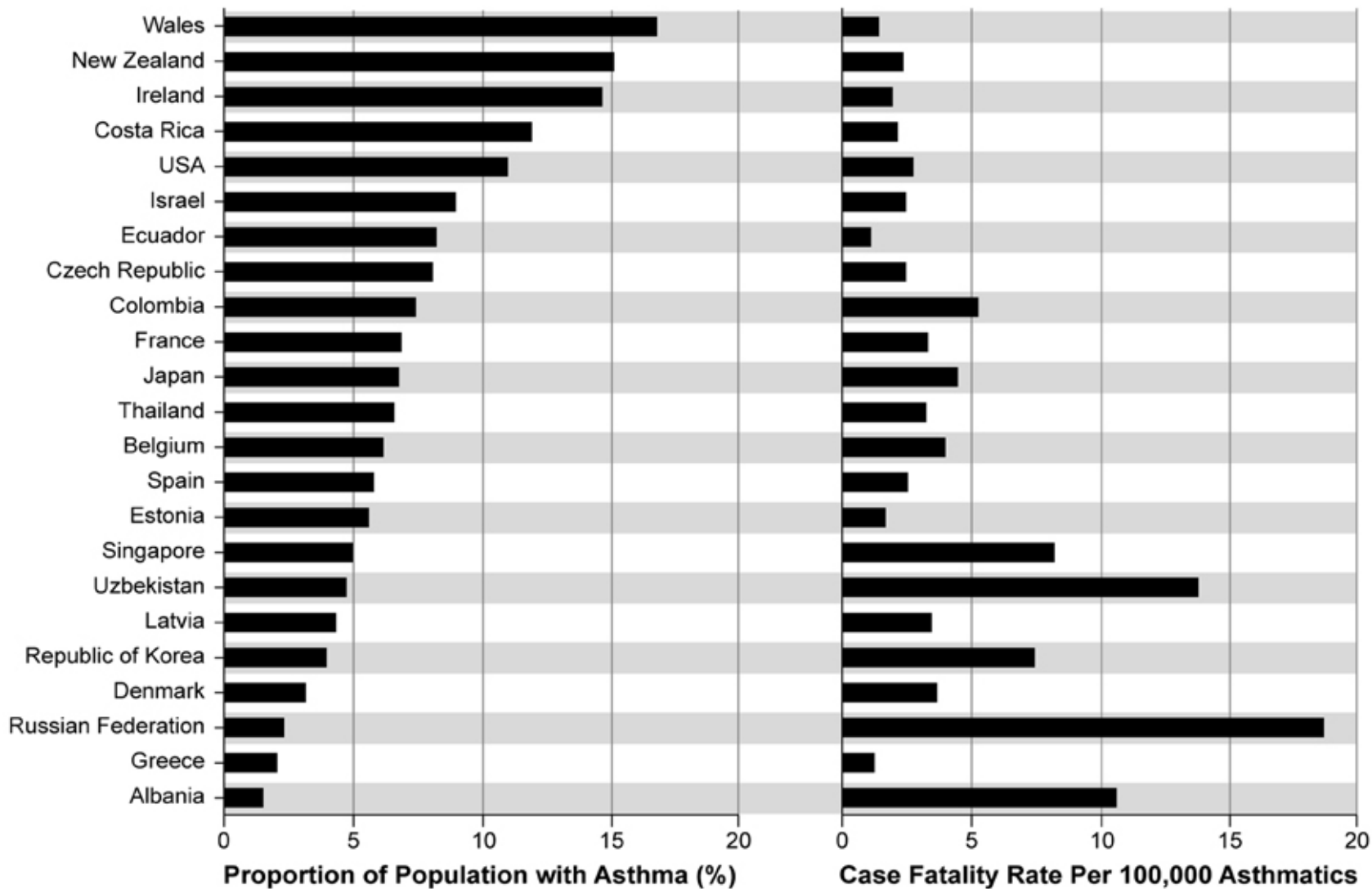


Prevalence of asthma in children aged 13-14 years





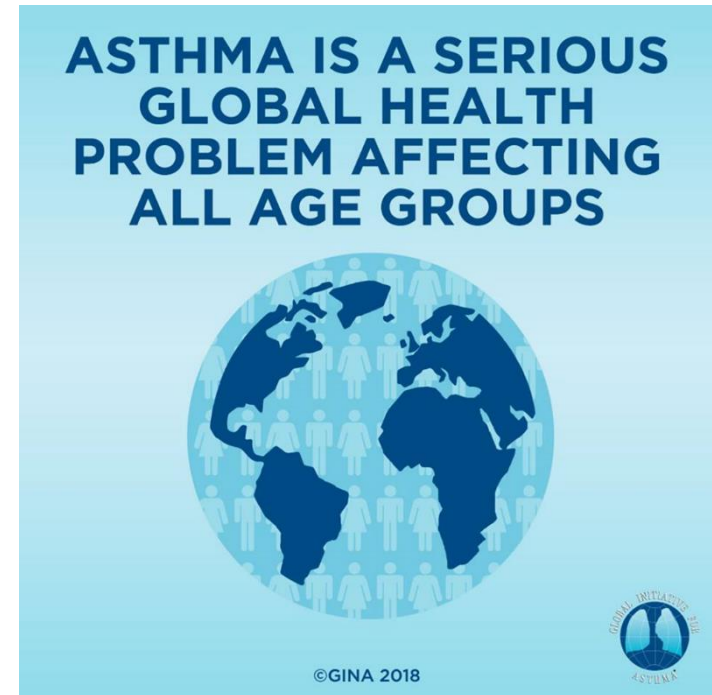
Asthma: Prevalence, Mortality



Source: Masoli M et al. Allergy 2004

Incidence and prevalence differ from country to country

- New Zealand about 30% (<5y.o.)
- Australia 25%
- UK 10-15 %
- France 7-10%
- Russia – 0,66% (MS RF 2002r.)
 - Moscow-1.1% (2016 r)
 - Sanct-Peterburg 1% (2016 r)
- Ucraina 0,5%
- Moldova 0,1%
 - 2015:1200-1500



There is the problem with early detection (diagnosis) of asthma in childhood

Asthma – the disease started in early age

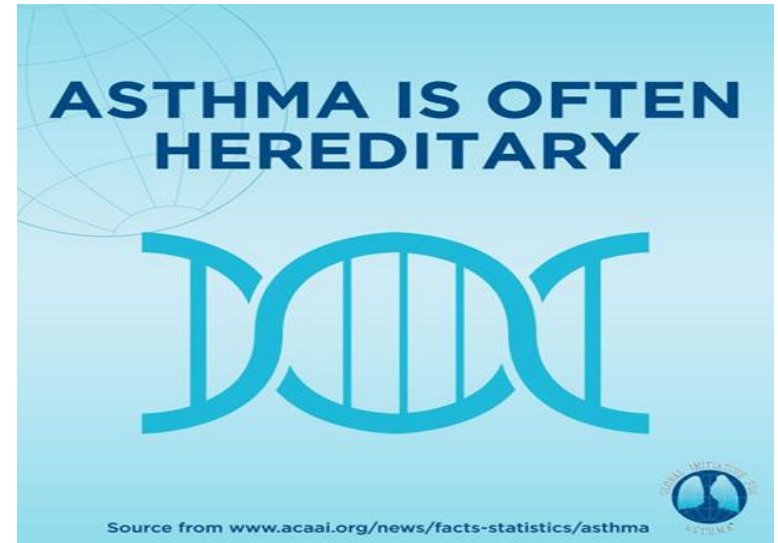
- In most children (about 50-80%) , asthma develops before age 5 years, and, in more than half, asthma develops before age 3 years.



4. RISK FACTORS, TRIGGERS, PATHOGENESIS

Host factors –

- Genetic
 1. Genes predisposing to atopy
 2. Genes predisposing to airway hyper responsiveness
- Obesity
- Sex There are gender differences. *Before puberty, the prevalence of asthma is 3 times higher in boys than in girls. During adolescence, the prevalence is equal among males and females. Adult-onset asthma is more common in women than in men.*

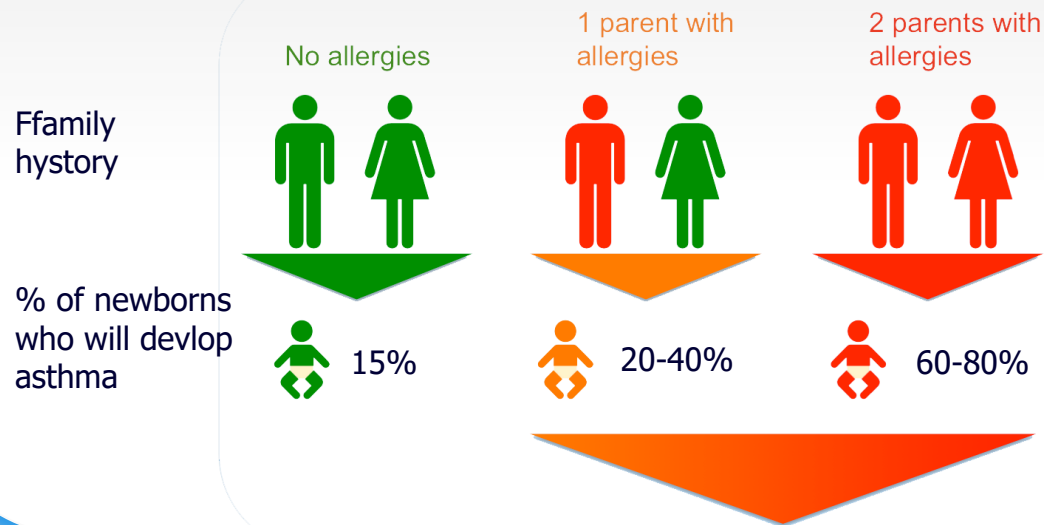


Newborn with family history of asthma has high risk to develop disease

► In Europe each 3-d child has high risk to develop asthma



FH+ - these newborns need preventive measures



Triggers, allergens –

- Indoor – Domestic mites, furred animals (dogs, cats, mice), cockroach allergens, fungi, molds, yeasts.
- Outdoor – Pollens, fungi, molds, yeasts.
- Infections (predominantly viral)
- Occupational sensitizers
- Tobacco smoke
- Passive smoking
- Active smoking
- Indoor/Outdoor air pollution
- Diet- food



Triggers

Non specific factors

- Psihogenic
- Exercises induced
- Meteo pathic
- Postnatal bisphenol A (BPA) exposure in the first years of a child's life is associated with significantly increased risk for wheeze and asthma. Feeding bottles, sippy cups, or other containers designed for infants may contain it.

Other factors

1. **Morfofunctional peculiarities of airway predisposing to obstruction:**

- Smooth muscles of bronchi are immature
- Hyperplasia of mucous glands with hyper secretion
- Predominating of colinergic system
- The pulmonary immune system is immature

2. **Perinatal and postnatal antecedents**

Assisted ventilation

Amniotic liquid aspiration

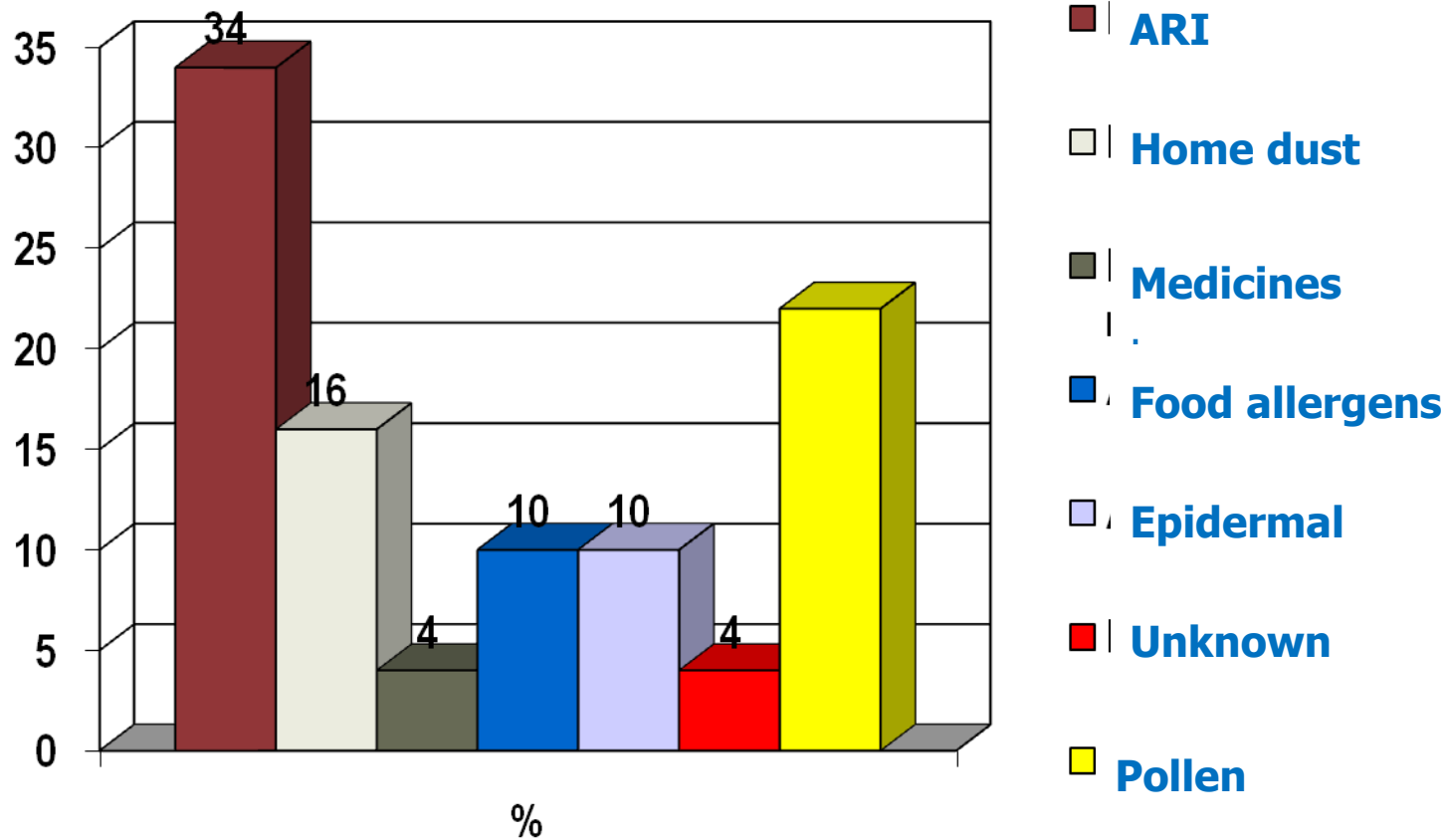
Bronhopulmonar dysplasia

3. **Environment pollution, cigarette smoking**

4. **Gastroesofagal reflux (20-30%)**

5. **Socioeconomic problems**

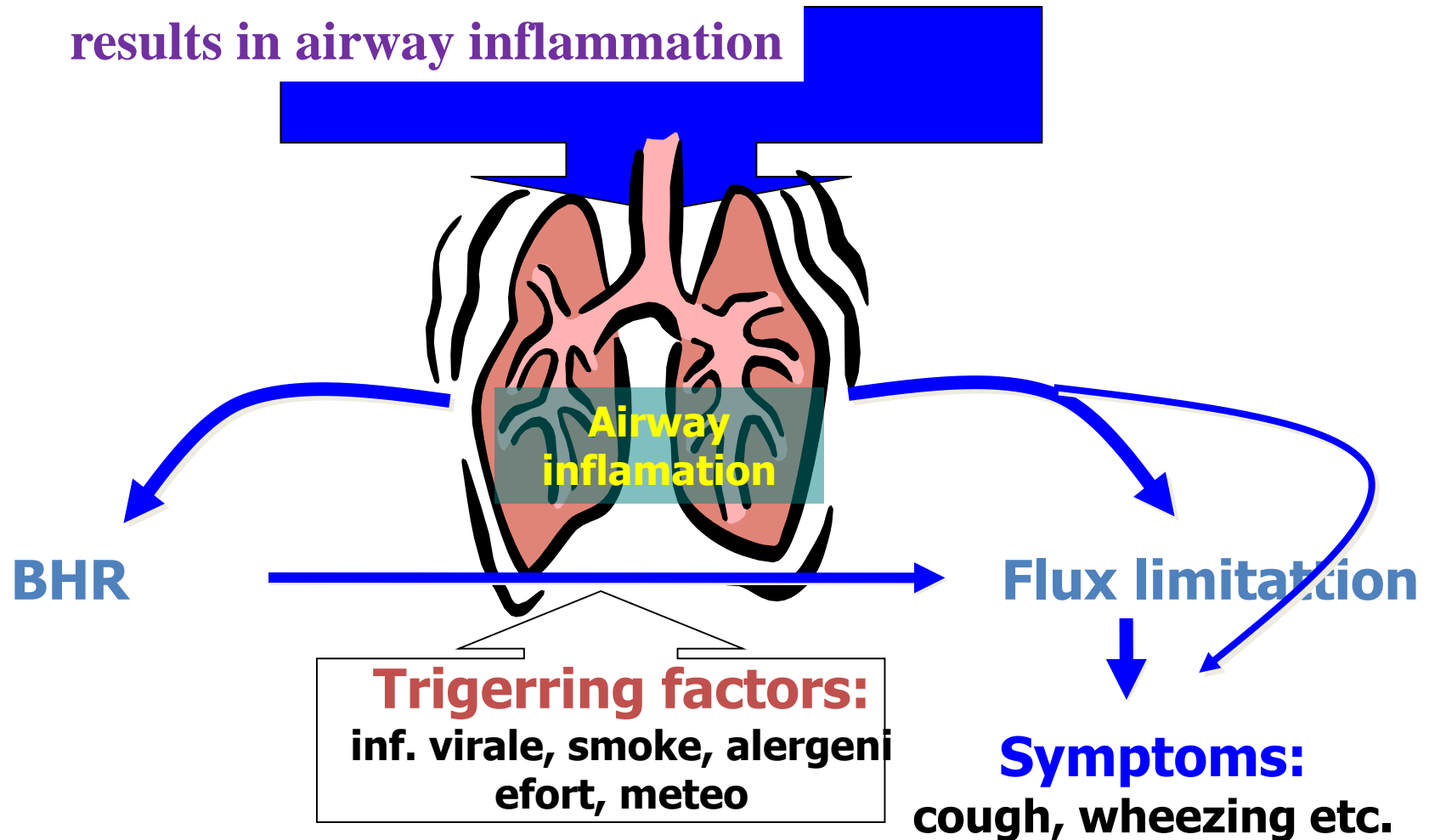
Comparative data about cause of exacerbation in BA collected from hystory (%)



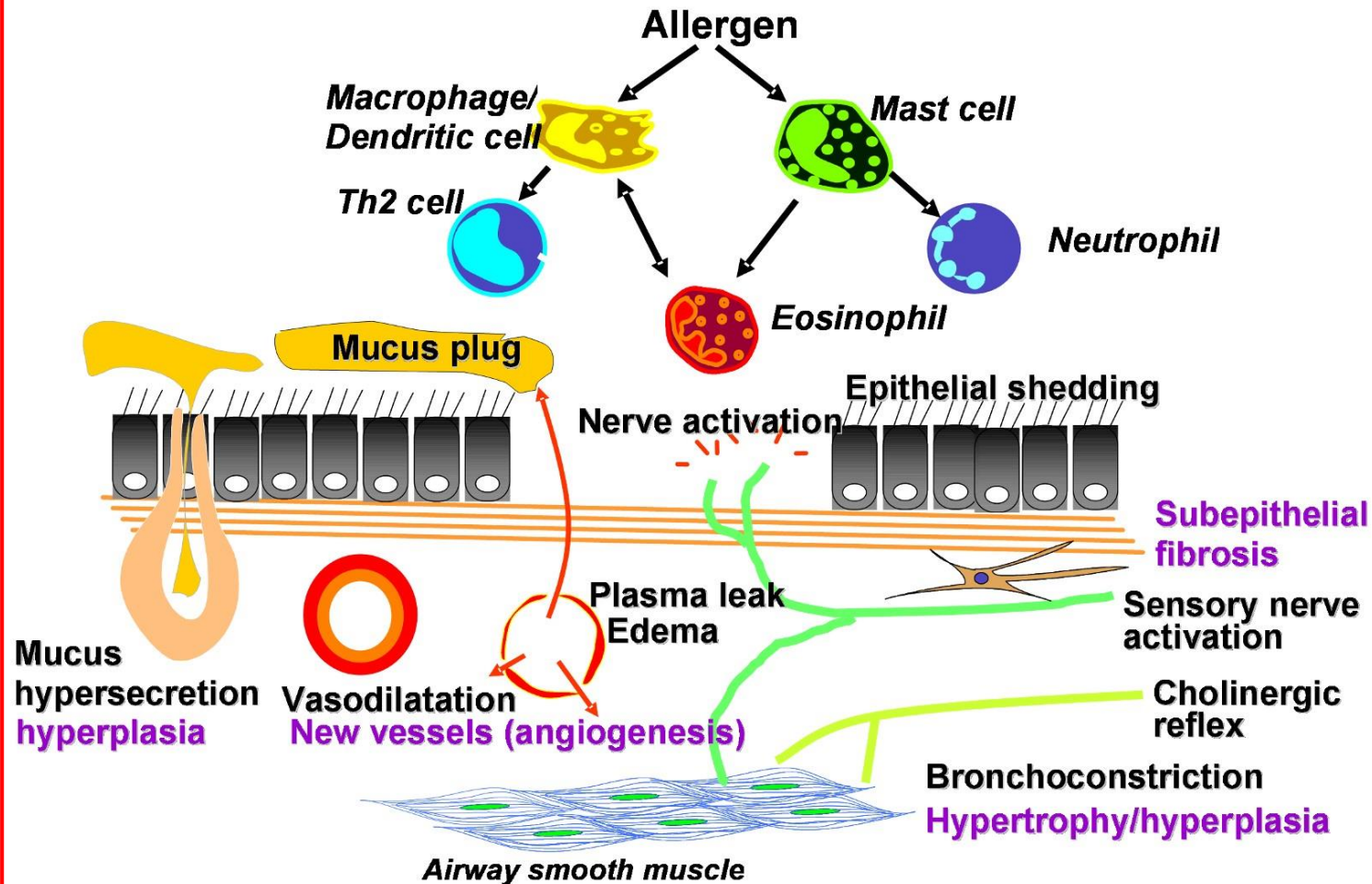
PATHOPHYSIOLOGY

- Asthma –multifactorial disease
- Interactions between genetic and environment factors

results in airway inflammation



Asthma Inflammation – Cells and Mediators



Asthma Inflammation

Inflammatory cells

Mast cells
Eosinophils
Th2 cells
Basophils
Neutrophils
Platelets

Structural cells

Epithelial cells
Sm muscle cells
Endothelial cells
Fibroblast
Nerves



Mediators

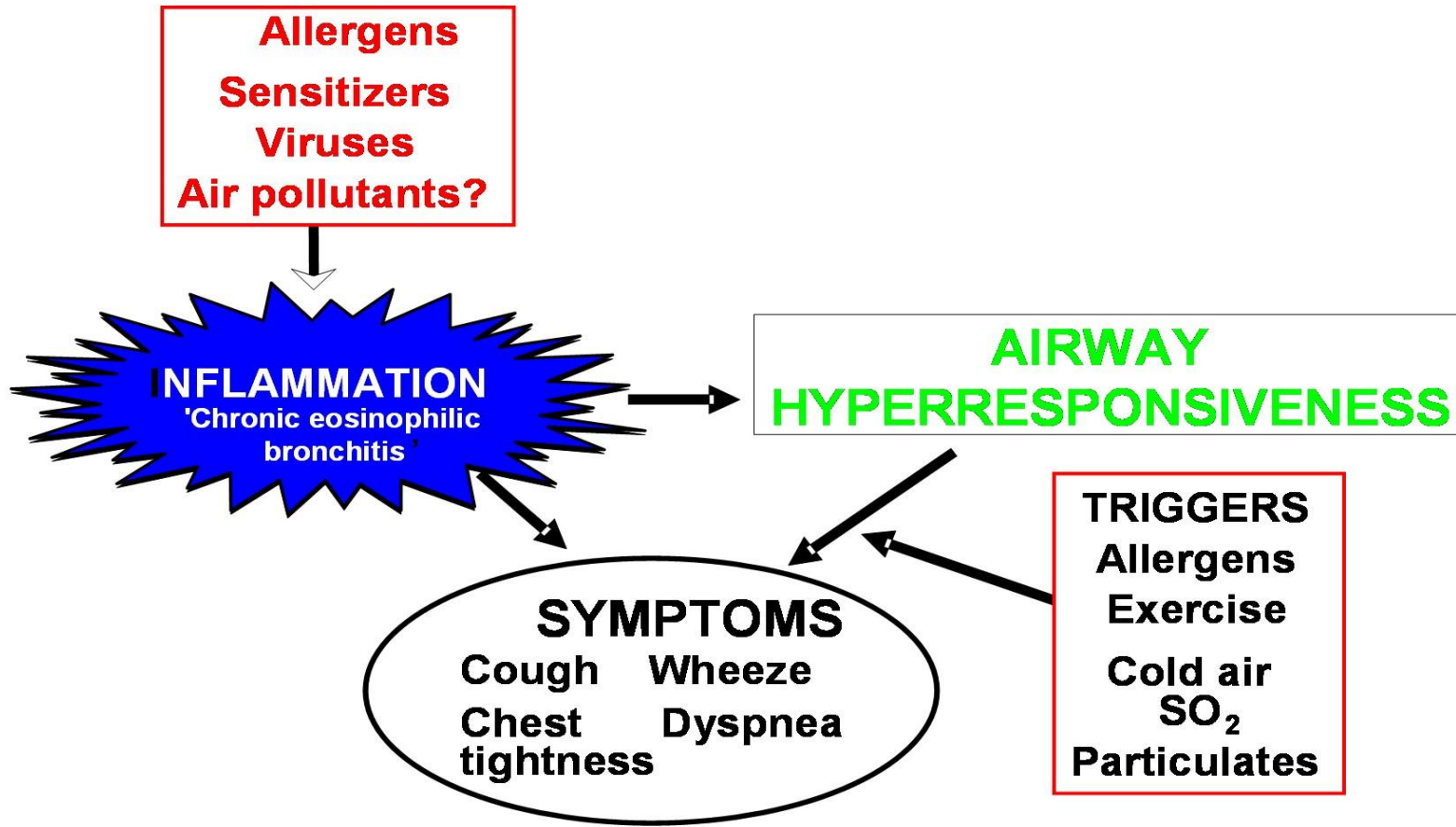
Histamine
Leukotrienes
Prostanoids
PAF
Kinins
Adenosine
Endothelins
Nitric oxide
Cytokines
Chemokines
Growth factors



Effects

Bronchospasm
Plasma exudation
Mucus secretion
AHR
Structural changes

Mechanism – Asthma Inflammation



Airway inflammation

in asthma may represent a loss of normal balance between two "opposing" populations of **T helper (Th) lymphocytes**.

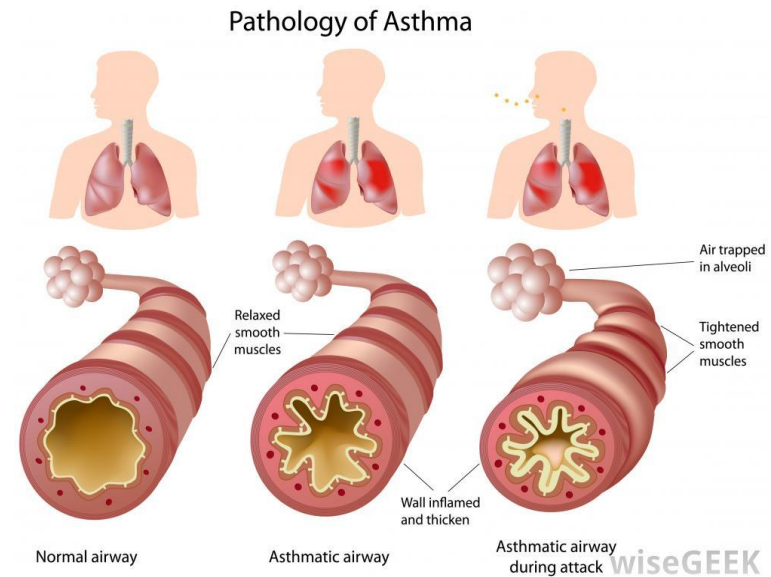
Two types of Th lymphocytes have been characterized: **Th1 and Th2**.

Th1 cells produce **interleukin (IL)-2** and **interferon- α (IFN- α)**, which are critical in cellular defense mechanisms in response to infection.

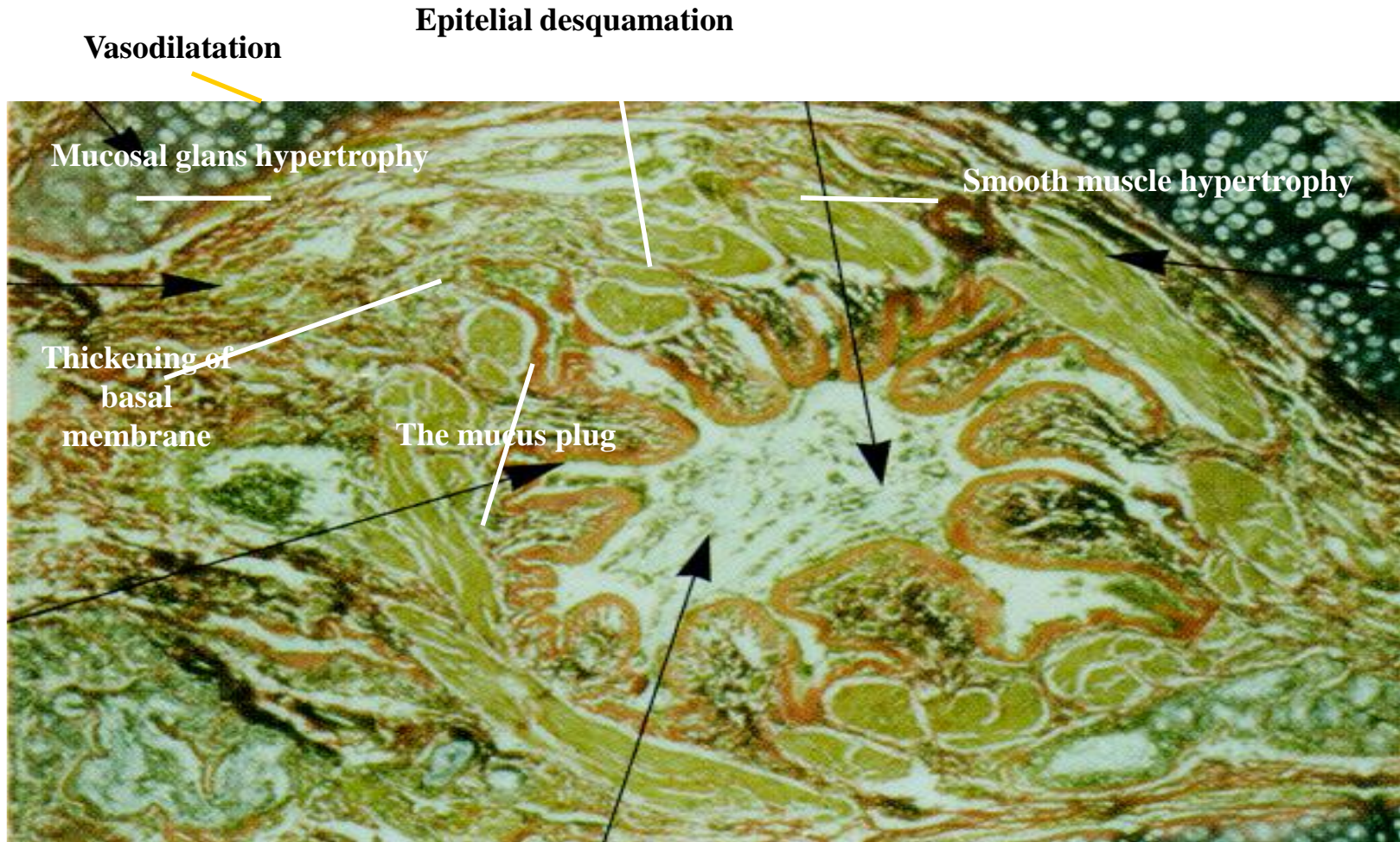
Th2, in contrast, generates a family of cytokines (**interleukin-4 [IL-4], IL-5, IL-6, IL-9, and IL-13**) that can mediate allergic inflammation.

PATHOPHYSIOLOGY

- **Bronchospasm,**
- **Mucosal edema**
- **Mucus plugs (hyper secretion)**
- **Airway inflammation - the main pathophysiologic mechanism**



MORFOPATHOLOGIC MODIFICATION ÎN SEVERE ASTHMA



5. CLINICAL SIGNS

- Recurrent Wheeze
- Recurrent Cough
- Recurrent Breathlessness
- Activity Induced Cough/Wheeze
- Nocturnal Cough/Breathlessness
- Tightness Of Chest

The asymptomatic period alternate with symptomatic

Wheezing

- A musical, high-pitched, whistling sound produced by airflow turbulence is one of the most common symptoms. The wheezing usually occurs during exhalation.
- In the mildest form, wheezing is only end expiratory.
- As severity increases, the wheeze lasts throughout expiration.
- In a more severe asthmatic episode, wheezing is also present during inspiration.
 - *Thus, wheezing is not necessary for the diagnosis of asthma. Furthermore, wheezing can be associated with other causes of airway obstruction, such as cystic fibrosis and heart failure.*

Coughing and chest tightness

- Cough may be the only symptom of asthma, especially in cases of exercise-induced or nocturnal asthma.
- Children with nocturnal asthma tend to cough after midnight, during the early hours of morning.
- Usually, the cough is nonproductive and nonparoxysmal.
- In addition, coughing may be present with wheezing.
 - *A history of tightness or pain in the chest may be present with or without other symptoms of asthma, especially in exercise-induced or nocturnal asthma.*

Typical features of Asthma

- Afebrile episodes
- Personal atopy
- Family history of atopy or asthma
- Exercise /Activity induced symptoms
- History of triggers
- Seasonal exacerbations
- Relief with bronchodilators

Other nonspecific symptoms

- Infants or young children may have:
 - a history of recurrent bronchitis, bronchiolitis, or pneumonia;
 - a persistent cough with colds;
 - and/or recurrent croup or chest rattling.

Most children with chronic or recurrent bronchitis have asthma.

6. DIAGNOSIS

- History Taking (ASK)
- Careful Physical Examination (LOOK)
- Investigations (PERFORM) –
 - **Pulmonary function tests (PFTs) above 5 years only** (spirometry, peakfluorometry)
 - **Fraction of exhaled nitric oxide (FeNO) test**
 - **Radiography:**
 - **Allergy testing: Eosinophil counting (in blood, bronchi, mucosa)**
 - **Histologic evaluation of the airways**

History taking (Ask)

Has the child had an attack or recurrent episode of wheezing (high-pitched whistling sounds when breathing out)?

Does the child have a troublesome cough which is particularly worse at night or on waking?

Is the child awakened by coughing or difficult breathing?

Does the child cough or wheeze after physical activity (like games and exercise) or excessive crying?

Does the child experience breathing problems during a particular season?

Questions about the development and treatment of the patient's disease should touch on the following:

- Age at onset and diagnosis
- Progression of symptoms (better or worse)
- Improvement with bronchodilators
- Use of oral corticosteroids

The clinician should ask whether any of the following precipitate and/or aggravate symptoms:

- Viral infections
- Environmental allergens
- Irritants (eg, smoke exposure, chemicals, vapors, dust)
- Exercise
- Emotions
- Home environment (eg, carpets, pets, mold)
- Stress
- Drugs (eg, aspirin, beta blockers)
- Foods
- Changes in weather

The presence of other conditions that may affect asthma should be determined.

- Such conditions may include the following:
- Thyroid disease
- Pregnancy
- Menses
- GER-gastroesophageal reflux
- Sinusitis
- Rhinitis

Exacerbation (acute episode, “flare-up”)

In an acute episode of asthma, symptoms vary according to the episode's severity.

Infants and young children suffering a severe episode display the following characteristics:

- Breathless during rest
- Not interested in feeding
- Sit upright
- Talk in words (not sentences)
- Usually agitated
- With imminent respiratory arrest, the child displays the aforementioned symptoms and is also drowsy and confused.

However, adolescents may not have these symptoms until they are in frank respiratory failure.

Duration of bronchoobstructive exacerbation

- 1-3 hours with maximum of intensity of 10-20 minutes,
- could be solved spontaneously or after therapy
- with prolonged crisis at infants and early age

Lung examination

- may reveal:
 - prolongation of the expiratory phase,
 - expiratory wheezing,
 - coarse crackles, or
 - unequal breath sounds.

In a child who is not sick, forced exhalation may reveal expiratory wheeze. Forced exhalation can be obtained by asking the child to blow hard (like blowing imaginary birthday candles) or, in the case of toddlers or infants, pushing on the abdomen may be used to cause forced exhalation.

Clubbing of the fingers is not a feature of straightforward asthma and indicates a need for more extensive evaluation and work-up to exclude other conditions, such as cystic fibrosis.

Severe exacerbation

- Signs :
 - Anxiety, orthopnea, cyanosis, transpiration
 - Thorax is enlarged, fixed in inspiration,
 - Hyperinflation
 - Bronchial crackles, sibilant or subcrepitant
 - Low or lack of stethoscopic pulmonary modification due to reduced pulmonary function (air trapping)
 - The liver and spleen are down

The end of the exacerbation producing the sensation of relief and improvement of functional pulmonary activity with expectoration of white (pearl) viscous sputum (most of the cases)

Findings in status asthmaticus with imminent respiratory arrest include the following:

(very severe condition)

- Duration of exacerbation > 6-8 hours
- Unresponsiveness to bronhodilators (Salbutamol)
- Paradoxical thoracoabdominal movement occurs
- Wheezing may be absent (in patients with the most severe airway obstruction)-silent lungs
- Severe hypoxemia may manifest as brady- cardia
- Pulsus paradoxus may disappear: This finding suggests respiratory muscle fatigue
- Hypoxemia $\text{PaO}_2 < 60 \text{ mm Hg}$
- Hypercapnia $\text{PaCO}_2 > 60 \text{ mm Hg}$
- Low % of Oxygen saturation

The severity of asthma exacerbation: classification

	mild	moderate	severe	Respiratory failure
Breathing	Can sleep Decubitus is possible	Prefer the sitting position ribcage seted to inspire(expanded)	Preferr the sitting/upright position, anterior bent.	
Speech	phrases	Short sentences	words	
Sensors	Restless irritation	Restless irritation	Restlless, nervous, irritant	inhibited
Respiratory rate	frequent	frequent	increased	
Chest indrawing	absence	presence	presence	Paradoxal breath movement
Wheezing	moderate,	Presence	expressed	absentce
Puls	normal	The upper limit of the norm	tachicardia	bradycardy
FEV1	>80%	60-80%	<60%	
PaO2	N	>60mmHg	<60mmHg	
PaCO2	<45mmHg	<45mmHg	>45mmHg	
SaO2	>95%	91-95%	<91%	

Variability:

- Symptoms
- Responses to therapy
- Triggers of the asthma
- + prognostic
- Types to the asthma at children

Findings in the absence of an acute episode

- . The physical findings between acute episodes vary with the severity of the asthma.
- During an outpatient visit, a patient with mild asthma may have normal findings on physical examination.
- Patients with more severe asthma are likely to have signs of chronic respiratory distress and chronic hyperinflation.

Findings in the absence of an acute episode in severe asthma

- Signs of atopy or allergic rhinitis, such as conjunctival congestion and inflammation may be present.
- The anteroposterior diameter of the chest may be increased because of hyperinflation. Hyperinflation may also cause an abdominal breathing pattern.

Diagnosis(continued)

- Investigations (PERFORM) –
 - **Pulmonary function tests (PFTs)** (spirometry, peakfluorometry)

In asthma, airways blockage results in reduced airflow with forced exhalation and smaller partial-expiratory lung volumes

For young children < 5 y.o. unable to perform spirometry. Other techniques:

- 1. Plethysmography**
- 2. Spirometry in rest (when sleep)**
- 3. Impulse oscillometry system (IOS)**
- 4. Tidal Breathing Analysis**

other:

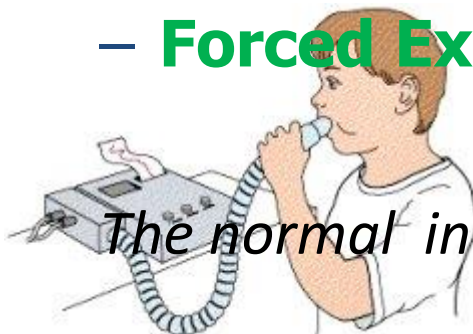
- ***Blood gases***
- ***Rx pulmonary,***
- ***Nuclear pulmonary investigation , scintigraphy***
(to exclude other pathology)



- ***Pulmonary Function Tests***

- **SPIROMETRY: > 5 y.o.**

- **Pulmon`'s capacity:**
- **PC-total vital capacity**
- **FVC- forced vital capacity;**
- **FEV₁- forced expiratory volume in 1 second;**
- **Forced Expiratory Ratio (FEV1/FVC)**
- **Forced Expiratory Flow (FEF 25% to 75%)**



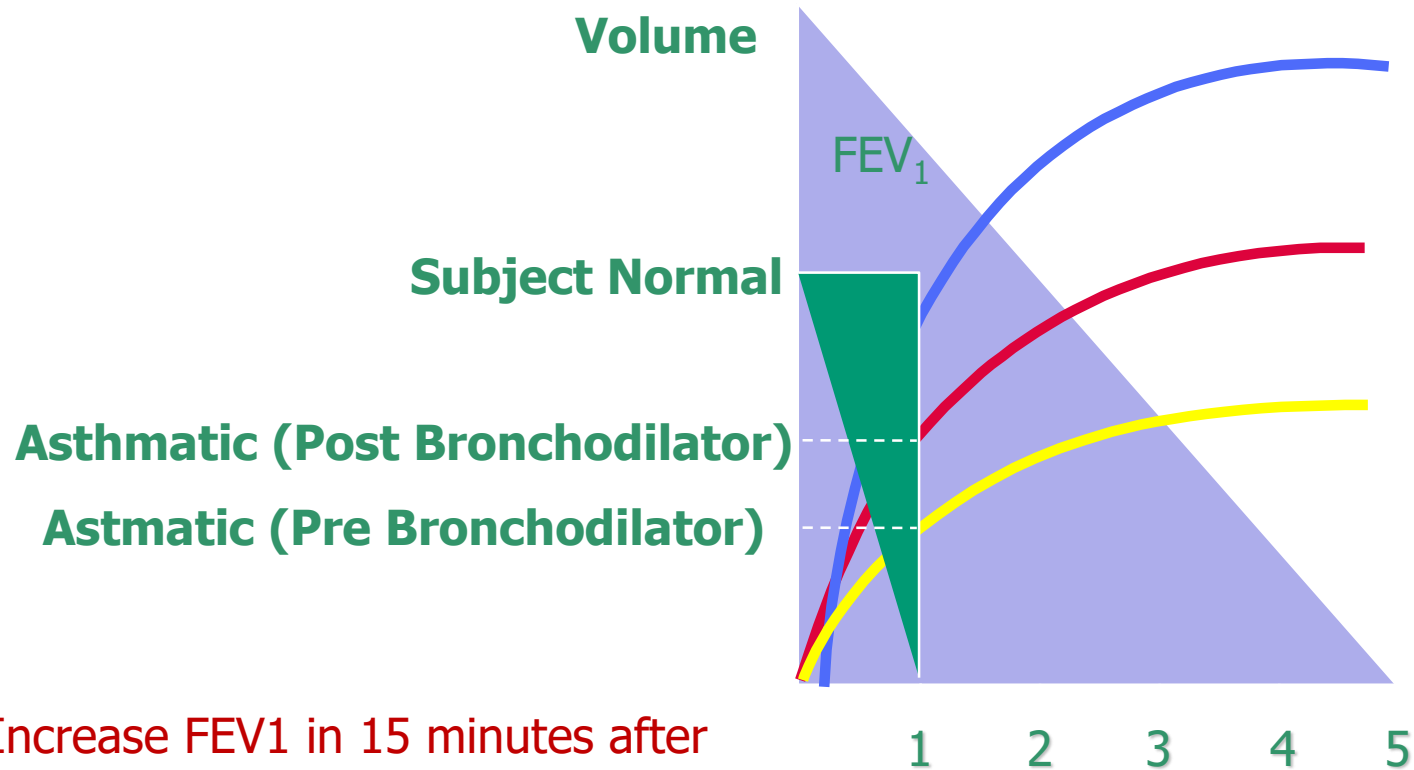
The normal indices: > 80% reported to predicted normative

USB PC Spirometer





The typical changes in spirometry(FEV_1) after Salbutamol



Increase FEV_1 in 15 minutes after Salbutamol inhalation $> 12\%$ - positive test for BA

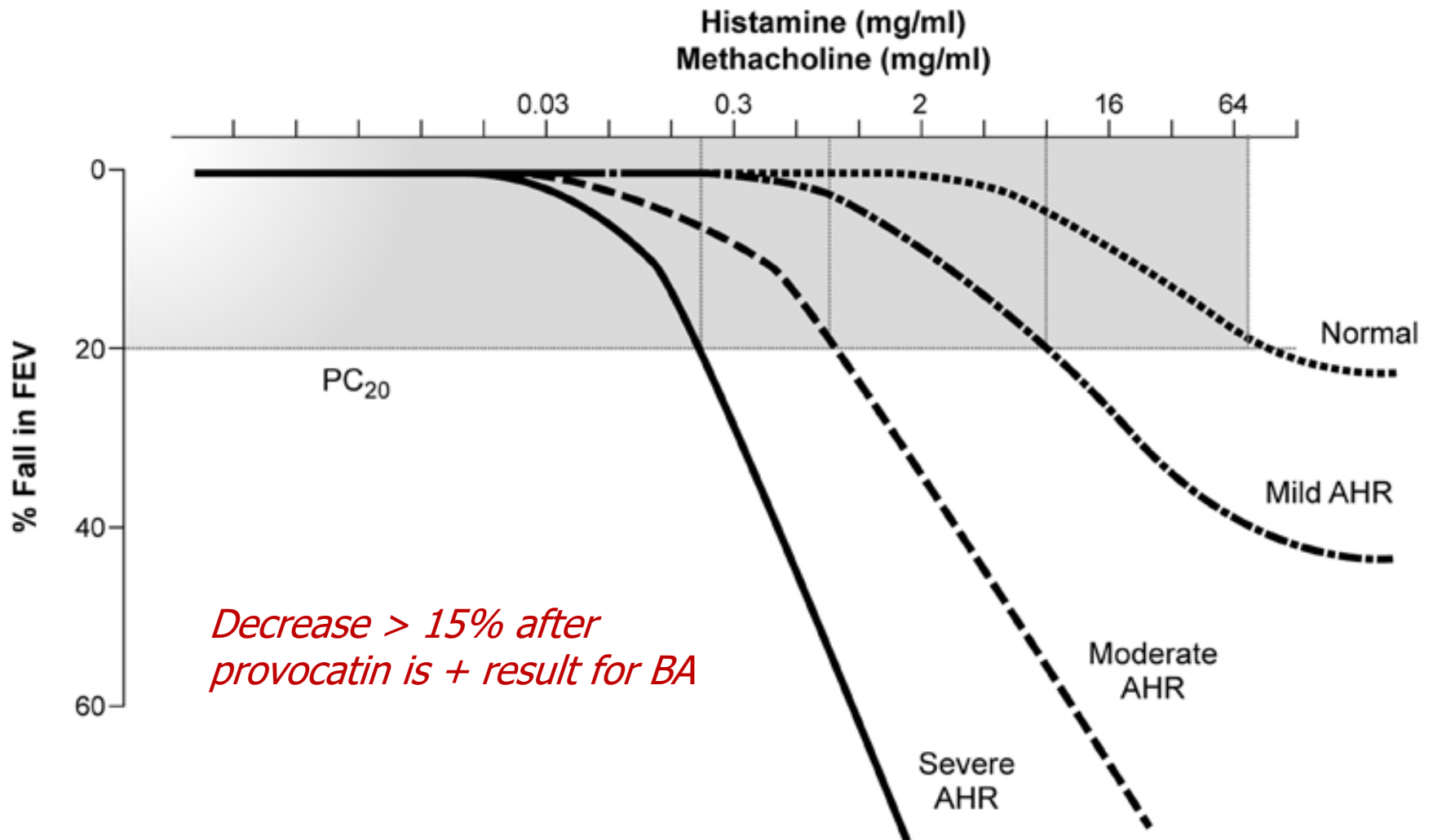
Nota: Each curve represented the FEV_1 of 3 consecutive measurements

Bronchoprovocation challenges

- inhaled methacholine, histamine, and cold or dry air
- **Exercise challenges** (aerobic exertion or “running” for 6–8 min) can help to identify children with **exercise-induced bronchospasm**.



Bronchial hyperreactivity – provocation test



Reversibility

- **Documentation of reversibility of airway obstruction after bronchodilator therapy is central to the definition of asthma.**
- **FEF 25-75 is a sensitive indicator of obstruction and may be the only abnormality in a child with mild disease.**

Peak expiratory flow (PEF) monitoring (*pneumotahography*)

- PEF (the maximum instantaneous flow debit at expiratory) Normal value :>80% of predicted
- MEF50(peak expiratory flow) at 50% of CV(vital capacity) or 25%;

PEF variation (between evening and morning) >20% is consistent with uncontrolled asthma

Peak-Flow-Meter

devices provide a simple and inexpensive home-use tool to measure airflow and can be helpful in a number of circumstances



Oscilometry with impulses (OI)

**Screening
method to
detect the
ventilation
disturbances**



Lung Function Abnormalities in Asthma

- Spirometry (in clinic)
- Airflow limitation

Low FEV1 (relative to percentage of predicted norms)

- **FEV1/FVC ratio <0.80**

Bronchodilator response (to inhaled β -agonist)

- **Improvement in FEV1 $\geq 12\%$ or ≥ 200 mL^[*]**

Exercise challenge

- **Worsening in FEV1 $\geq 15\%$ ^[*]**

Daily peak flow or FEV 1 monitoring: day to day and/or
AM-to-PM variation **$\geq 20\%$ ^[*]**

FEV₁, forced expiratory volume in 1 sec; FVC, forced vital capacity.

Additional studies

are not routinely necessary, but they may be useful when the clinician is considering alternative diagnoses.

- Eosinophil counts (increasing) and
- IgE levels may be useful when allergic factors are suspected.

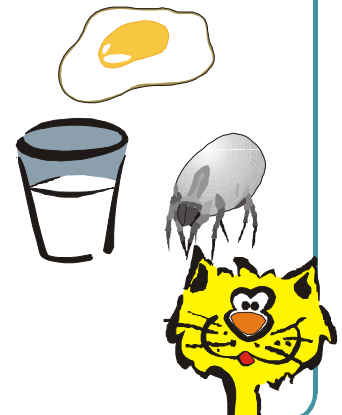


Phadiatop® **Infant**



Identification
>9 of 10

Egg
Milk
Peanut
Ticks
Home dust
Cat
Dog
Pollens



Fraction of Exhaled Nitric Oxide and interleukin-5 Testing

- Measuring the fraction of exhaled nitric oxide (FeNO) has proved useful as a noninvasive marker of airway inflammation. Due to the high cost of equipment, FeNO measurement is used primarily as a research tool at present.
- Measuring the level of interleukin-5 in exhaled breath condensate is a possible way of titrating asthma progress, , significant predictors of an asthma exacerbation.

Radiography and CT Scan

- Include chest radiography in the initial workup if the asthma does not respond to therapy as expected. In addition to typical findings of hyperinflation and increased bronchial markings, a chest radiograph may reveal evidence of parenchymal disease, atelectasis, pneumonia, congenital anomaly, or a foreign body.
- In a patient with an acute asthmatic episode that responds poorly to therapy, a chest radiograph helps in the diagnosis of complications such as pneumothorax or pneumomediastinum.
- Consider using sinus radiography and CT scanning to rule out sinusitis.

Radiography and CT Scan

Posteroanterior chest radiograph demonstrates a **pneumomediastinum** in bronchial asthma. Mediastinal air is noted adjacent to the anteroposterior window and airtrapping extends to the neck, especially on the right side.

Lateral chest radiograph demonstrates a **pneumomediastinum** in bronchial asthma. Air is noted anterior to the trachea (same patient as in the previous image).



Asthma. **High-resolution CT** scan of the thorax obtained during inspiration demonstrates airtrapping in a patient with asthma. **Inspiratory findings are normal.**

High-resolution CT scan of the thorax obtained **during expiration** demonstrates **a mosaic pattern** of lung attenuation in a patient with asthma. Lucent areas (arrows) represent areas of **airtrapping** (same patient as in the previous image).



The **specificity of HRCT** for bronchial asthma **is limited** by the similarity of its changes to those of other diseases, such as bronchiectasis, chronic bronchitis, emphysema, and bronchopulmonary aspergillosis

Complications

- Immediate
 - Spontaneously pneumotorax
 - Subcutaneous Emphysema
 - Mediastinal Emphysema
 - Rib Fractures
 - Segmental atelectasis (due to mucus plug)
- Late
 - Bronchi superinfection
 - Intercurrent Pneumonia

Iatrogenic

- Steroid abuse
 - Corticoddependence
 - Kushingoid Syndrom
 - Osteoporosis
 - Arterial hypertnsion
 - Ulcer
 - Infections
- Beta-adrenergic abuse
 - Irritability
 - Digital Tremor
 - Muscular Cramps
 - Tachycardie, extrasystolia
 - Arterial hypertension
- Aminophylin abuse
 - Anxiety, irritability, convulsions, sleepness

Diagnosing BA at children < 5 y.o.

Asthma Predictive Index

- Identify high risk children (< 5 y.o.):
 - ≥ 4 wheezing episodes in the past year
(at least one must be MD diagnosed)

PLUS

- One major criterion

- Parent with asthma
- Atopic dermatitis
- Aero-allergen sensitivity

OR

- Two minor criteria

- Food sensitivity
- Peripheral eosinophilia ($\geq 4\%$)
- Wheezing not related to infection

7. DIFFERENTIAL DIAGNOSES OF ASTHMA IN CHILDREN

Condition	Typical features
Recurrent viral respiratory infections	Mainly cough, runny congested nose for <10 days; wheeze usually mild; no symptoms between infections
Gastroesophageal reflux	Cough when feeding; recurrent chest infections; vomits easily especially after large feeds; poor response to asthma medications
Foreign body aspiration	Episode of abrupt severe cough and/or stridor during eating or play; recurrent chest infections and cough; focal lung signs
Tracheomalacia or bronchomalacia	Noisy breathing when crying or eating, or during URTIs; harsh cough; inspiratory or expiratory retraction; symptoms often present since birth; poor response to asthma treatment
Tuberculosis	Persistent noisy respirations and cough; fever unresponsive to normal antibiotics; enlarged lymph nodes; poor response to BD or ICS; contact with someone with TB
Congenital heart disease	Cardiac murmur; cyanosis when eating; failure to thrive; tachycardia; tachypnea or hepatomegaly; poor response to asthma medications

Condition	Typical features
Cystic fibrosis	Cough starting shortly after birth; recurrent chest infections; failure to thrive (malabsorption); loose greasy bulky stools
Primary ciliary dyskinesia	Cough and recurrent mild chest infections; chronic ear infections and purulent nasal discharge; poor response to asthma medications; situs inversus (in ~50% children with this condition)
Vascular ring	Respirations often persistently noisy; poor response to asthma medications
Bronchopulmonary dysplasia	Infant born prematurely; very low birth weight; needed prolonged mechanical ventilation or supplemental oxygen; difficulty with breathing present from birth
Immune deficiency	Recurrent fever and infections (including non-respiratory); failure to thrive
Hyperventilation syndrome	
Vocal cord dysfunction	
Pulmonary edema	
Collagen vascular disease	
Reactive airway disease	

GINA - Global Initiative for Asthma

Consensus on Asthma since 1992

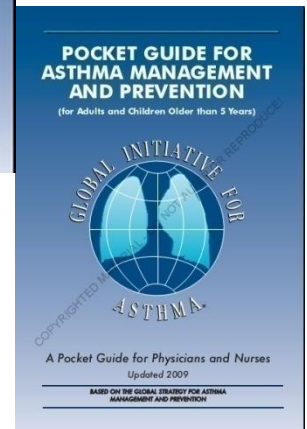
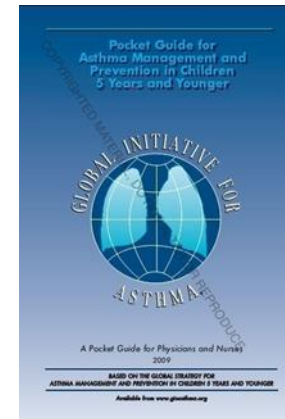
Global Strategy for Asthma Management and Prevention 2015

GINA proposes the Guides on Asthma Management .

Each 2 years are updated

The last – 2019

www.ginasthma.org



8. ASTHMA CLASSIFICATION:

Grades of severity:

For adults and children age > 5, GINA 2018

CLASSIFICATION	DAYS WITH SYMPTOMS	NIGHTS WITH SYMPTOMS	FEV ₁ or PEF ^[*] % Predicted Normal	FEV ₁ or PEF ^[*] % Predicted Normal
Severe persistent	Continual	Frequent	≤60	>30
Moderate persistent	Daily	>1/wk	>60—<80	>30
Mild persistent	>2/wk, but <1 time/day	>2/mo	≥80	20–30
Mild intermittent	≤2/wk	<2/mo	≥80	<20

GINA assessment of symptom control

A. Symptom control

In the past 4 weeks, has the patient had:		Well-controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms more than twice a week?	Yes <input type="checkbox"/> No <input type="checkbox"/>	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• Reliever needed for symptoms* more than twice a week?	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• Any activity limitation due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			

* Excludes reliever taken before exercise, because many people take this routinely

Assessment of risk factors for poor asthma outcomes

Risk factors for exacerbations include:

- Ever intubated for asthma
- Uncontrolled asthma symptoms
- Having ≥ 1 exacerbation in last 12 months
- Low FEV₁ (measure lung function at start of treatment, at 3-6 months to assess personal best, and periodically thereafter)
- Incorrect inhaler technique and/or poor adherence
- Smoking
- Obesity, pregnancy, blood eosinophilia

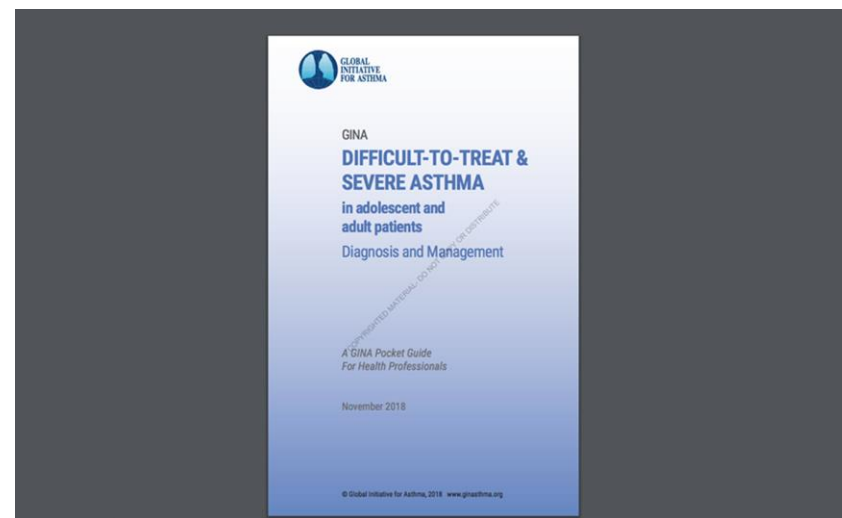
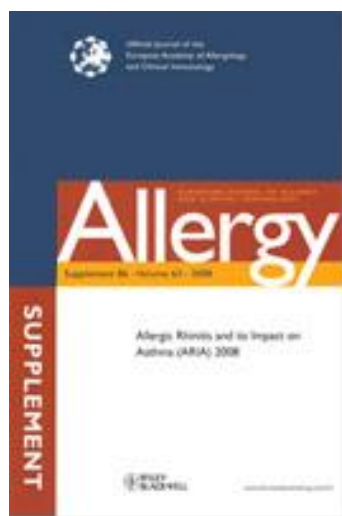
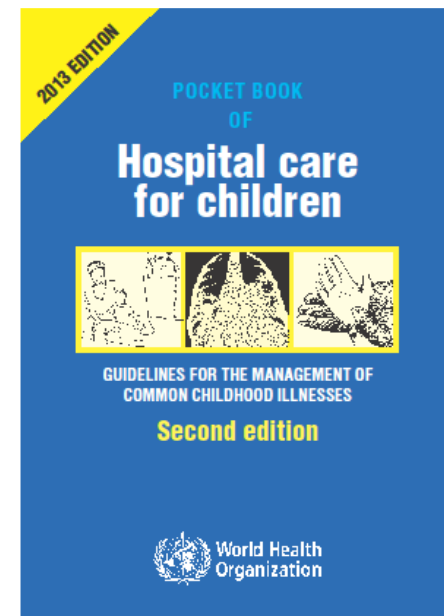
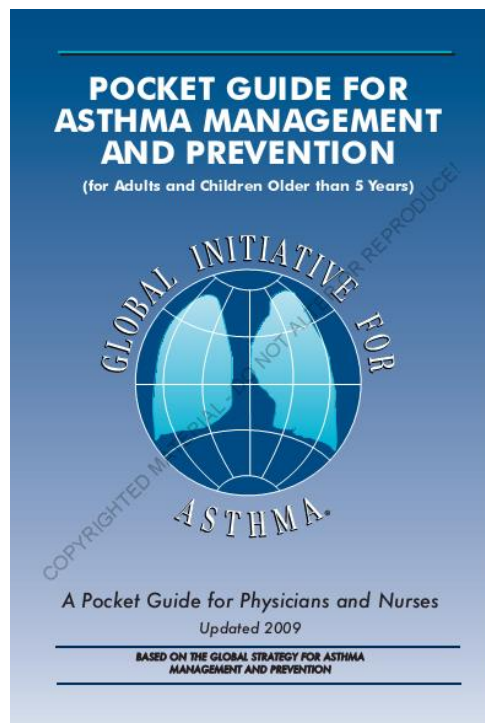
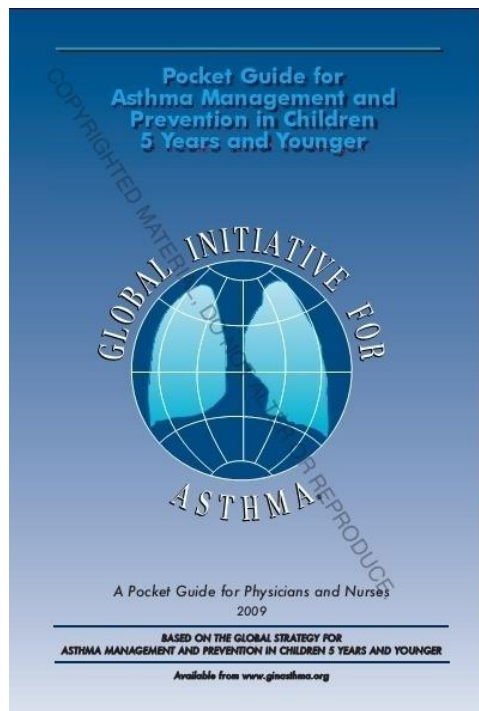
Risk factors for fixed airflow limitation include:

- No ICS treatment, smoking, occupational exposure, mucus hypersecretion, blood eosinophilia

9. ASTHMA THERAPY

Five interrelated components of therapy are required to achieve and maintain control of asthma-

1. Develop Patient/Doctor partnership
2. Identify and reduce exposure to risk factors
3. Assess, treat, and monitor asthma
4. Manage asthma exacerbations
5. Special considerations



Develop Patient/Doctor partnership -

Patients can learn to –

1. Avoid risk factors
2. Take medications correctly
3. Understand the difference between controller and reliever medications
4. Monitor their status using symptoms and, if relevant, PEF
5. Recognize signs that asthma is worsening and take action
6. Seek medical help as appropriate

Identify and reduce exposure to risk factors -

- Measures to prevent the development of asthma and asthma exacerbations by avoiding or reducing exposure to risk factors should be implemented wherever possible.
- Reducing patients exposure to some categories of risk factors improves the **control of asthma and reduces medication needs**.

Manage asthma in a continuous

- **Assess**
- **Adjust** treatment (pharmacological and non-pharmacological)
- **Review** the response

Teach and reinforce essential skills

- *Inhaler skills*
- *Adherence*
- *Guided self-management education*
 - *Written asthma action plan*
 - *Self-monitoring*
 - *Regular medical review*



Asthma medications

Classified into **Controllers** and **Relievers**

- **Controllers** – medications to be taken on daily long term basis.
- **Relievers** – medications to be used on as-needed basis to relieve symptoms quickly.

9.1. Relief medications include the following

- **O₂**
- **Short-acting bronchodilators**
- **Systemic corticosteroids**
- **Ipratropium bromide**
- **Methylxanthines, short acting**
- **Magnesium sulphates**

Selective short-acting β_2 -agonists (SABA)

albuterol,

fenoterol,

levalbuterol,

terbutalin,

pirbuterol.

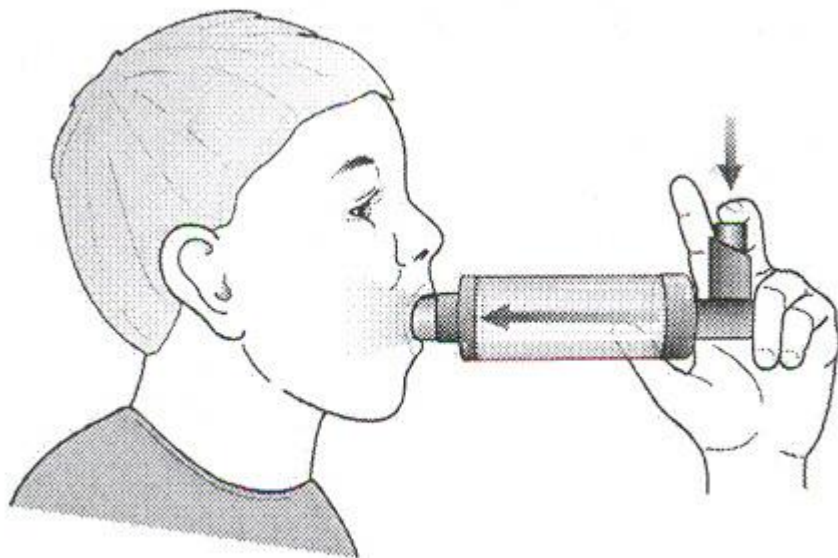


- **Choosing an inhaler device for children with asthma *** -

Age group	Preferred device	Alternative device
Younger than 4 years	Pressurized metered-dose inhaler plus dedicated spacer with face mask	Nebulizer with face mask
4-5 years	Pressurized metered-dose inhaler plus dedicated spacer with mouthpiece	Nebulizer with mouthpiece
Older than 6 years	Dry powder inhaler or breath actuated pressurized metered-dose inhaler or pressurized metered-dose inhaler with spacer with mouthpiece	Nebulizer with mouthpiece







Salbutamol (Ventolin)

- Inhalation way to relief – is the best
 - Doses: 0,05-0,15 mg/Kg/dose. *Gaz vector: oxygen*

**IN EMERGENCY: 3 times with breaks each 10-15 MIN.
after each inhalation –need evaluation**

1dose=100 mcg

***1 hour** : < 5 years 2 puffs x 3 times = 6 puffs
> 5 years 4 puffs x 3 times = 12 puffs*

- *if persist :*
 - Give initial dose of oral prednisolone (1-2mg/kg up to maximum of 20mg for children <2 years; 30 mg for 2-5 years) and reffer

Initial management of asthma exacerbations in children ≤ 5 years

Therapy	Dose and administration
Supplemental oxygen	24% delivered by face mask (usually 1L/min) to maintain oxygen saturation 94-98%
Inhaled SABA	2–6 puffs of salbutamol by spacer, or 2.5mg by nebulizer, every 20 min for first hour, then reassess severity. If symptoms persist or recur, give an additional 2-3 puffs per hour. Admit to hospital if >10 puffs required in 3-4 hours.
Systemic corticosteroids	Give initial dose of oral prednisolone (1-2mg/kg up to maximum of 20mg for children <2 years; 30 mg for 2-5 years)
Additional options in the first hour of treatment	
Ipratropium bromide	For moderate/severe exacerbations, give 2 puffs of ipratropium bromide 80mcg (or 250mcg by nebulizer) every 20 minutes for one hour only
Magnesium sulfate	Consider nebulized isotonic MgSO_4 (150mg) 3 doses in first hour for children ≥ 2 years with severe exacerbation

Salbutamol (albuterol)

Salbutamol, iv, in perfusion, PEV continuing,
0,2µg/Kg/min increasing dose to 0,5µg/Kg/min

Indication: when inhalation is imposible

NOTES! *Frequently SABA administration can cause Bronchial Hyperreactivity and can worsening clinical course of BA*

SABA therapy

Need to supervise the patient during 1 hour after exacerbation.

- If the patient is reponding + to SABA , but the new episodes appearing each hour during in 3-4 hours , is need to repeat SABA+ oral CS :
- If the patient doesn't respond after 10 doses of SABA – needs referral
- If no other exacerbations during 24 hours – no other therapy needed.

In addition:

***CS orally 1-2 mg/kg/day - max 20mg/kg/day at children < 2 years
and no >30 mg/kg/d for children 2-5 y.o***

3- 5 days (D)

Anticholinergic medication

- Ipratropium bromid (Atrovent)
- Oxytropium bromid
- Tiotropium bromid (Spiriva)

Efficiency – in **30 min**

Combined medication –with SABA-
synergic activity.

Systemic corticosteroids CS

Prednizolon (Methylprednizolon)

Dexamethasoni

Prednizolon :

I/V or I/M 1,5-2,0 mg/kg (or equivalent of prednisolone)

to maintain % **cortisol 100–150 / μ g /100 mL** în plasma

Orally 0,5-1,0 mg/kg – 3-5-10 days (or equivalent of prednisolone)

Methylxantines:Theophylline (*Euphyllin, Theo-24, Theochron, Uniphyl*)

is available in

- **short-acting and**
- **long-acting formulations.**

Because of the need to monitor **serum concentrations**, this agent is used **infrequently**.

The dose and frequency depend on the particular product selected.

Euphyllini, short acting methylxantine

- Indications: lack of efficiency of Salbutamol therapy , IGS
- Not as routine!
- In ICU (intensive care units) !
- Doses:
 - saturation: 6-7 mg/Kg iv, slowly , sol 2,4%
 - Maintaining , PEV (continuing perfusion): 0,4 mg/Kg/hour (>5 y.o.)
0,9 mg/kg /hour(<5y.o.)
- Monitoring of plasma concentration (requested):
 - Efficient: 10µg/ml
- Toxic: > 15 µg/Ml

Magnesium sulphate

- **In ICU** in cases of Status Asthmaticus
- Doses: 25-75 mg/Kg, iv, slowly
- Or inhalation via nebulizer
- Adequate hydration

The treatment not recommended during the exacerbations relief

- sedatives,
- mucolytics
- fiziotherapy
- hyperhydration (perfusion with increased volume)
- routin antibiotics if not associated with infections

Indications for immediate transfer to hospital for children ≤ 5 years

Transfer immediately to hospital if ANY of the following are present:

Features of severe exacerbation at initial or subsequent assessment

- Child is unable to speak or drink
- Cyanosis
- Subcostal retraction
- Oxygen saturation $<92\%$ when breathing room air
- Silent chest on auscultation

Lack of response to initial bronchodilator treatment

- Lack of response to 6 puffs of inhaled SABA (2 separate puffs, repeated 3 times) over 1-2 hours
- Persisting tachypnea* despite 3 administrations of inhaled SABA, even if the child shows other clinical signs of improvement

Unable to be managed at home

- Social environment that impairs delivery of acute treatment
- Parent/carer unable to manage child at home

Referral to ICU

- Patients need artificial ventilation,
- General danger signs
- Do not responded to emergency treatment with bronhodilators after 3 inhalations .
 - Worsening PEF
 - Hypoxia
 - Hypercapnia
 - Metabolic acidosis
 - Difficult breathing
 - Respiratory arrest
 - Unconscious or lethargic
- **The protocol PALS is applied**

Discharge from emergency/ICU

1. The patients stable during 3-4 hours after Salbutamol inhalation with recommendations at home
2. PEF and or FEV1 >75%
3. SpO2 > 94%.
4. Exacerbation is considering as deficiency of “Control therapy”

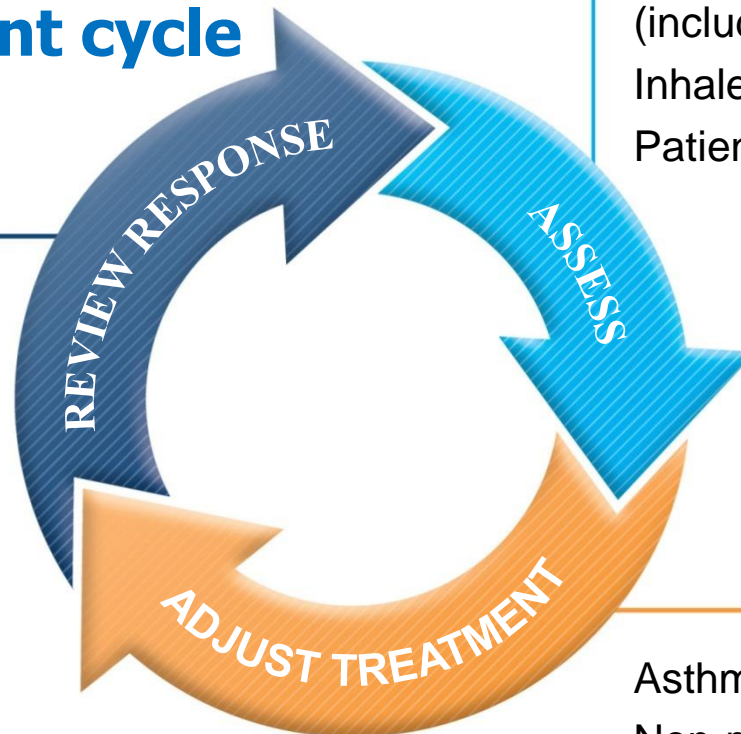
Plan at discharge:

- *Check technique at every opportunity – “Can you show me how you use your inhaler at present?”*
- *Identify errors with a device-specific checklist*
- *Update the “control” therapy*
- *Written plan with indication of necessary doses for emergency if needed*
- *Follow up to family doctor in 48 hours*
- *Follow up to allergologist in 2 months*
- *Consider other consultations if needed*

9.2.”Controller” therapy

The control-based asthma management cycle

Symptoms
Exacerbations
Side-effects
Patient satisfaction
Lung function



Diagnosis
Symptom control & risk factors
(including lung function)
Inhaler technique & adherence
Patient preference

Asthma medications
Non-pharmacological strategies
Treat modifiable risk factors

Asthma control medications

Control agents include the following:

- **Inhaled corticosteroids**
- **Inhaled cromolyn or nedocromil**
- **Long-acting bronchodilators**
- **Theophylline, long acting**
- **Leukotriene modifiers**
- **Biologic therapy**
- **Allergen immunotherapy**

'Low dose' inhaled corticosteroids (mcg/day) for children ≤ 5 years



Inhaled corticosteroid	Low daily dose (mcg)
Beclometasone dipropionate (HFA)	100
Budesonide (pMDI + spacer)	200
Budesonide (nebulizer)	500
Fluticasone propionate (HFA)	100
Ciclesonide	160
Mometasone furoate	Not studied below age 4 years
Triamcinolone acetonide	Not studied in this age group

- This is not a table of equivalence
- A low daily dose is defined as the dose that has not been associated with clinically adverse effects in trials that included measures of safety

Low dose inhaled corticosteroids mcg/day for children <5 y.o.

Inhaled corticosteroid	Total low daily dose (mcg)
Beclometasone dipropionate (HFA)	100
Budesonide (pMDI + spaser)	200
Budesonide (nebulizer)	500
Fluticasone propionate (HFA)	100
Ciclesonide (HFA)	160
Mometasone furoate	Not studied for age < 4 y.o.

Low, medium and high dose inhaled corticosteroids

Children 6–11 years

Inhaled corticosteroid	Total daily dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (CFC)	100–200	>200–400	>400
Beclometasone dipropionate (HFA)	50–100	>100–200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebulas)	250–500	>500–1000	>1000
Ciclesonide (HFA)	80	>80–160	>160
Fluticasone propionate (DPI)	100–200	>200–400	>400
Fluticasone propionate (HFA)	100–200	>200–500	>500
Mometasone furoate	110	≥220–<440	≥440
Triamcinolone acetonide	400–800	>800–1200	>1200

- This is not a table of equivalence, but of estimated clinical comparability
- Most of the clinical benefit from ICS is seen at low doses
- High doses are arbitrary, but for most ICS are those that, with prolonged use, are associated with increased risk of systemic side-effects

Low, medium and high dose inhaled corticosteroids

Adults and adolescents (≥ 12 years)

Inhaled corticosteroid	Total daily dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (CFC)	200–500	>500–1000	>1000
Beclometasone dipropionate (HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (HFA)	80–160	>160–320	>320
Fluticasone propionate (DPI or HFA)	100–250	>250–500	>500
Mometasone furoate	110–220	>220–440	>440
Triamcinolone acetonide	400–1000	>1000–2000	>2000

- This is not a table of equivalence, but of estimated clinical comparability
- Most of the clinical benefit from ICS is seen at low doses
- High doses are arbitrary, but for most ICS are those that, with prolonged use, are associated with increased risk of systemic side-effects

Side effects of topical Inhalator corticosteroid

- Oral candidoses,
- dysphagia,
- dysphonia.

Solutions:

- ☐ - need to use spaser,
- ☐ - is indicated to gargle after inhalation with plain water or 1% sol. of Sodium bicarbonates

Safety Considerations With ICS Therapy

- Local effects
 - Oropharyngeal effects
 - Oral candidiasis
 - Pharyngitis
 - Hoarseness/dysphonia
- Systemic effects
 - Suppression of hypothalamic-pituitary-adrenal (HPA) axis
 - Growth suppression
 - Changes in bone mineral density and bone metabolism
 - Ophthalmologic effects: cataracts and glaucoma
 - Skin thinning and bruising



Dahl R. Respir Med. 2006;100:1307-1317.
Lipworth BJ. Arch Intern Med. 1999;159:941-955.

EDGE 95

Adverse reactions after CS therapy

- Suprarenal inhibition
- Osteoporoses
- Growth impairment

ICS – minimal side effect

Only orally CS for long tie- causing adverse reactions.

Cromones

Antiinflammatory, efficient in mild asthma in exercise-induceing asthma

- *Sodium Cromoglicat, Nedocromil*

inhaled, aerosol, ,reducing specific and non-specific bronchial hyperreactivity.

- The clinical efficiency is significant lower than ICS

Long acting methylxantines

Theophyllini

(*Teopec, Theo-dur, Spophyllin retard, Duraphyllin, Theo-300 etc*)

Only in combination with CSI

Long acting β_2 -agonists LABA

- *Salmeterol (Serevent),*
- *Formoterol (Foradil)*

Maintained bronhodilation about 12 hours

:Indications:

- prevent and treat by physical activity
- severe asthma therapy

***Administration in combination with
antiinflammatory medications as CSI !!!!***

Combined medications for inhalation

- Fluticasone propionate/salmeterol (pMDI)
-DPI)
- Budesonide/formoterol (controlr, reliever) pMDI
DPI
- Beclomethasone/formoterol(pMDI)
- Mometasone/formoterol(pMDI)

pMDI = pressurized metered dose inhaler; DPI = dry powder inhaler

Leukotriene Modifiers

Antileucotriens – as antagonists of leucotrien receptors and impeding the leucotrien synthesis receptorilor leucotrienice

- *Sodium Montelukast* – 6 months-5 years 4 mg/1/day
- 5-14 yars - (5 mg) ;
- > 14 ani – 10mg;
- *Zafirlucast de natriu (Acolat)* – 10 mgx 2/day

BIOLOGIC THERAPY

Inhibitors of allergic mediators

- **Omalizumab (Anti-IgE antibody).**
- **Mepolizumab (Anti-IL-5 de antibody).**
- **Reslizumab, antibody anti-IL-5**
- **Dupilumab (Anti-IL-4 receptors α antibody).**

Anti IgE- omalizumab

Omalizumab is a recombinant, DNA-derived, humanized IgG monoclonal antibody that binds selectively to human IgE on surface of mast cells and basophils.

It reduces mediator release, which promotes allergic response.

It is indicated for moderate-to-severe persistent asthma in patients who react to perennial allergens in whom symptoms are not controlled by inhaled corticosteroids.

Stepwise management – additional components

REMEMBER TO...

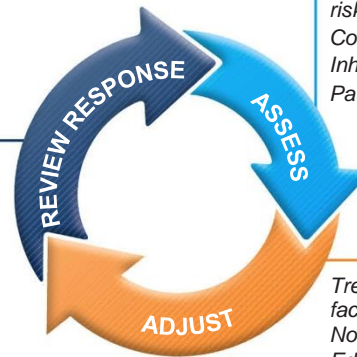
- Provide guided self-management education
- Treat modifiable risk factors and comorbidities
- Advise about non-pharmacological therapies and strategies
- Consider stepping up if ... uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first
- Consider stepping down if ... symptoms controlled for 3 months
+ low risk for exacerbations. Ceasing ICS is not advised.

Adults & adolescents 12+ years

Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations
Side-effects Lung
function
Patient satisfaction



Confirmation of diagnosis if necessary
Symptom control & modifiable
risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient goals

Treatment of modifiable risk
factors & comorbidities
Non-pharmacological strategies
Education & skills training
Asthma medications

Asthma medication options:

Adjust treatment up and down for
individual patient needs

PREFERRED CONTROLLER

to prevent exacerbations
and control symptoms

Other
controller options

PREFERRED RELIEVER

Other
reliever option

STEP 1

As-needed low
dose
ICS-formoterol *
Low dose ICS
taken whenever
SABA is taken †

STEP 2

Daily low dose inhaled corticosteroid (ICS),
or as-needed low dose ICS-formoterol *
Leukotriene receptor antagonist (LTRA), or
low dose ICS taken whenever SABA taken †

STEP 3

Low dose
ICS-LABA

Medium dose
ICS, or low dose
ICS+LTRA #

STEP 4

Medium dose
ICS-LABA

High dose ICS,
add-on
tiotropium, or
add-on LTRA #

STEP 5

High dose
ICS-LABA
Refer for
phenotypic
assessment
± add-on
therapy,
e.g. tiotropium,
anti-IgE,
anti-IL5/5R,
anti-IL4R

Add low dose
OCS, but
consider
side-effects

As-needed low dose ICS-formoterol *

As-needed low dose ICS-formoterol ‡

As-needed short-acting β_2 -agonist (SABA)

* Off-label; data only with budesonide-formoterol (bud-form)

† Off-label; separate or combination ICS and SABA inhalers

‡ Low-dose ICS-form is the reliever for patients prescribed bud-form or BDP-form maintenance and reliever therapy

Consider adding HDM SLIT for sensitized patients with allergic rhinitis and FEV₁ >70% predicted

Step 1 – ‘preferred’ controller option

- Step 1 is for patients with symptoms less than twice a month, and with no exacerbation risk factors

As-needed low dose ICS-formoterol (off-label)

- Evidence
 - Indirect evidence from SYGMA 1 of large reduction in severe exacerbations vs SABA-only treatment in patients eligible for Step 2 therapy (*O’Byrne, NEJMed 2018*)
- Values and preferences
 - High importance given to reducing exacerbations
 - High importance given to avoiding conflicting messages about goals of asthma treatment between Step 1 and Step 2
 - High importance given to poor adherence with regular ICS in patients with infrequent symptoms, which would expose them to risks of SABA-only treatment

Step 1 - other controller option

Low dose ICS taken whenever SABA is taken (off-label)

- Evidence
 - Indirect evidence from studies in patients eligible for Step 2 treatment (BEST, TREXA, BASALT)
- Values and preferences
 - High importance given to preventing severe exacerbations
 - Lower importance given to small differences in symptom control and the inconvenience of needing to carry two inhalers
 - Combination ICS-SABA inhalers are available in some countries, but approved only for maintenance use

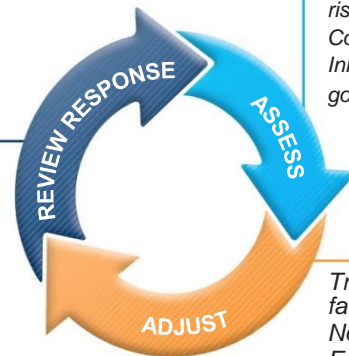
Children 6-11 years



Personalized asthma management:

Assess, Adjust, Review response

Symptoms
Exacerbations Side-effects Lung function
Child and parent satisfaction



Confirmation of diagnosis if necessary Symptom control & modifiable risk factors (including lung function) Comorbidities Inhaler technique & adherence Child and parent goals

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Education & skills training
Asthma medications

Asthma medication options:

Adjust treatment up and down for individual child's needs

PREFERRED CONTROLLER

to prevent exacerbations and control symptoms

RELIEVER

Other controller options

STEP 1

Low dose ICS taken whenever SABA taken*; or daily low dose ICS

STEP 2

Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)

Leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*

STEP 3

Low dose ICS-LABA, or medium dose ICS

Low dose ICS+LTRA

STEP 4

Medium dose ICS-LABA
Refer for expert advice

High dose ICS-LABA, or add-on tiotropium, or add-on LTRA

STEP 5

Refer for phenotypic assessment ± add-on therapy, e.g. anti-IgE

Add-on anti-IL5, or add-on low dose OCS, but consider side-effects

As-needed short-acting β_2 -agonist (SABA)

* Off-label; separate ICS and SABA inhalers; only one study in children

Children < 5 y.o.

4 Steps of controller therapy

PREFERRED CONTROLLER CHOICE	STEP 1	STEP 2	STEP 3	STEP 4
		Daily low dose ICS	Double 'low dose' ICS	Continue controller & refer for specialist assessment
	Other controller options	Leukotriene receptor antagonist (LTRA) Intermittent ICS	Low dose ICS + LTRA	Add LTRA Inc. ICS frequency Add intermittent ICS
RELIEVER	As-needed short-acting beta ₂ -agonist (all children)			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern consistent with asthma and asthma symptoms not well-controlled, or ≥3 exacerbations per year Symptom pattern not consistent with asthma but wheezing episodes occur frequently, e.g. every 6–8 weeks. Give diagnostic trial for 3 months.	Asthma diagnosis, and not well-controlled on low dose ICS First check diagnosis, inhaler skills, adherence, exposures	Not well- controlled on double ICS

Step-up Therapy

- Indications: Symptoms, need for quick-relief medication, exercise intolerance, decreased lung function
 - May need a short course of oral steroids.
- Continue to monitor.
 - Follow and reassess every 1–6 months
 - Step down when appropriate.

Step-down Therapy

Step down once control is achieved:

- After 2–3 months
- 25% reduction over 2–3 months

Follow-up monitoring:

- Every 1–6 months
- Assess symptoms.
- Review medication use.
- Objective monitoring (PEF or spirometry)
- Review medication.

Check adherence with asthma medications

- Poor adherence:
 - Contributes to uncontrolled asthma symptoms and risk of exacerbations and asthma-related death
- Contributory factors
 - Unintentional (e.g. forgetfulness, cost, confusion) and/or
 - Intentional (e.g. no perceived need, fear of side-effects, cultural issues, cost)
- How to identify patients with low adherence:
 - Ask an empathic question, e.g. “*Do you find it easier to remember your medication in the morning or the evening?*”, or
“*Would you say you are taking it 3 days a week, or less, or more?*”
 - Check prescription date, label date and dose counter
 - Ask patient about their beliefs and concerns about the medication



Assessment of Future Risk

Risk of decline

Each exacerbation
need reevaluation of
"controller" therapy

risk

used

- Frequent exacerbations
- Even mild exacerbations require care
- Low FEV₁, exposure to cigarette smoke, high dose of medications

Allergen Immunotherapy

The administration of low then sequentially increasing doses of allergens in patients with IgE mediated diseases

Duration of therapy –individually -3-4 and more years

The tolerance to triggers are restored

Immunotherapy

- Allergen skin testing should be considered to determine possible allergen triggers
- Highly effective; disease modifying
- Candidates
 - Moderate to severe symptoms
 - Lack of improvement with other modalities
 - Presence of comorbid conditions
 - Evidence of specific IgE sensitization based on testing
- Risk of anaphylaxis
- Oral drops and low dose (provocation-neutralization technique) immunotherapy have not been proven effective in clinical studies

Non-pharmacological interventions

- **Avoidance of tobacco smoke exposure**
 - Provide advice and resources at every visit; advise against exposure of children to environmental tobacco smoke (house, car)
- **Physical activity**
 - Encouraged because of its general health benefits. Provide advice about exercise-induced bronchoconstriction
- **Occupational asthma**
 - Ask patients with adult-onset asthma about work history. Remove sensitizers as soon as possible. Refer for expert advice, if available
- **Avoid medications that may worsen asthma**
 - Always ask about asthma before prescribing NSAIDs or beta-blockers
- **(Allergen avoidance)**
 - (Not recommended as a general strategy for asthma)
- **See GINA Box 3-9 and online Appendix for details**

Treating modifiable risk factors

- **Provide skills and support for guided asthma self-management**
 - This comprises self-monitoring of symptoms and/or PEF, a written asthma action plan and regular medical review
- **Prescribe medications or regimen that minimize exacerbations**
 - ICS-containing controller medications reduce risk of exacerbations
 - For patients with ≥ 1 exacerbations in previous year, consider low-dose ICS/formoterol maintenance and reliever regimen*
- **Encourage avoidance of tobacco smoke (active or ETS)**
- **For patients with severe asthma**
 - Refer to a specialist center for consideration of add-on medications and/or sputum-guided treatment
- **For patients with confirmed food allergy:**
 - Appropriate food avoidance
 - Ensure availability of injectable epinephrine for anaphylaxis

*Approved only for low dose beclometasone/formoterol and low dose budesonide/formoterol

Identify patients at risk of asthma-related death

- Patients at increased risk of asthma-related death should be identified
 - Any history of near-fatal asthma requiring intubation and ventilation
 - Hospitalization or emergency care for asthma in last 12 months
 - Not currently using ICS, or poor adherence with ICS
 - Currently using or recently stopped using OCS
 - (indicating the severity of recent events)
 - Over-use of SABAs, especially if more than 1 canister/month
 - Lack of a written asthma action plan
 - History of psychiatric disease or psychosocial problems
 - Confirmed food allergy in a patient with asthma
- Flag these patients for more frequent review

Assessing control

“well-controlled” asthma

- daytime symptoms less than 2 days per week
- night awakenings secondary to asthma less than 2 times per month
- ability to perform activities without limitations
- less than 2 steroid bursts per year
- FEV_1 greater than or equal to 80% predicted
- FEV_1/FVC 80% (>5 years old) and 85% (< 5y.o)



New medications (cytokine modifiers) in asthma therapy..

Experimental stage.

- **Agonists PPAR γ** (Peroxisome proliferator-activated receptor gamma) antiinflammatory.
- **Inhibitor of Mastocyte cells**
- **Stem Cells Factor (SCF)**
- **Inhibitor of spleen and thyroid Kinase - SYK**
(Spleen tyrosine kinase)
- Antagonist, inhibitors
- Anti PG –LT-IL- TNF- α (tumor necrosis factor),
- **Phosphodiesterase Inhibitoris**
- **Kinase Inhibitors**
- Adhesie **Molecular** Blockators and other under experimental study

> 50 citokins are important in BA

10. Prognosis

- Some findings suggest a poor prognosis if asthma develops in children younger than 3 years, unless it occurs solely in association with viral infections.
- Individuals who have asthma during childhood have significantly lower forced expiratory volume in 1 second (FEV₁), higher airway reactivity, and more persistent bronchospastic symptoms than those with infection-associated wheezing.
- Children with mild asthma who are asymptomatic between attacks are likely to improve and be symptom-free later in life.
- Children with asthma appear to have less severe symptoms as they enter adolescence, but half of these children continue to have asthma.
- Asthma has a tendency to remit during puberty, with a somewhat earlier remission in girls. However, compared with men, women have more BHR.

11. Primary prevention of asthma

- **The development and persistence of asthma are driven by gene-environment interactions**
 - *For children, a ‘window of opportunity’ exists in utero and in early life, but intervention studies are limited*
- **For intervention strategies including allergen avoidance**
 - Strategies directed at a single allergen have not been effective
 - Multifaceted strategies may be effective, but the essential components have not been identified

Current recommendations for asthma prevention are:

- Avoid exposure to tobacco smoke in pregnancy and early life
- Encourage vaginal delivery
- Advise breast-feeding for its general health benefits
- Where possible, avoid use of paracetamol (acetaminophen) and broad-spectrum antibiotics in the first year of life

12. Asthma Education

- Define asthma and explain treatment options
- Need to adhere to treatment plan
- Discuss patient's fear about asthma and its treatment
- Conduct regularly scheduled follow-up office visits
- Provide written asthma action plan
 - Treatment schedule, peak flow zones, and emergency numbers

Asthma Control Test™



Know your asthma score – ACT now

Step 1: Circle your score for each question and write the number in the box. Please answer as honestly as possible. This will help you and your doctor discuss what your asthma is really like.



In the **past 4 weeks**, how much of the time did your asthma keep you from getting as much done at work, school or home?

All of the time	1	Most of the time	2	Some of the time	3	A little of the time	4	None of the time	5	SCORE
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During the **past 4 weeks**, how often have you had shortness of breath?

More than once a day	1	Once a day	2	3 to 5 times a week	3	Once or twice a week	4	Not at all	5	
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During the **past 4 weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	1	2 to 3 nights a week	2	Once a week	3	Once or twice	4	Not at all	5	
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During the **past 4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as salbutamol)?

3 or more times per day	1	1 or 2 times per day	2	2 or 3 times a week	3	Once a week or less	4	Not at all	5	
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How would you rate your **asthma control** during the **past 4 weeks**?

Not controlled	1	Poorly controlled	2	Somewhat controlled	3	Well controlled	4	Completely controlled	5	
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2: Add up your score to get your total.

TOTAL

3: See below to find out what your score means.

Score: 25 – Congratulations!

You have **TOTAL CONTROL** of your asthma. You have no symptoms and asthma-related limitations. Continue your treatment as prescribed by your doctor and see your doctor or nurse if your condition changes.

Score: 20 to 24 – On Target

Your asthma may be **WELL CONTROLLED** but not **TOTALLY CONTROLLED**. Continue your treatment as prescribed by your doctor and see your doctor or nurse as they may be able to help you aim for **TOTAL CONTROL**.

Score: less than 20 – Off Target

Your asthma may **NOT BE CONTROLLED**. Your doctor or your nurse can recommend an asthma action plan to help improve your asthma control.



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