BRONCHIAL ASTHMA
IN CHILDREN

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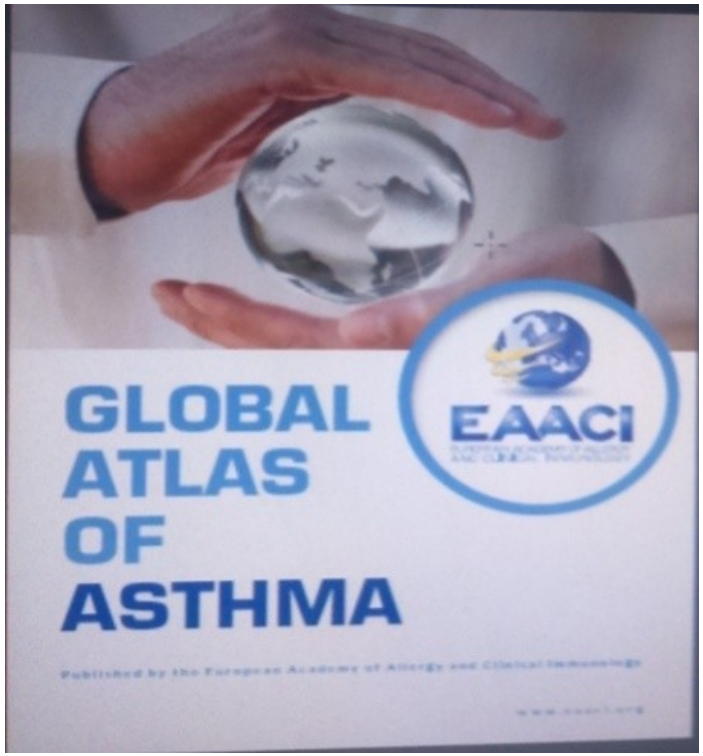


LESSON PLAN

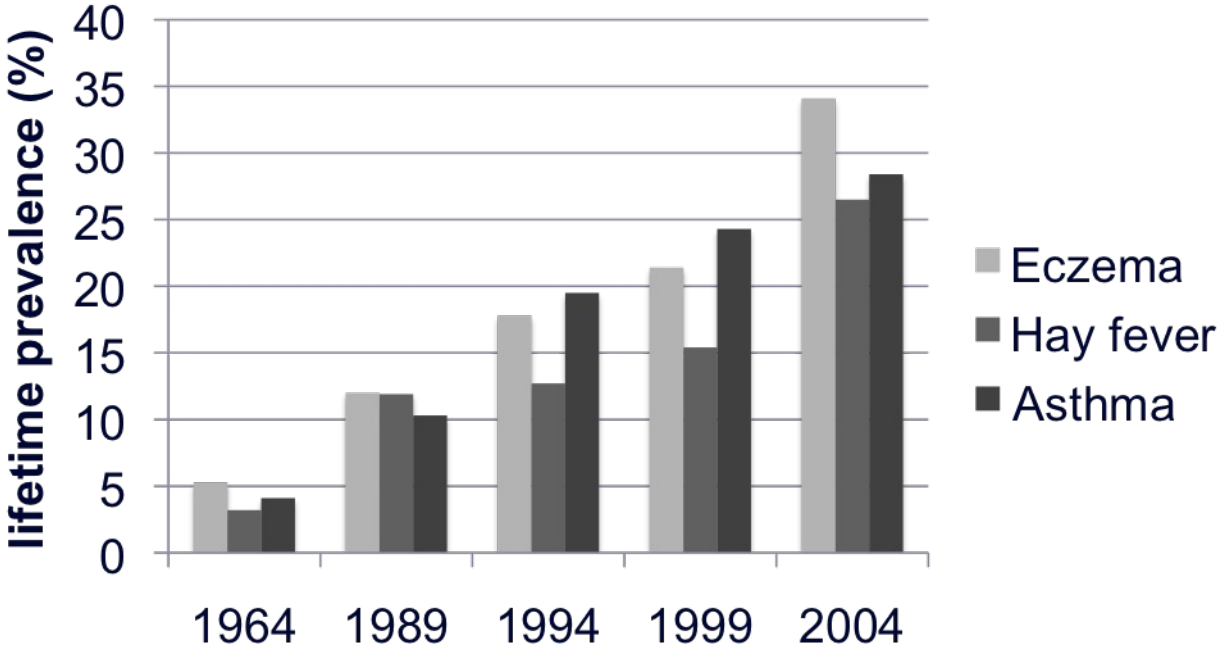
1. Background
2. Definition
3. Epidemiology
4. Risk factors, triggers, pathogenesis
5. Clinical signs
6. Diagnosis. Asthma Predictive index
7. Differential diagnosis
8. Asthma classification
9. Asthma therapy
   - 9.1. The “reliever” therapy, according to child age
   - 9.2. The “controller” therapy,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

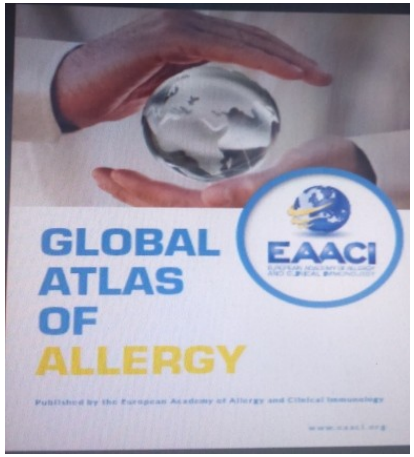
1. BACKGROUND

- 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 continuosly of the patients with allergic desease in developed countres

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





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

Burden of asthma

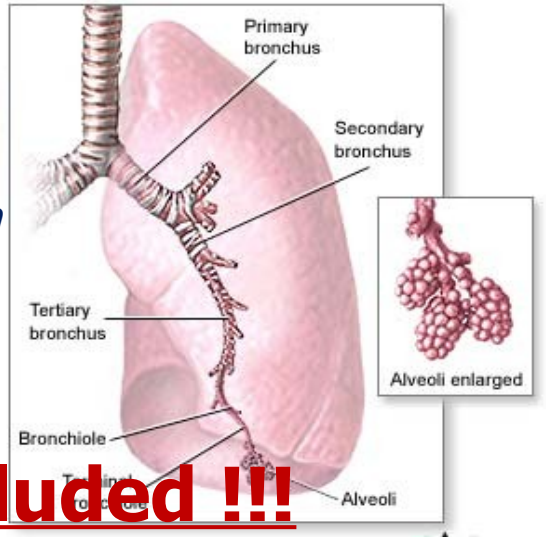
- Health care expenditure on asthma is very high
  - Developed economies might expect to spend 1-2 % of total health care expenditures on asthma.
  - Developing economies likely to face increased demand due to increasing prevalence of asthma
  - Poorly controlled asthma is expensive
  - However, investment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

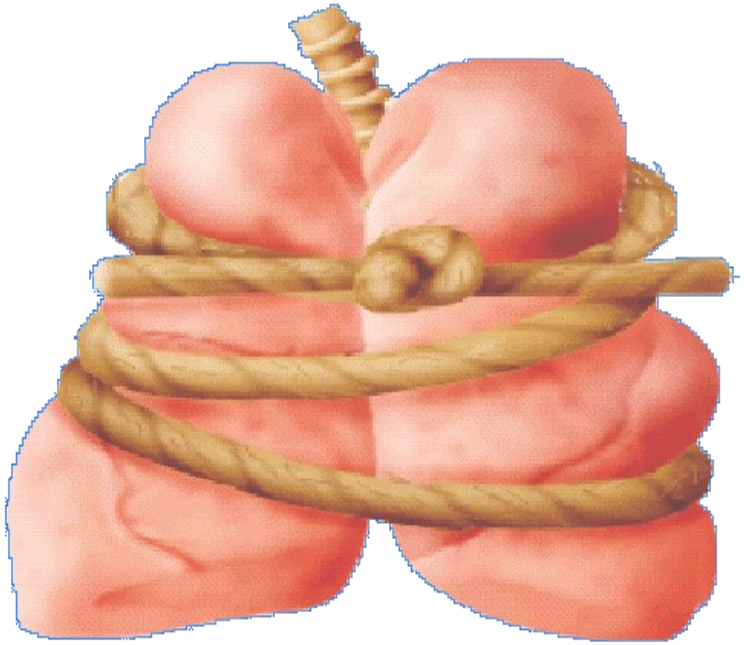
- ***Inflammation and edema***
- ***Bronchial smooth-muscle spasm***
- ***Mucous plugging***



AND

Alternative diagnoses are excluded !!!

3. EPIDEMIOLOGY

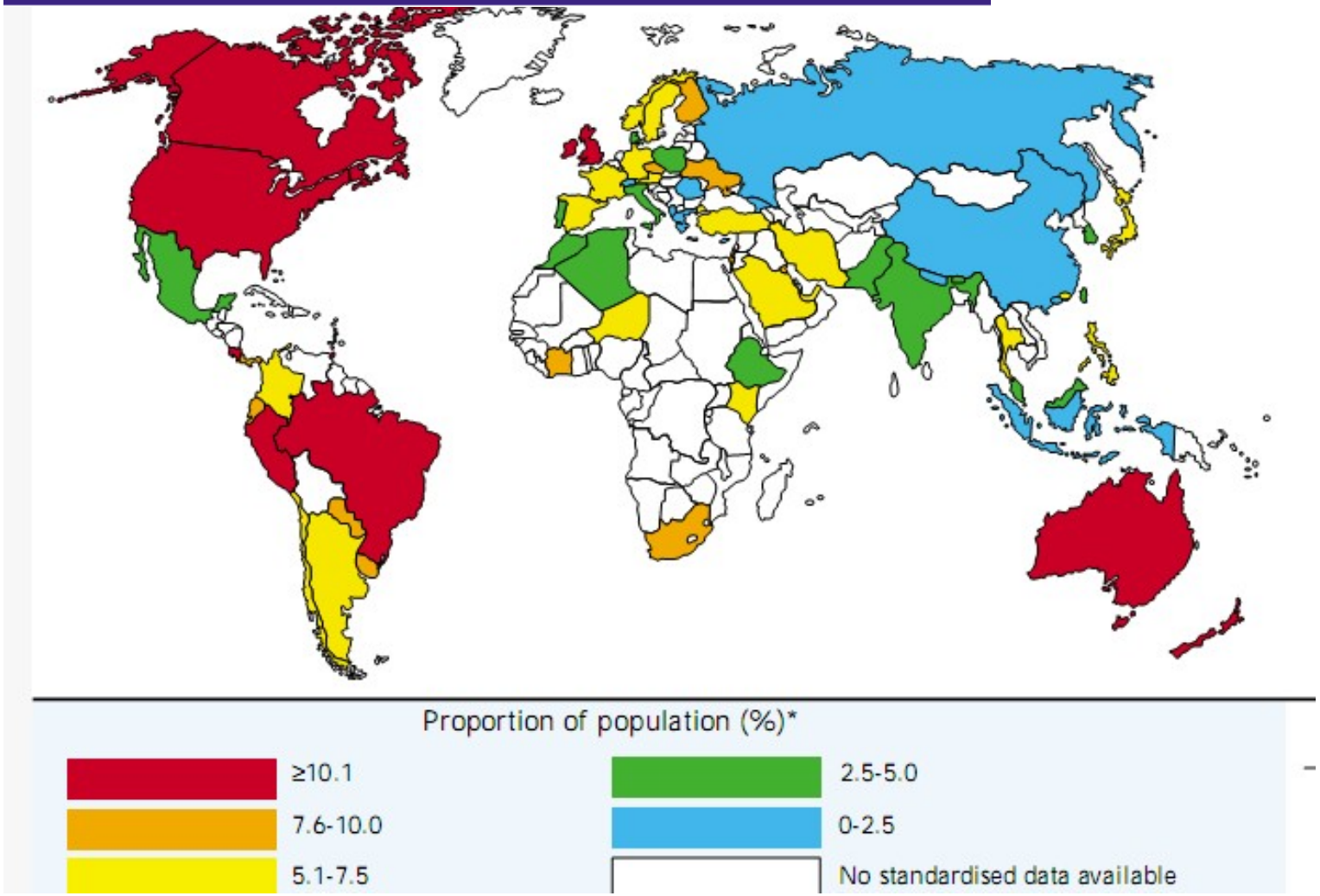


Asthma is a major cause of school and work absence

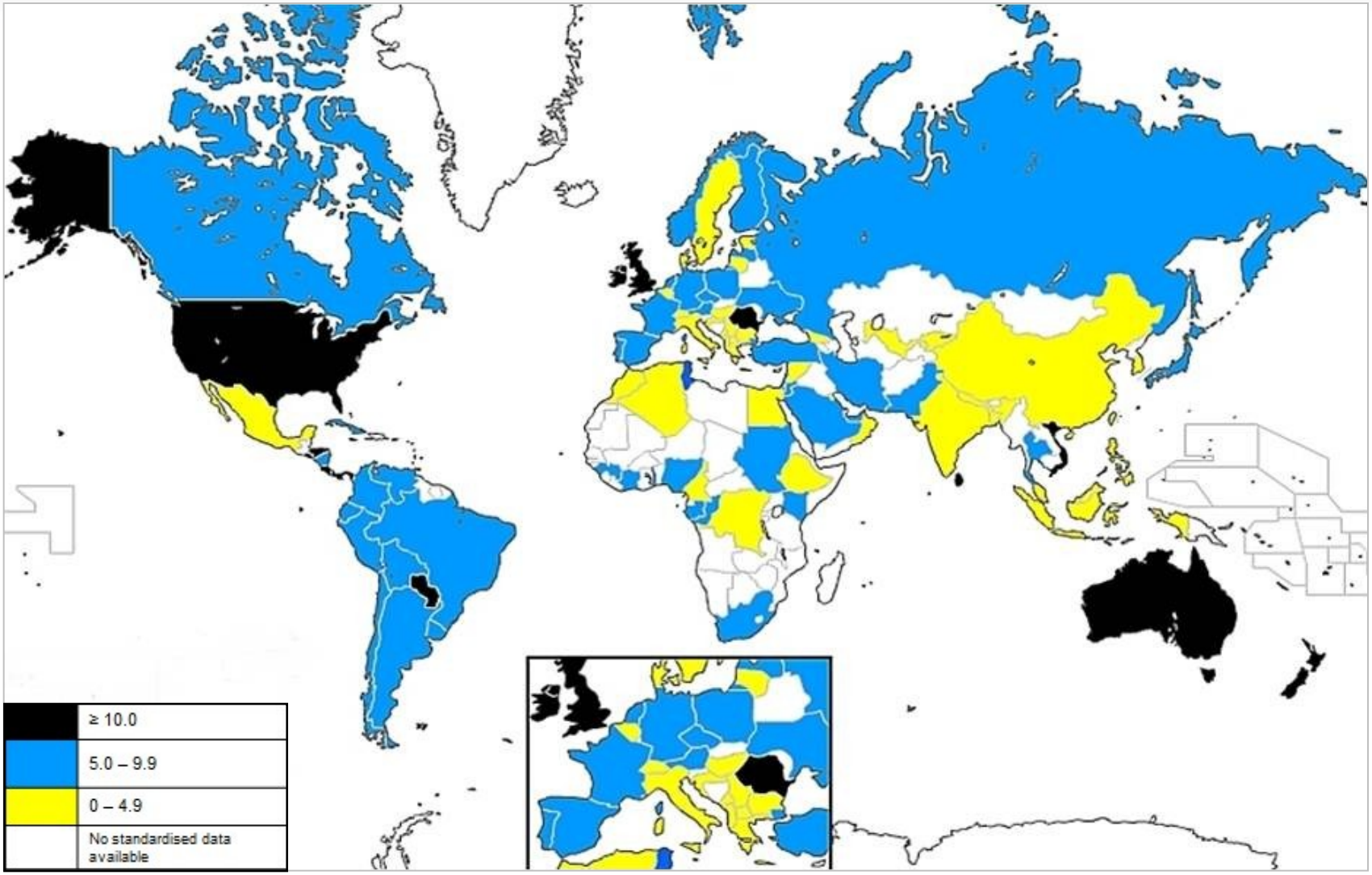
250,000Annually, the World Health Organization (WHO) has estimated that 15 million disability-adjusted life-years are lost and

asthma deaths are reported worldwide.[(2008).

World Map of the Prevalence of Clinical Asthma

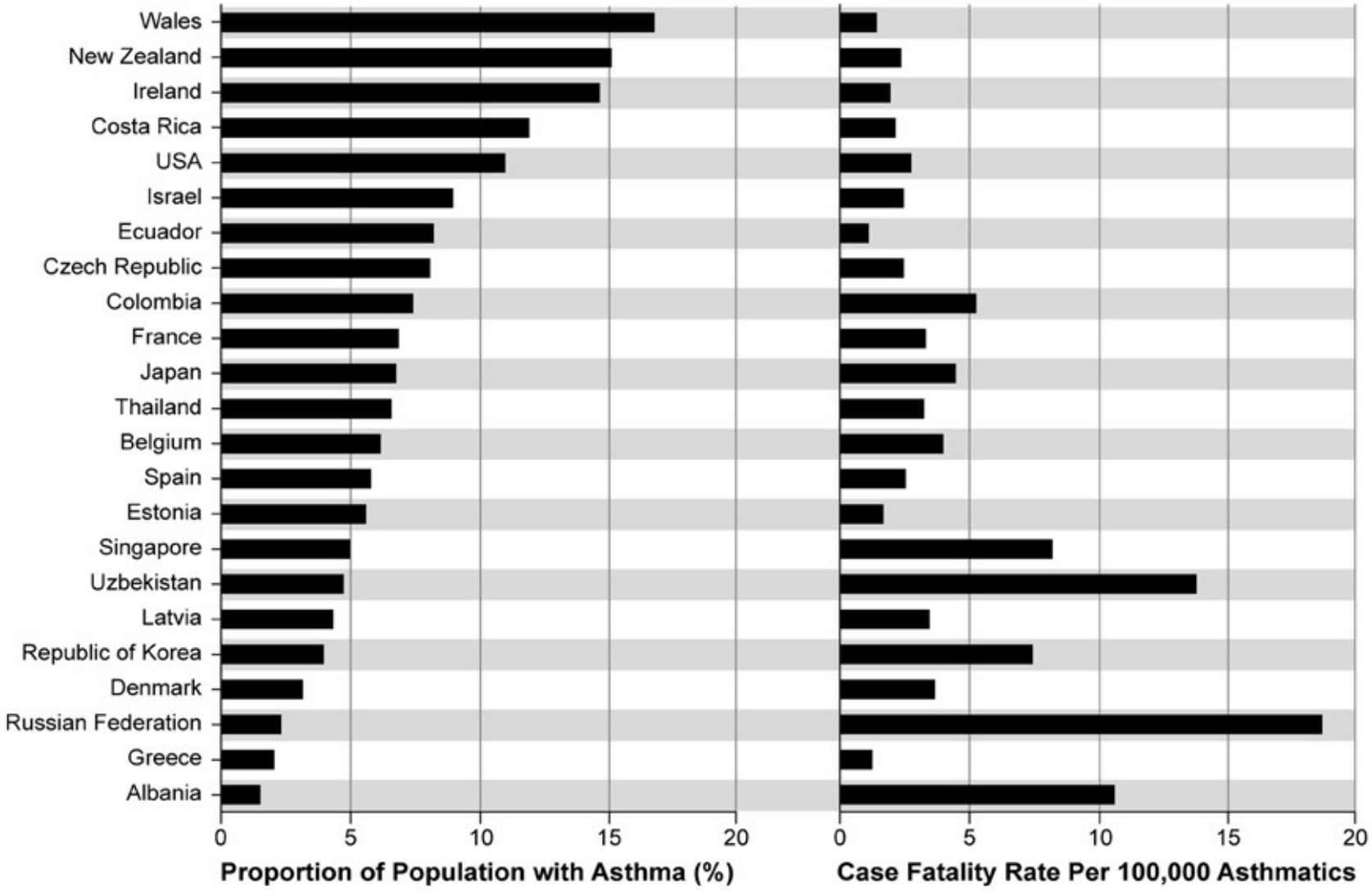


Prevalence of asthma in children aged 13-14 years



GINA 2015 Appendix Box A1-1; figure provided by R Beasley

Asthma: Prevalence, Mortality



Source: Masoli M et al. Allergy 2004

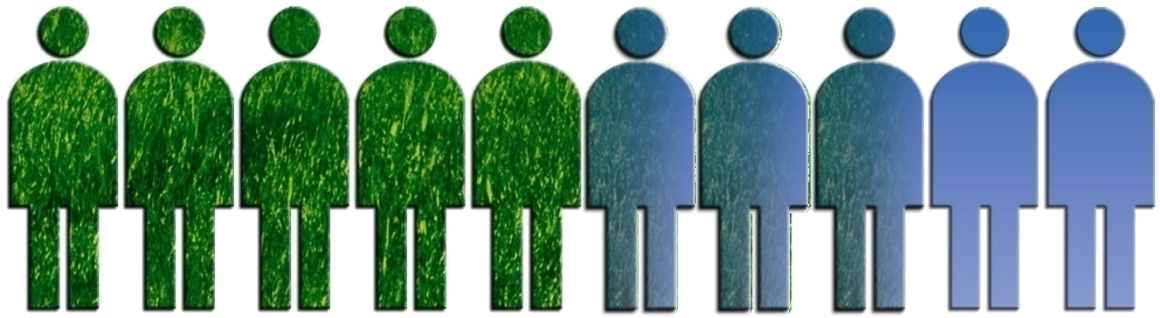
Incidence and prevalence differ from country to country

- **New Zeland about30%(<5y.o.)**
- **Australia 25%**
- **UK 10-15 %**
- **France 7-10%**
- **Ucraina 0,5%**
- **Moldova 0,1%**
  - **2015:1200-1500**

There is the problem with early detecti
astma in childhood

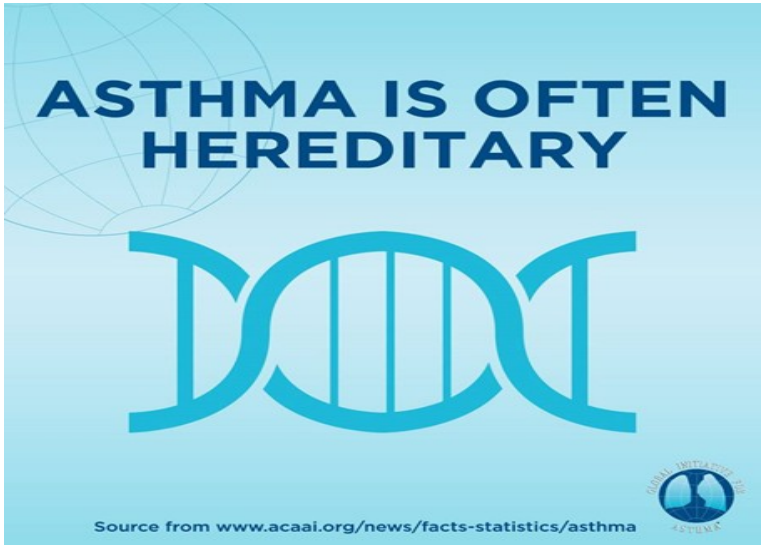
Asthma – the disease started in early age

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



Адаптировано из: Boner AL, Martinati LC *Eur Respir Rev* 1997;7:3–7; National Asthma Education and Prevention Program, 2003. Publication No. 02-5074.

4. RISK FACTORS, TRIGGERS, PATHOGENESIS



Host factors –

- Genetic

1. Genes predisposing to atopy

2. Genes predisposing to airway hyper responsiveness

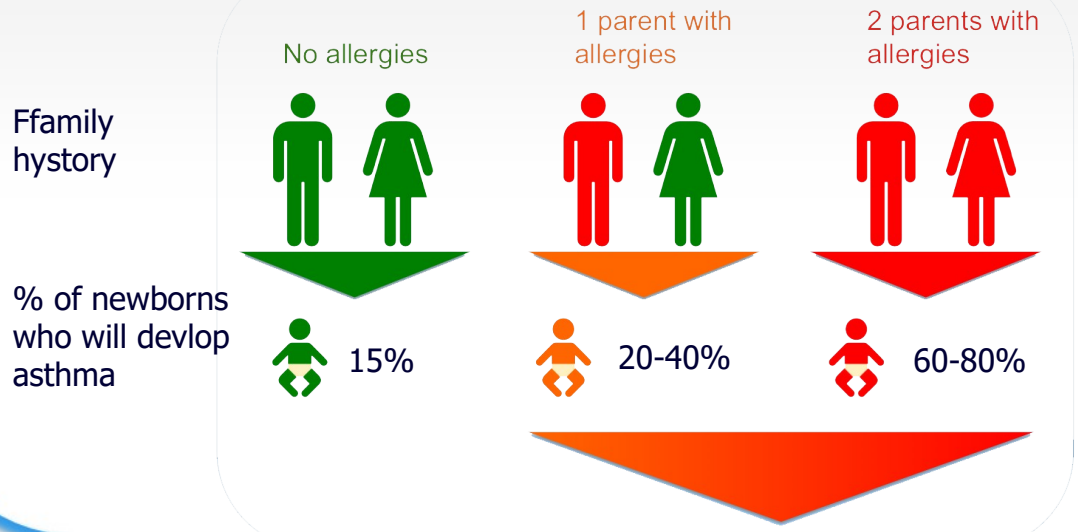
- Obesity
- Sex There are gender differences. ***Before puberty, the prevalence of asthma is 3 times higher in boys than in girls. During adolescence, the prevalence is equal among males and females. Adult-onset asthma is more common in women than in men.***

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

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

FH+ FH+ FH+

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

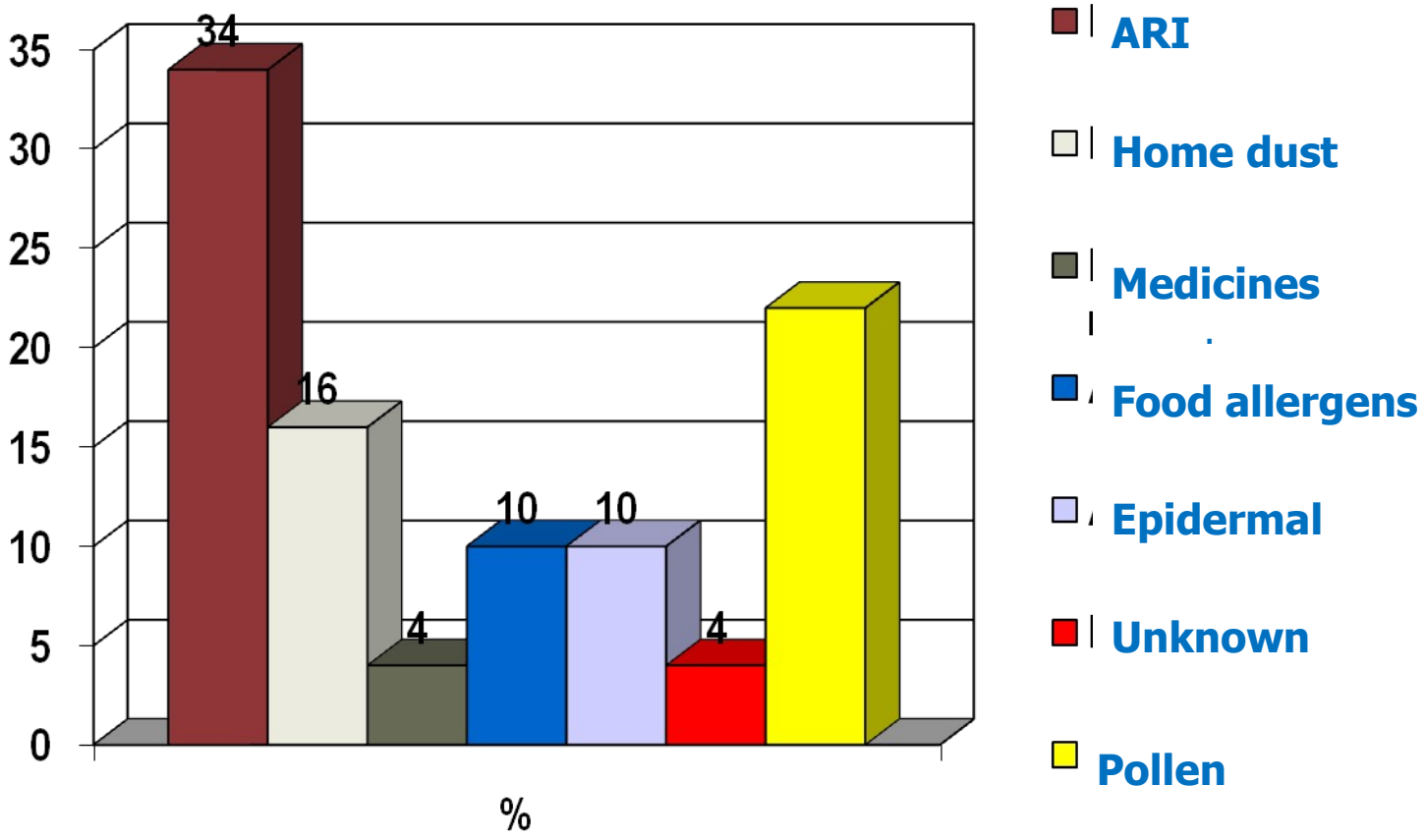
Bronhopulmonar dysplasia

3. **Environment pollution, cigarette smoking**

4. Gastroesofagal reflux (20-30%)

5. Socioeconomic problems

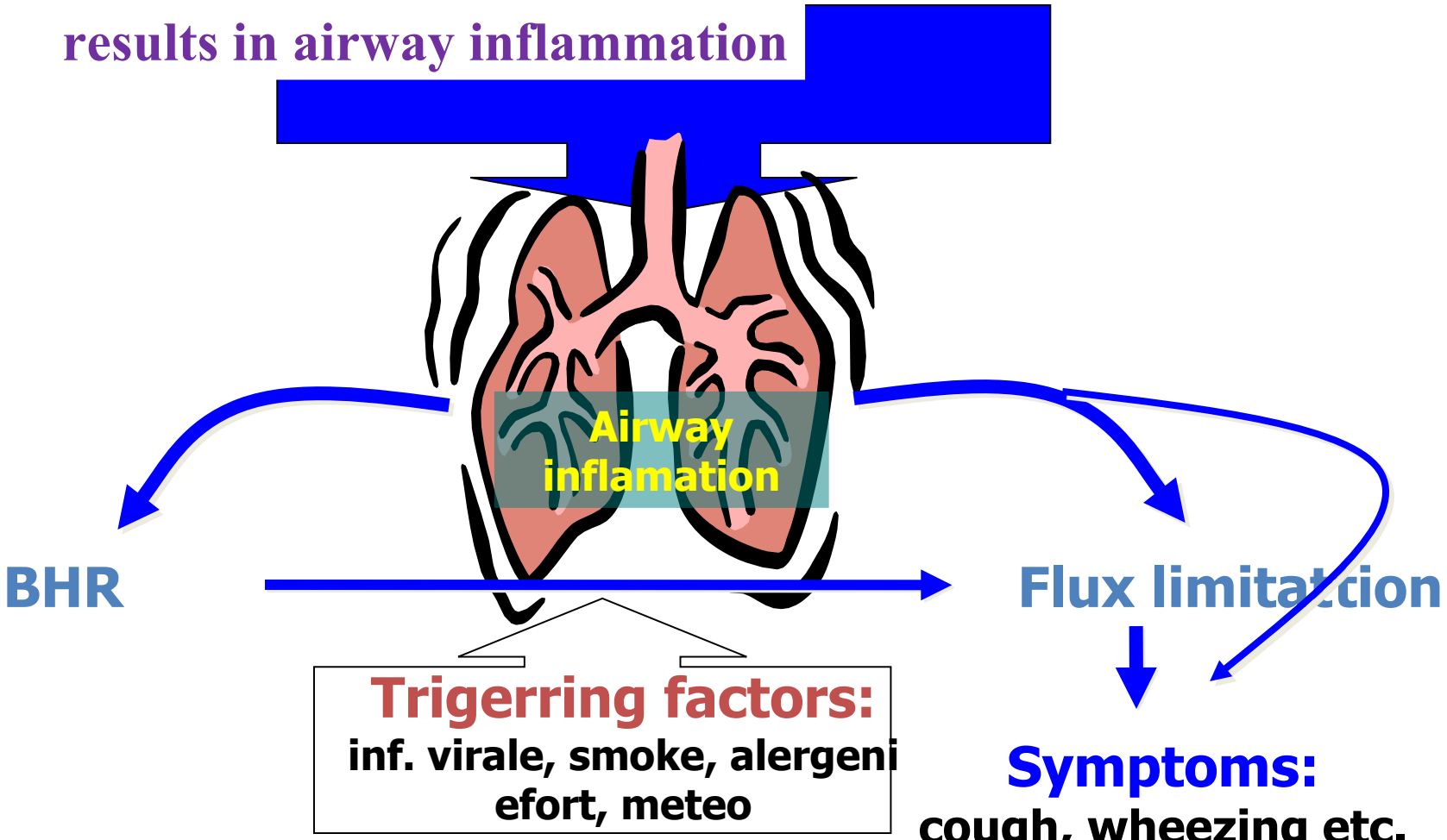
Comparative data about cause of exacerbation in BA collected from hystory (%)



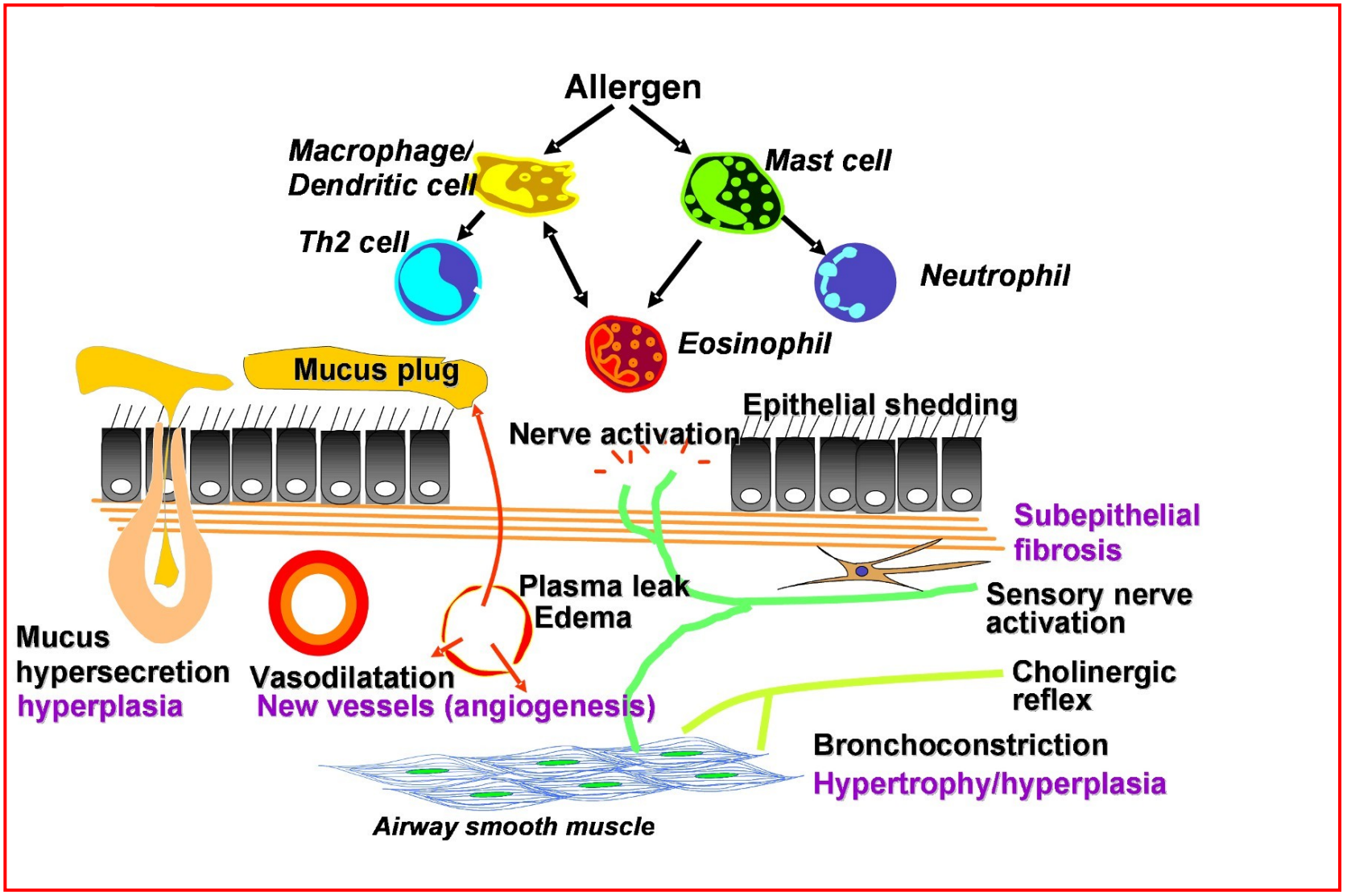
PATHOPHYSIOLOGY

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

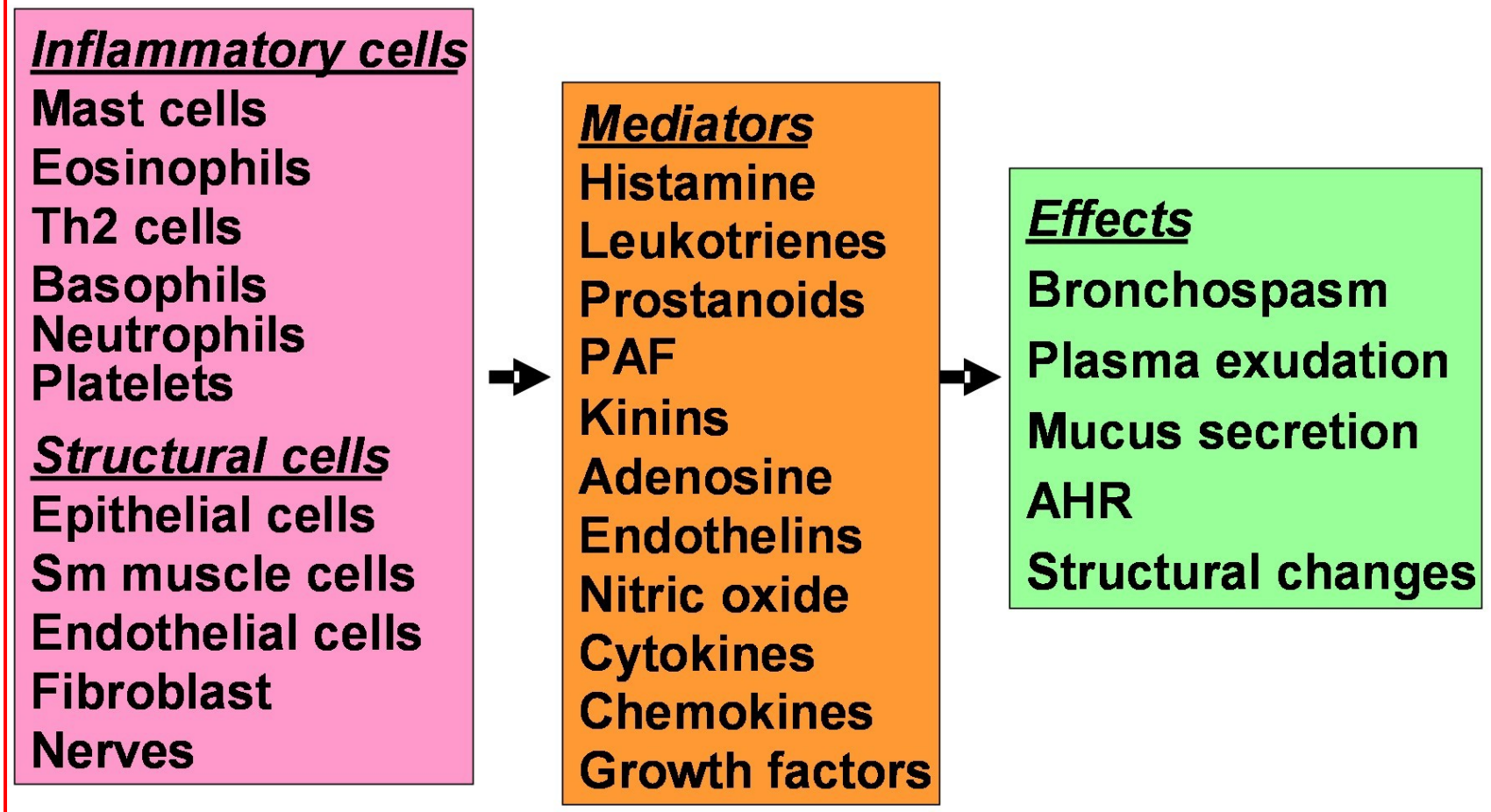
results in airway inflammation



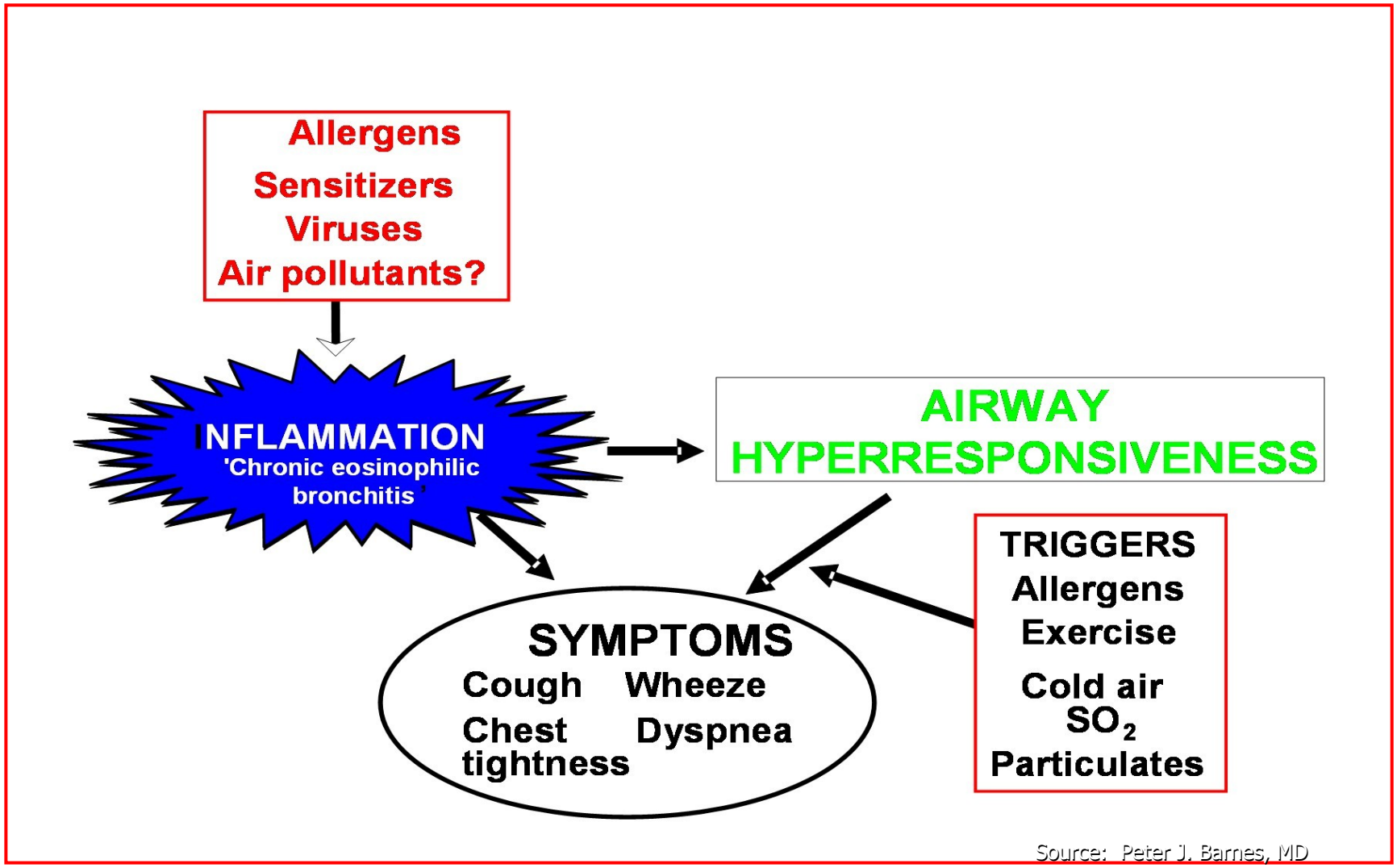
Asthma Inflammation – Cells and Mediators



Asthma Inflammation



Mechanism – Asthma Inflammation



Airway inflammation

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

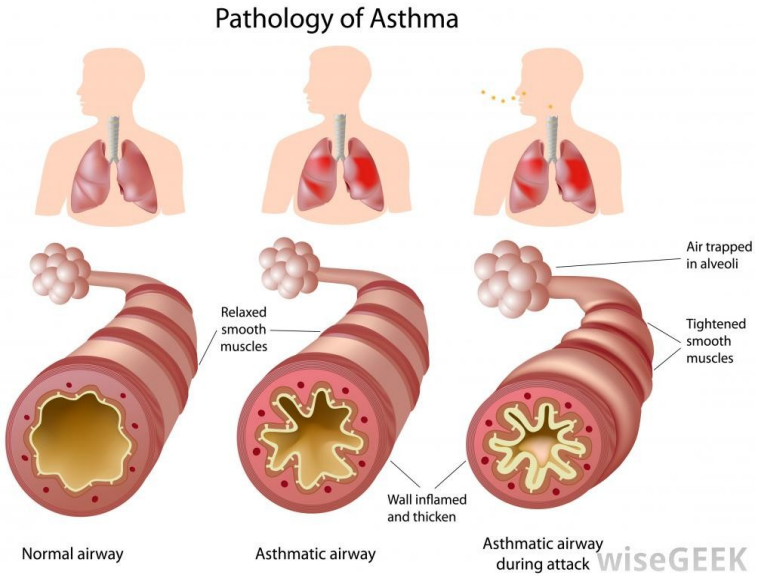
Two types of Th lymphocytes have been characterized: **Th1 and Th2.**

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.

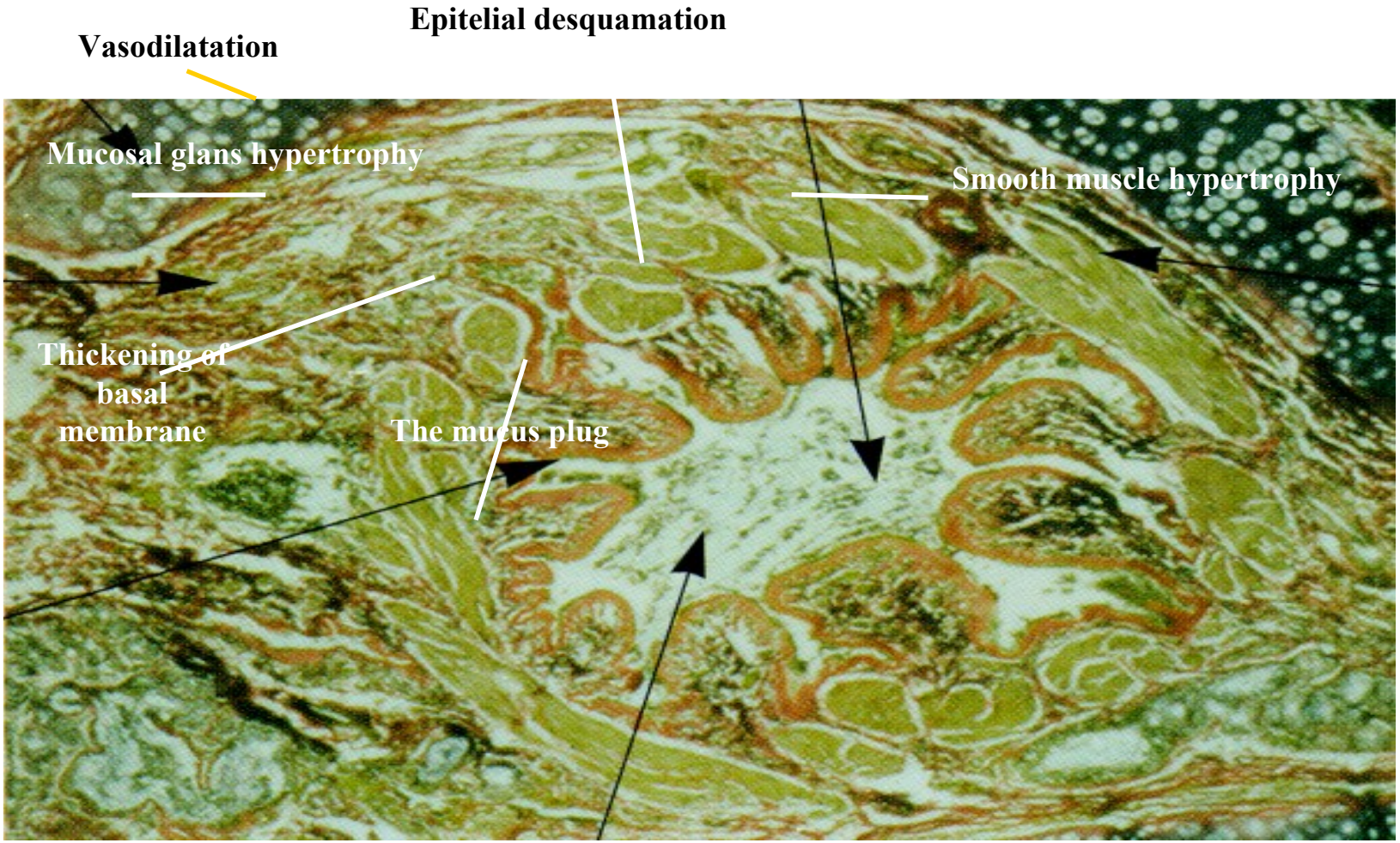
PATHOPHYSIOLOGY

- **Bronchospasm,**
- **Mucosal edema**



- **Mucus plugs (hyper secretion)**
- **Airway inflamation - the main pathophysiologic mechanism**

MORFOPATHOLOGIC MODIFICATION ÎN SEVERE ASTHMA



Natural History of Asthma, Current Issues in Respiratory Medicine, 1999

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

Asthma by Consensus, GINA 2015

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

Asthma by Consensus, GINA 2015

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) testin**
  - **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-gastroesophagal 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 bronhoobstructive exacerbation

- 1-3 hours with maximum of intensity of 10-20 minutes,
- could be solved spontaneusly 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

- Singns :
  - Anxiety, othopnea, cyanosis,transpiration
  - Thorax is enlarged, fixed in inspiration,
  - Hypersonority
  - Bronchial crackles, sibilant or subcrepitant
  - Low or lack of stetoacustic pulmonar modification due to reduced pulmonary function (air debits)
  - The liver and spleen are down

The end of the exacerbation producing the sensation of relief and improvement of functional pulmnary activity with expectoration of white)pearl) viscouse 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 bronhodilatators (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 PaO_2 < 60 mm Hg
- Hypercapnia $PaCO_2$ > 60 mm Hg
- Low % of Oxygen saturation

The severity of asthma exacerbation: classification

	mild	moderate	severe	Respiratory failure
Breathing	Can sleep Decubitus is posibil	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	bradicardy
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 asthm
- + 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.
- Hyperinflation may also cause an abdominal breathing pattern.
- Signs of atopy or allergic rhinitis, such as conjunctival congestion and inflammation may be present.

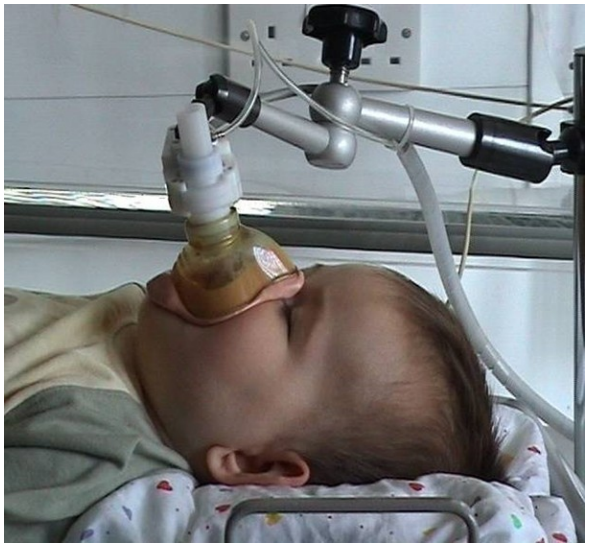
Diagnosis(continued)

- 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**

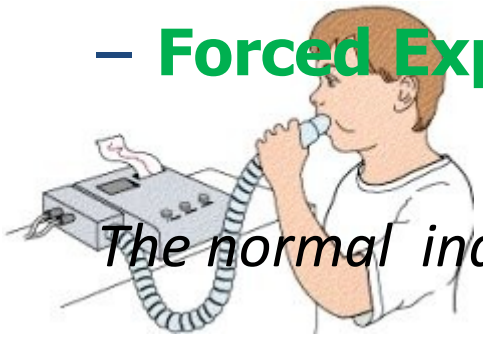


other:

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

- ***Pulmonary Function Tests***
- **SPIROMETRY: > 5 y.o.**
  - **Pulmon`s capacity:**

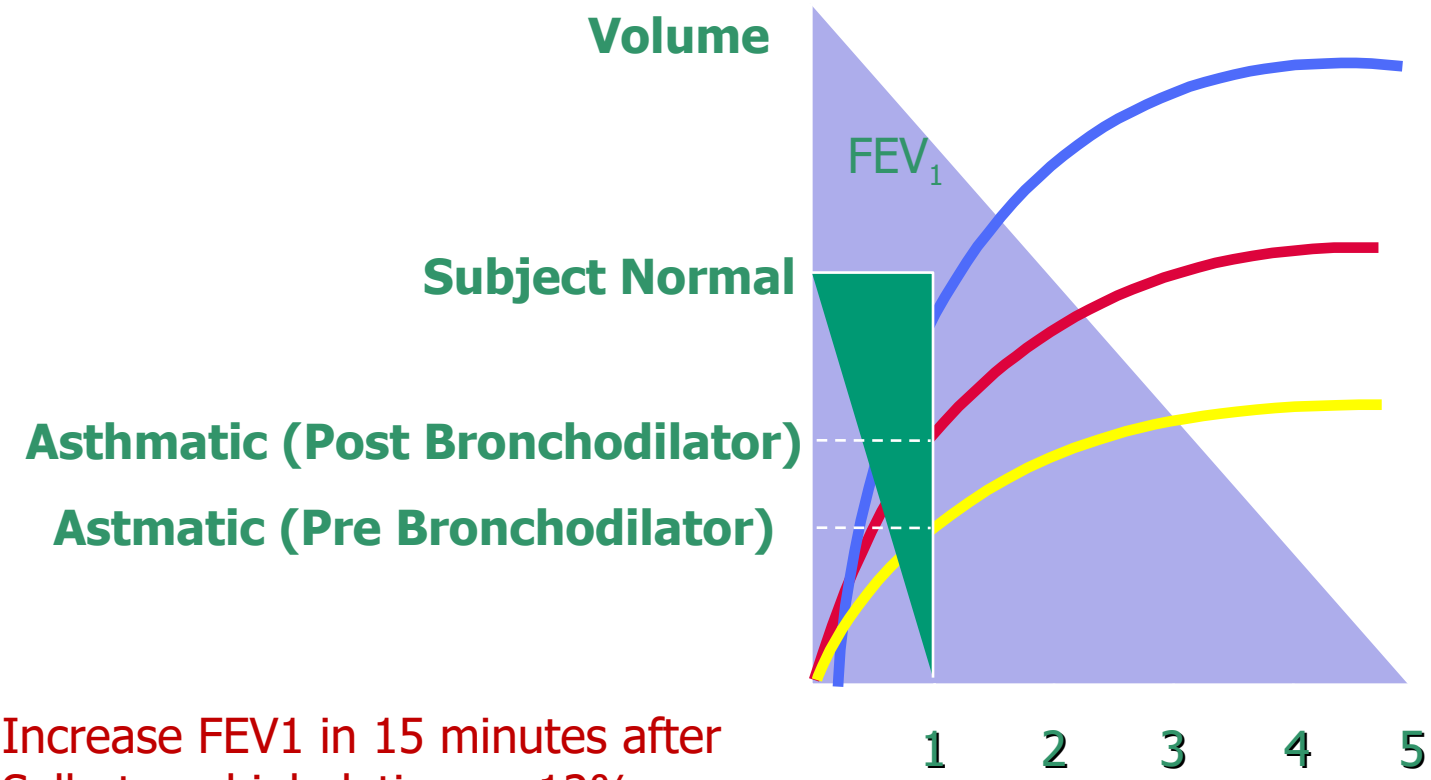
  - **PC-total vital capacity**
  - **FVC- forced vital capacity;**
  - **FEV_{1-} forced expiratory volume in 1 second;**
  - **Forced Expiratory Ratio (FEV1/FVC)**
  - **Forced Expiratory Flow (FEF 25% to 75%)**



The normal indices: > 80% reported to predicted normative

USB PC Spirometer

The typical changes in spirometry(FEV_1) after Salbutamol



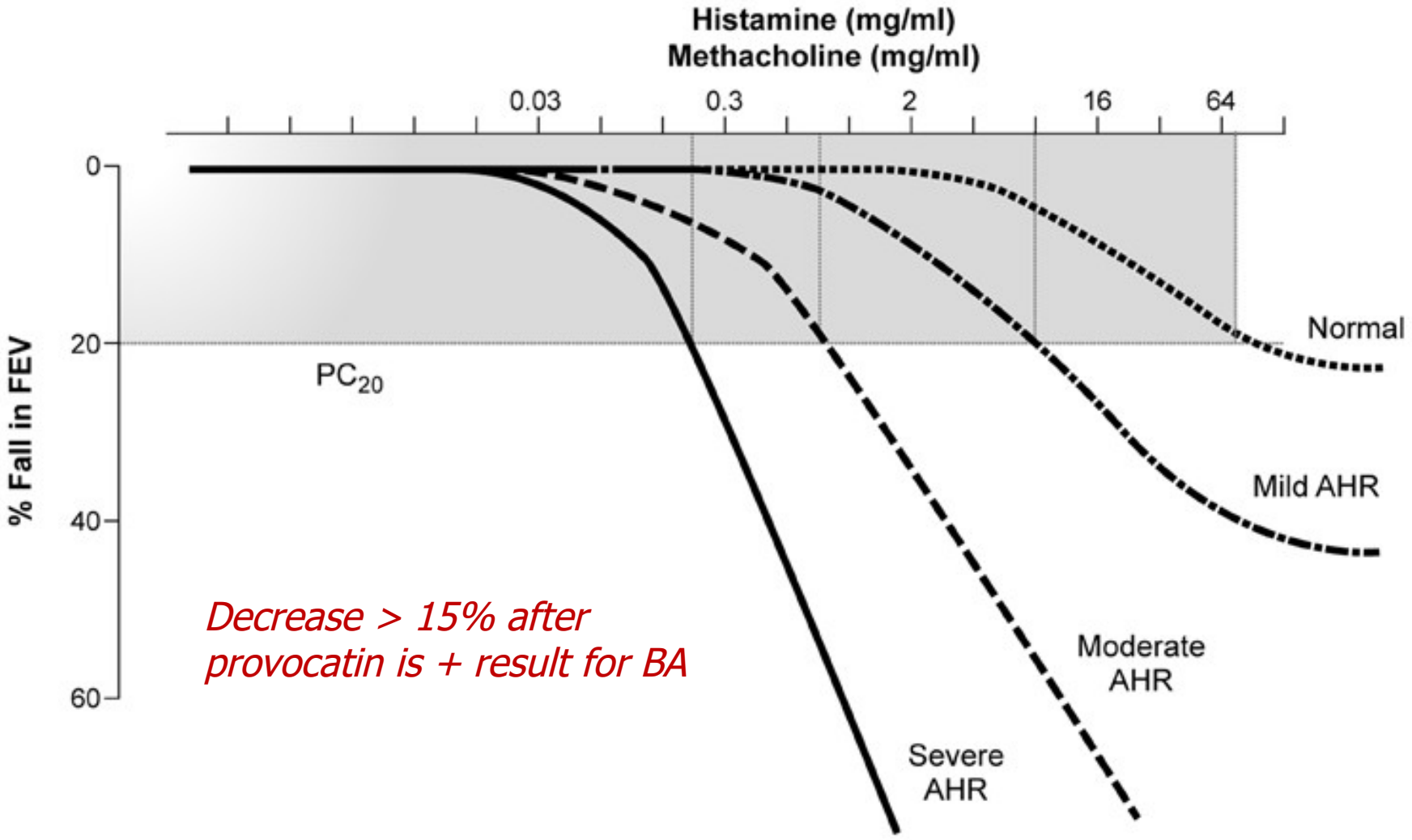
Increase FEV1 in 15 minutes after Salbutamol inhalation > 12% - pozsitive test for BA

Nota: Each curve represented the FEV_1 of 3consecutive 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 bron chospasm.**

Bronchial hyperreactivity – provocation test



Decrease > 15% after provocatin is + result for BA

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

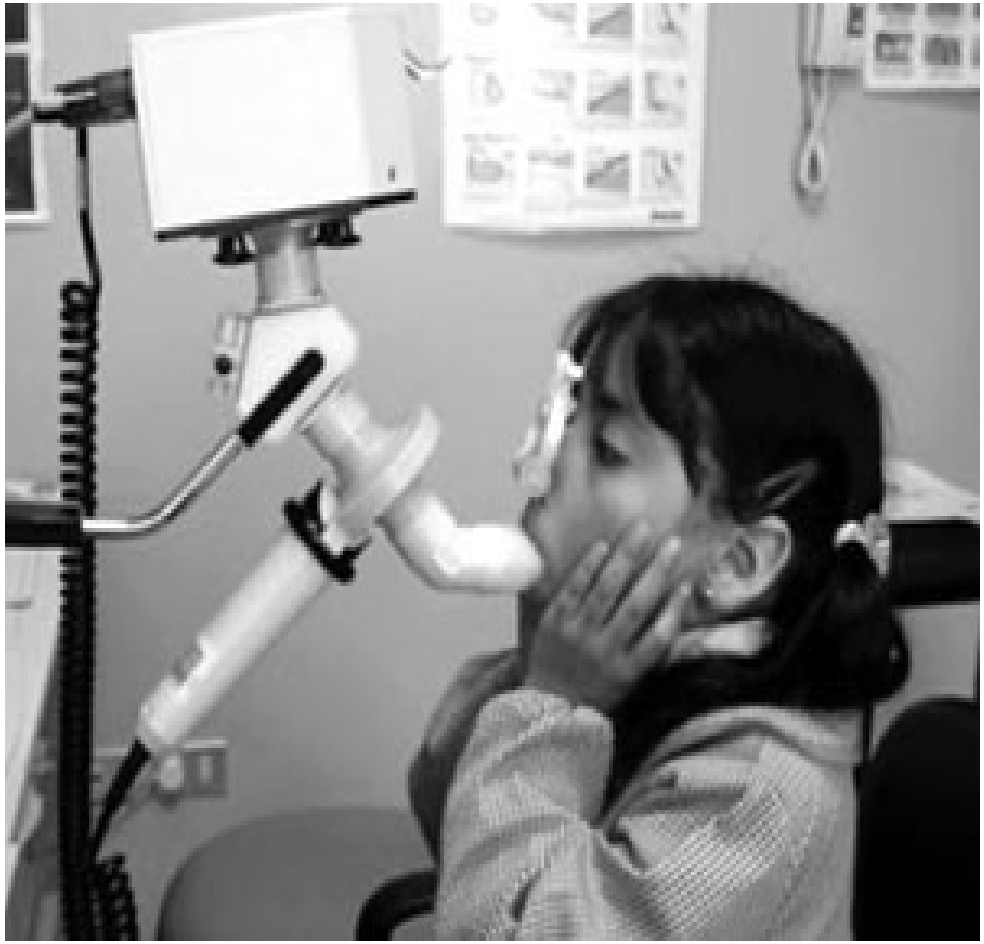
PEF variation (between eveneng and morning) >20% is consistent with uncontrolled asthma

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 ≥12%** or ≥200 mL[*]

Exercise challenge

- **Worsening in FEV1 ≥15%**[*]

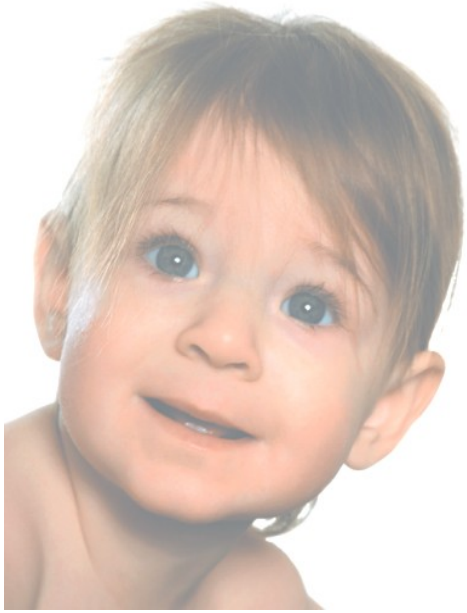
Daily peak flow or FEV 1 monitoring: day to day and/or AM-to-PM variation **≥20%**[*]

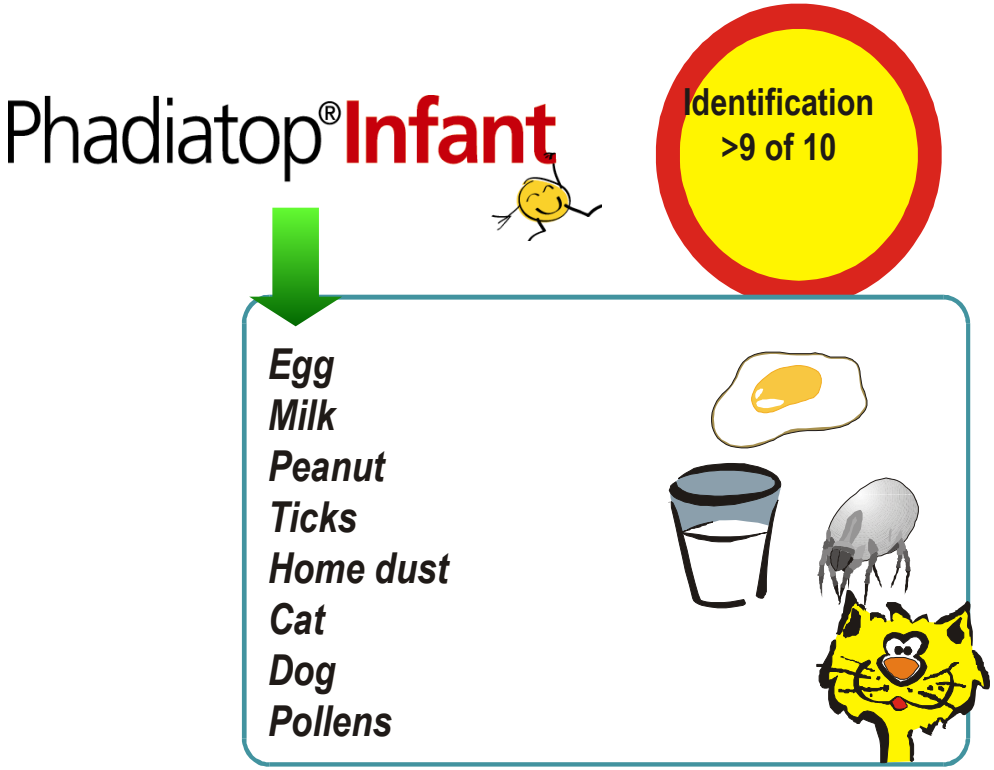
FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity.

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.





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

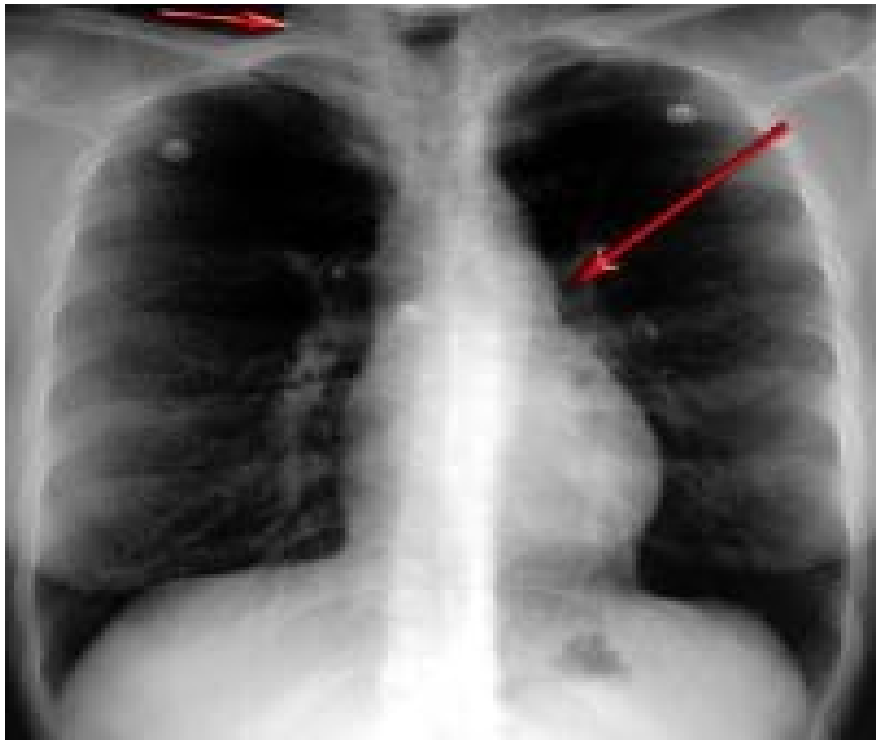
- Include chest radiography in the initial workup if the asthma does not respond to therapy as expected. In addition to typical findings of hyperinflation and increased bronchial markings, a chest radiograph may reveal evidence of parenchymal disease, atelectasis, pneumonia, congenital anomaly, or a foreign body.

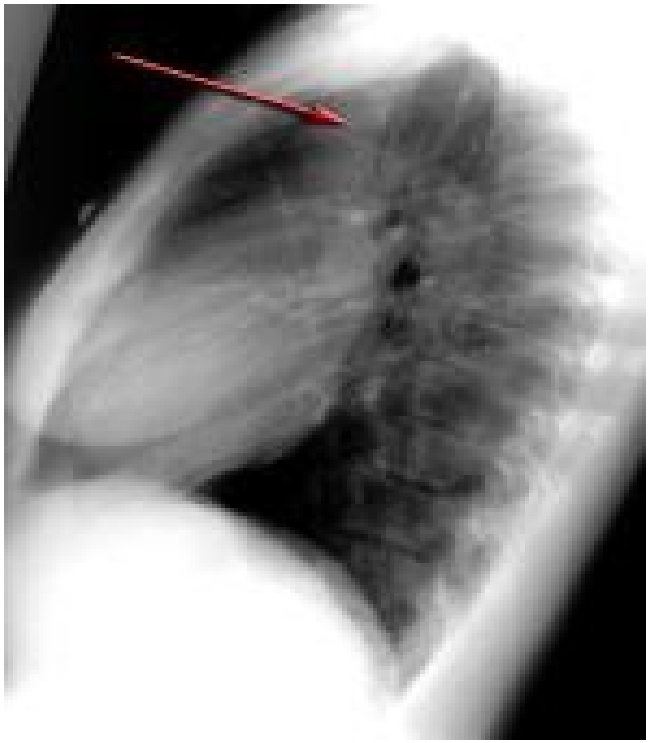
- In a patient with an acute asthmatic episode that responds poorly to therapy, a chest radiograph helps in the diagnosis of complications such as pneumothorax or pneumomediastinum.
- Consider using sinus radiography and CT scanning to rule out sinusitis.

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.

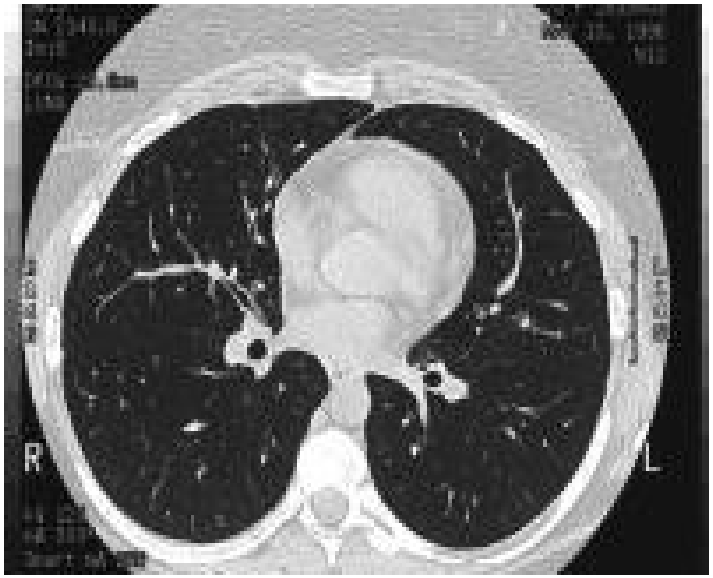
Lateral chest radiograph demonstrates **a pneumomediastinum** in bronchial asthma. Air is noted anterior to the trachea (same patient as in the previous image).

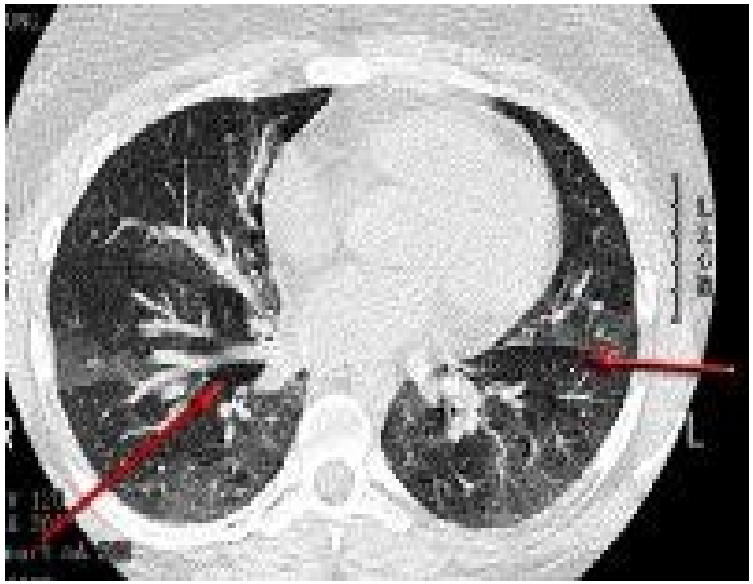




Asthma. **High-resolution CT** scan of the thorax obtained during inspiration demonstrates airtrapping in a patient with asthma. **Inspiratory findings are normal.**

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
  - Spontaneusly pneumotorax
  - Subcutaneus Emphysema
  - Mediastinal Emphysema
  - Rib Fractures
  - Segmental atelectasis (due to mucus plug)
- Late
  - Bronchi superinfection
  - Intercurrent Pneumonia

Iatrogenic

- Steroid abuse
  - Corticodependence
  - Kushingoid Syndrom
  - Osteoporosis
  - Arterial hypertnsion
  - Ulcer
  - Infections
- Beta-adrenergic abuse
  - Iritability
  - Digital Tremor
  - Muscular Cramps
  - Tachycardie, extrasystolia
  - Arterial hypertension
- Aminophylin abuse
  - Anxiety, iritability, 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

- <u>One major criterion</u>
  - Parent with asthma
  - Atopic dermatitis
  - Aero-allergen sensitivity

OR

- <u>Two minor criteria</u>
  - Food sensitivity
  - Peripheral eosinophilia (≥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; situsinversus (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 disfunction	
Pulmonary edema	
Collagen vascular disease	
Reactive airway disease	

GINA - Global Initiative for Asthma

Consensus on Asthma since 1992

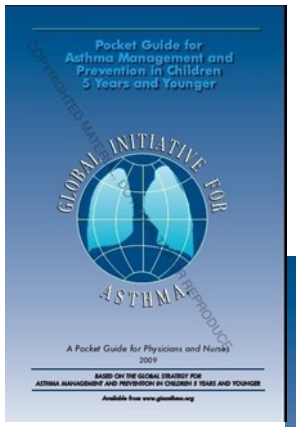
Global Strategy for Asthma Management and Prevention 2015

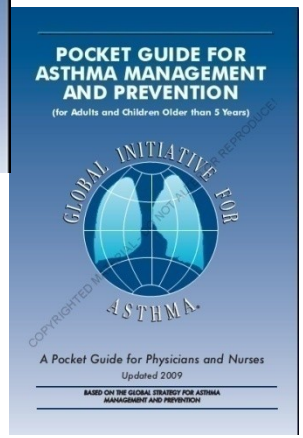
GINA proposes the Guides on Asthma Management .

Each 2 years are updated

The last – 2019

www.ginasthma.org





The Global Initiative for Asthma (GINA)

- GINA was established by the WHO and NHLBI in 1993
  - To increase awareness about asthma
  - To improve asthma prevention and management through a coordinated worldwide effort
  - GINA is independent, funded only by the sale and licensing of its reports and figures
- The GINA report is a global evidence-based strategy that can be adapted for local health systems and medicine availability
  - ~500,000 copies of GINA reports downloaded each year from 100 countries
  - Practical focus: multiple flow-charts and tables
- The GINA strategy report is updated every year
  - Twice-yearly cumulative review of new evidence across the whole asthma strategy
  - The Science Committee reviews published GRADE reviews, when available
  - Careful attention is paid to clinical relevance of study designs and generalizability of populations
  - Extensive external review before publication
- For detailed description of GINA methodology, see www.ginasthma.com/aboutus/methodology

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❑ No❑	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma? Yes❑ No❑			
• Reliever needed for symptoms* more than twice a week? Yes❑ No❑			
• Any activity limitation due to asthma? Yes❑ No❑			

* 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 FEV_1 (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:

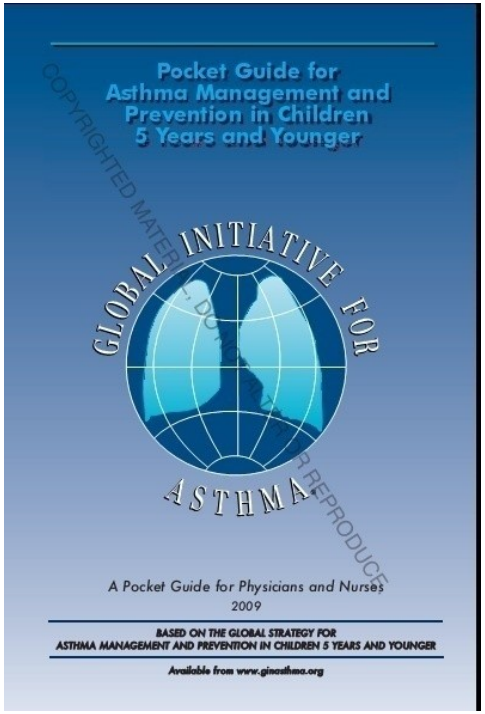
- No ICS treatment, smoking, occupational exposure, mucus hypersecretion, blood eosinophilia

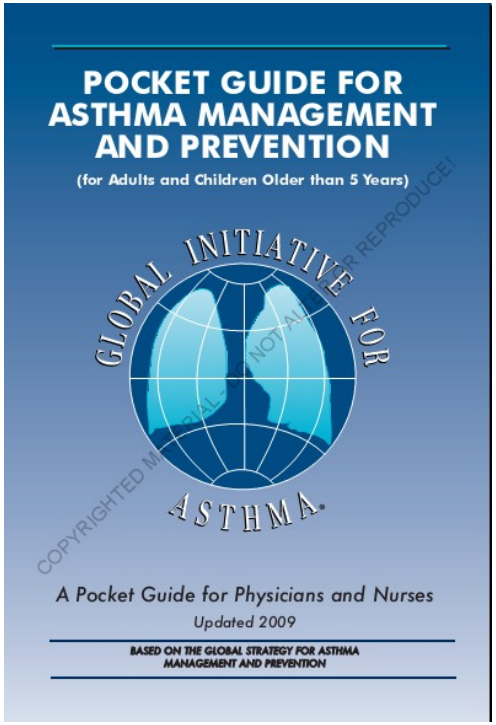
GINA 2015, Box 2-2B (3/4)

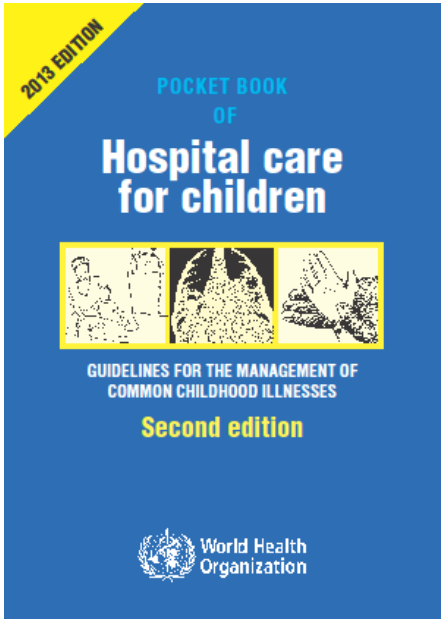
9. ASTHMA THERAPY

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

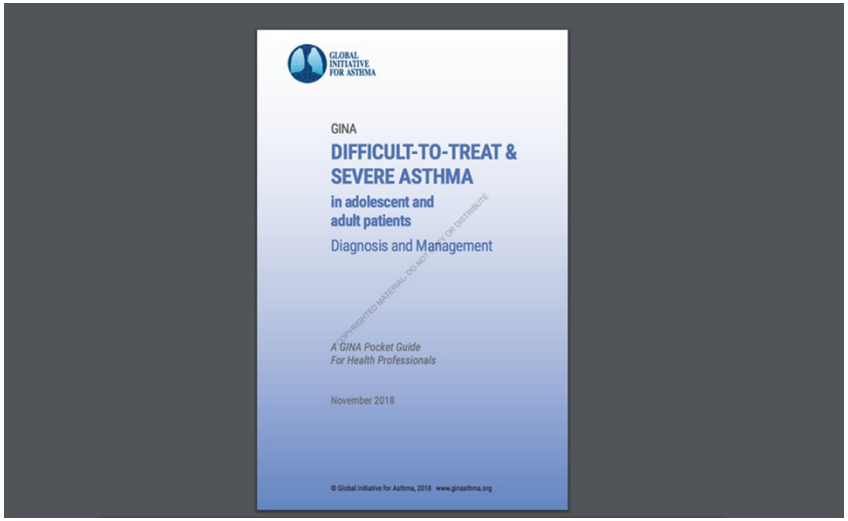

Pocket Guide for
Asthma Management and
Prevention in Children
5 Years and Younger
GLOBAL INITIATIVE FOR ASTHMA
A Pocket Guide for Physicians and Nurses
2009
BASED ON THE GLOBAL STRATEGY FOR
ASTHMA MANAGEMENT AND PREVENTION IN CHILDREN 5 YEARS AND YOUNGER
Available from www.ginasthma.org


POCKET GUIDE FOR
ASTHMA MANAGEMENT
AND PREVENTION
(for Adults and Children Older than 5 Years)
GLOBAL INITIATIVE FOR ASTHMA
A Pocket Guide for Physicians and Nurses
Updated 2009
BASED ON THE GLOBAL STRATEGY FOR ASTHMA
MANAGEMENT AND PREVENTION


2013 EDITION
POCKET BOOK
OF
Hospital care
for children
GUIDELINES FOR THE MANAGEMENT OF
COMMON CHILDHOOD ILLNESSES
Second edition
World Health
Organization


Allergy
SUPPLEMENT
Allergic Rhinitis and its Impact on
Asthma (ARIA) 2008


Allergy


GLOBAL INITIATIVE FOR ASTHMA
GINA
DIFFICULT-TO-TREAT &
SEVERE ASTHMA
in adolescent and
adult patients
Diagnosis and Management
A GINA Pocket Guide
For Health Professionals
November 2018

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
- Ipratrpium bromid
- Methyxantines, 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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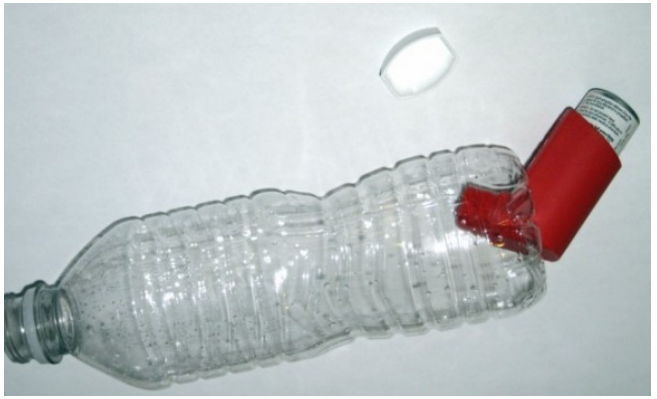
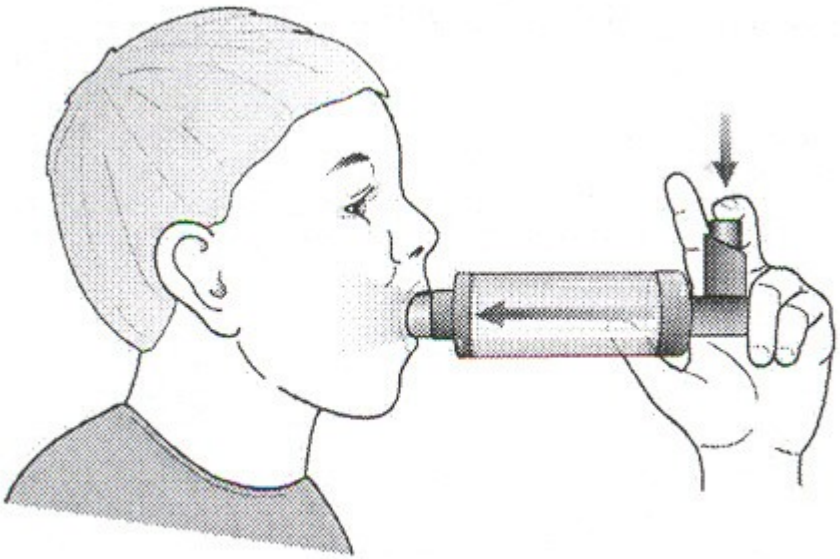
AeroChamber
SCIENCEphotoLIBRARY


Salamol CFC
100 micrograms



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123RF


www.charamedical.com
CE

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

I 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

GINA treatment figure for adults and adolescents (≥12 years)

- Treatment options are shown in two tracks
  - This was necessary to clarify how to step treatment up and down with the same reliever
- **Track 1, with low dose ICS-formoterol as the reliever, is the preferred strategy**
  - Preferred because of the evidence that using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever, with similar symptom control and lung function
- **Track 2, with SABA as the reliever, is an 'alternative' (non-preferred) strategy**
  - Less effective than Track 1 for reducing severe exacerbations
  - Use Track 2 if Track 1 is not possible; can also consider Track 2 if a patient has good adherence with their controller, and has had no exacerbations in the last 12 months
  - Before considering a regimen with SABA reliever, consider whether the patient is likely to continue to be adherent with daily controller – if not, they will be exposed to the risks of SABA-only treatment

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
Magnesiumsulfate	Consider nebulized isotonic $MgSO_4$ (150mg) 3 doses in first hour for children ≥2 years with severe exacerbation

GINA 2015, Box 6-11 (2/2)

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 /µg /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 releif

- sedatives,
- mucolitics
- 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 nt responded to emergency treatment with bronhodilatators after 3 inhalations .
  - Worsening PEF
  - Hipoxia
  - Hipercapnia
  - Methabolic acidosis
  - Difficult breathing
  - Respiratory arrest
  - Unconscious or lethargic
- **The protocol PALS is apllied**

Discharge from emergency/ICU

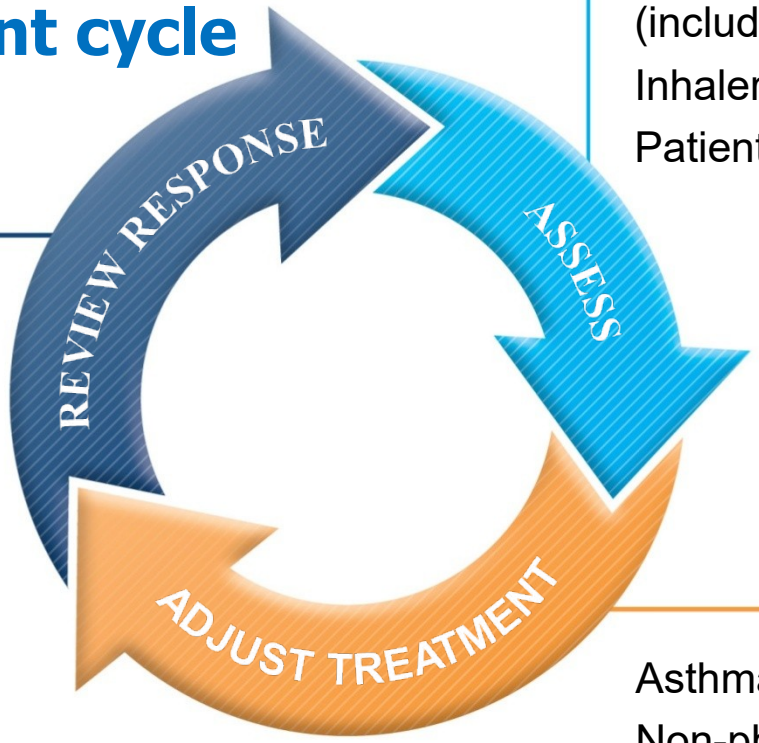
1. The patiens stable during 3-4 hours after Salbutamol inhalation with recommendations at home
2. PEF and or FEV1 >75%
3. SpO2 > 94%.
4. Exacerbation is considering as deficiency of “Control therapy”

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 indicatin of necessary doses for emergency if needed*
- *Follow up to family doctor in 48 hours*
- *Follow up to allergolog in 2 months*
- *Consider other consultations if needed*

9.2."Contoller" therapy

The control-based asthma management cycle



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

Symptoms
Exacerbations
Side-effects
Patient satisfaction
Lung function

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 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 (nebules)	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

GINA 2015, Box 3-6 (2/2)

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

GINA 2015, Box 3-6 (1/2)

Side effects of topical Inhalator corticosteroid

- **Oral candidoses,**
- **dysphagia,**
- **dysphonia.**

Solutions:

- ❑ - need to use spaser,
- ❑ - is indicated to gargle after inhalation

with plane water or 1% sol. of Sodium bicarbonates

Adverse reactions after CS therapy

- Suprarenal inhibition
- Osteoporoses
- Growth impairment

ICS – minimal side effect

Only orally CS for long tie- causing adverse reactions.

Cromones

Antiinflamatory, efficient in mild asthma in exercice-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*
- *Formoterol*

Maintained bronhodilation about 12 hours

:Indications:

- **prevent and treat by physical activity**
- **severe asthma therapy**

Administration in combination with antiinflamatory medications as CSI !!!!

Combined medications for inhalation

- **Fluticasone propionate/salmeterol** (p***MDI***) - ***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 Montelucast*** – **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).**

(continued)

- Anti-IL4R* (dupilumab) for severe eosinophilic/Type 2 asthma
  - Not suggested if blood eosinophils (current or historic) >1500/µl
  - Dupilumab now also approved for children ≥6 years with severe eosinophilic/Type 2 asthma, not on maintenance OCS *(Bacharier, NEJMed 2021)*
- Anti-TSLP* (tezepelumab) now approved for severe asthma (age ≥12 years)
  - Greater clinical benefit with higher blood eosinophils and/or higher FeNO

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5 Anti-IL5R	Mepolizumab (SC) Reslizumab (IV) Benralizumab (SC)	≥6 years ≥18 years ≥12 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
Anti-IL4R	Dupilumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥12 years	Severe asthma	

**Check local eligibility criteria for specific biologic therapies; TSLP: thymic stromal lymphopoietin*

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.

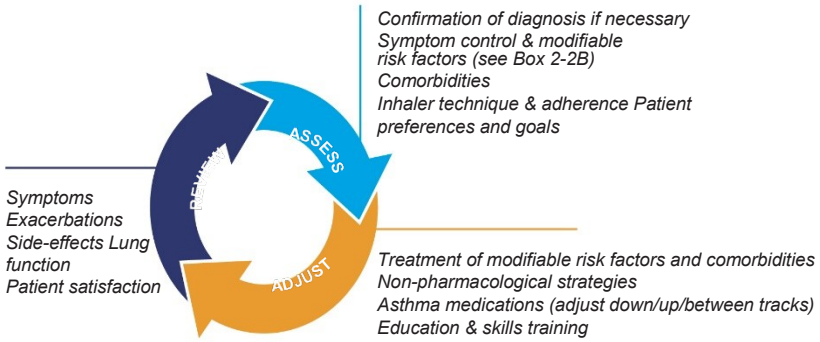
Stepwise management – additional components

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
for individual patient needs



CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2
As-needed low dose ICS-formoterol

STEP 3
Low dose maintenance ICS-formoterol

STEP 4
Medium dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1
Take ICS whenever SABA taken

STEP 2
Low dose maintenance ICS

STEP 3
Low dose maintenance ICS-LABA

STEP 4
Medium/high dose maintenance ICS-LABA

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

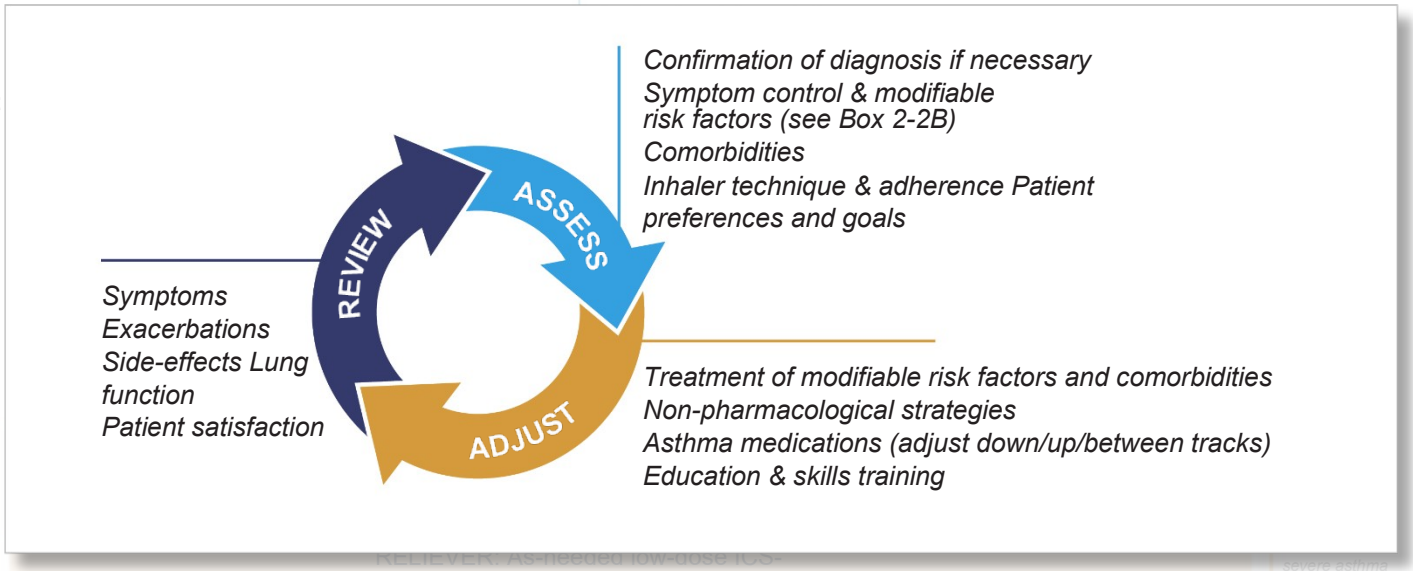
RELIEVER: As-needed short-acting beta$_2$-agonist

Other controller options for either track (limited indications, or less evidence for efficacy or safety)

	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3		
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed short-acting beta$_2$-agonist

Other controller options for either track (limited indications, or less evidence for efficacy or safety)		Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1
Take ICS whenever SABA taken

STEP 2
Low dose maintenance ICS

STEP 3
Low dose maintenance ICS-LABA

STEP 4
Medium/high dose maintenance ICS-LABA

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed short-acting beta$_2$-agonist

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER**

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
	Low dose	Low dose maintenance	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE,

Other controller options for either track (limited indications, or less evidence for efficacy or safety)					
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

Step 1 – 'preferred' controller option

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

<u>As-needed low dose ICS-formoterol (off-label)</u>

- 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

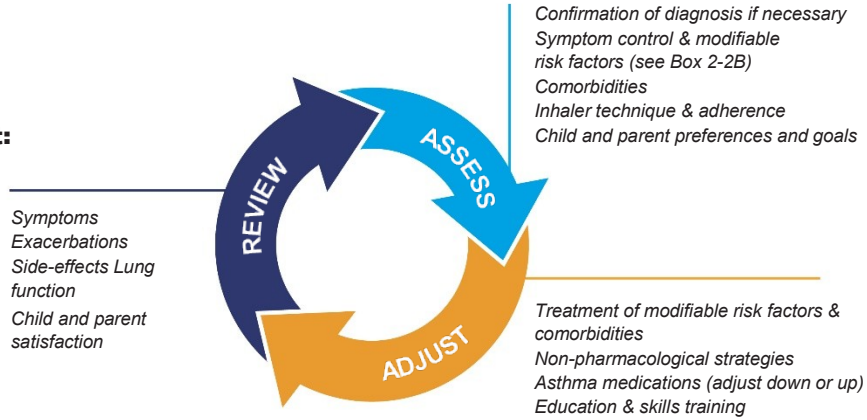
Step 1 - other controller option

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



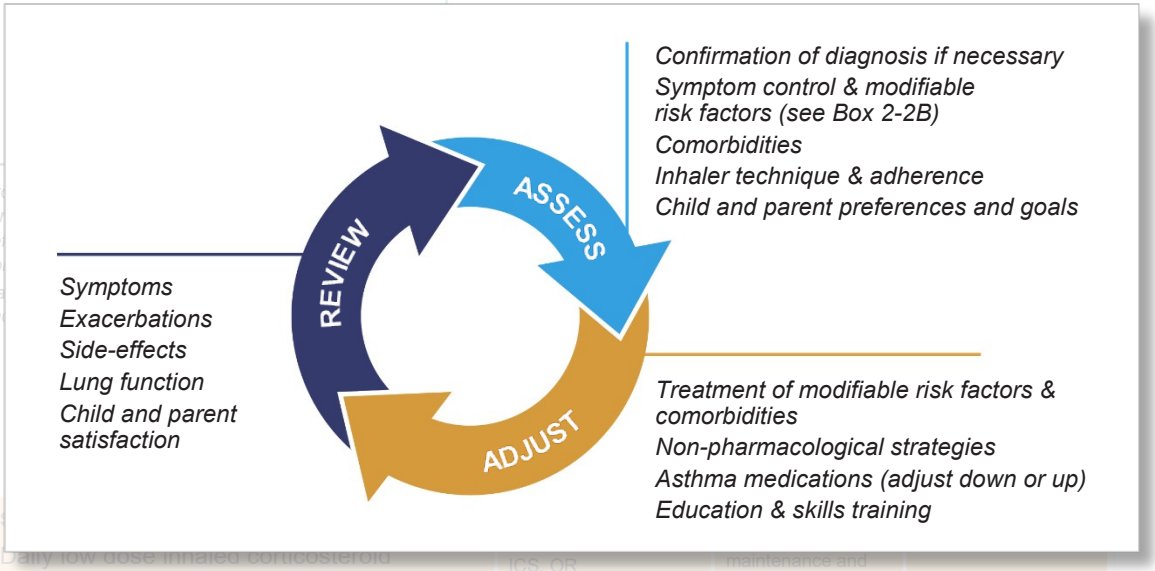
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS- LABA, OR medium dose ICS, OR very low dose* ICS-formoterol maintenance and reliever (MART)	Medium dose ICS-LABA, OR low dose† ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4R
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*Add-on anti-IL5 or, as last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed short-acting beta$_2$-agonist (or ICS-formoterol reliever in MART in Steps 3 and 4)				

**Very low dose: BUD-FORM 100/6 mcg*
†Low dose: BUD-FORM 200/6 mcg (metered doses).

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	ICS, OR very low dose* ICS-formoterol maintenance and reliever (MART)	maintenance and reliever therapy (MART). Refer for expert advice	
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*Add-on anti-IL5 or, as last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed short-acting beta$_2$-agonist (or ICS-formoterol reliever in MART in Steps 3 and 4)				

*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken				
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*				
RELIEVER	As-needed short-acting beta$_2$-agonist (or ICS-formoterol reliever in MART in Steps 3 and 4)				

Children 6-11 years

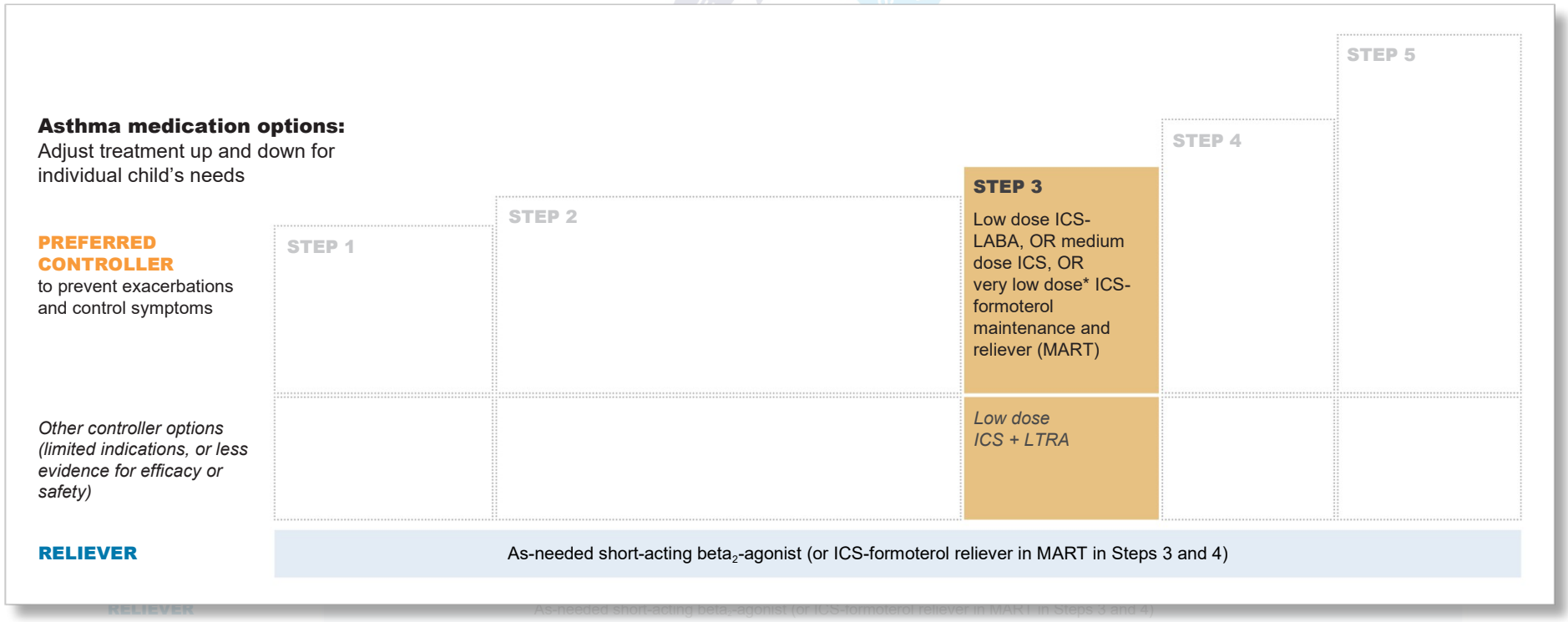
Personalized asthma management:
Assess, Adjust, Review

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)			
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*			
RELIEVER	As-needed short-acting beta$_2$-agonist (or ICS-formoterol reliever in MART in Steps 3 and 4)				

Children 6-11 years

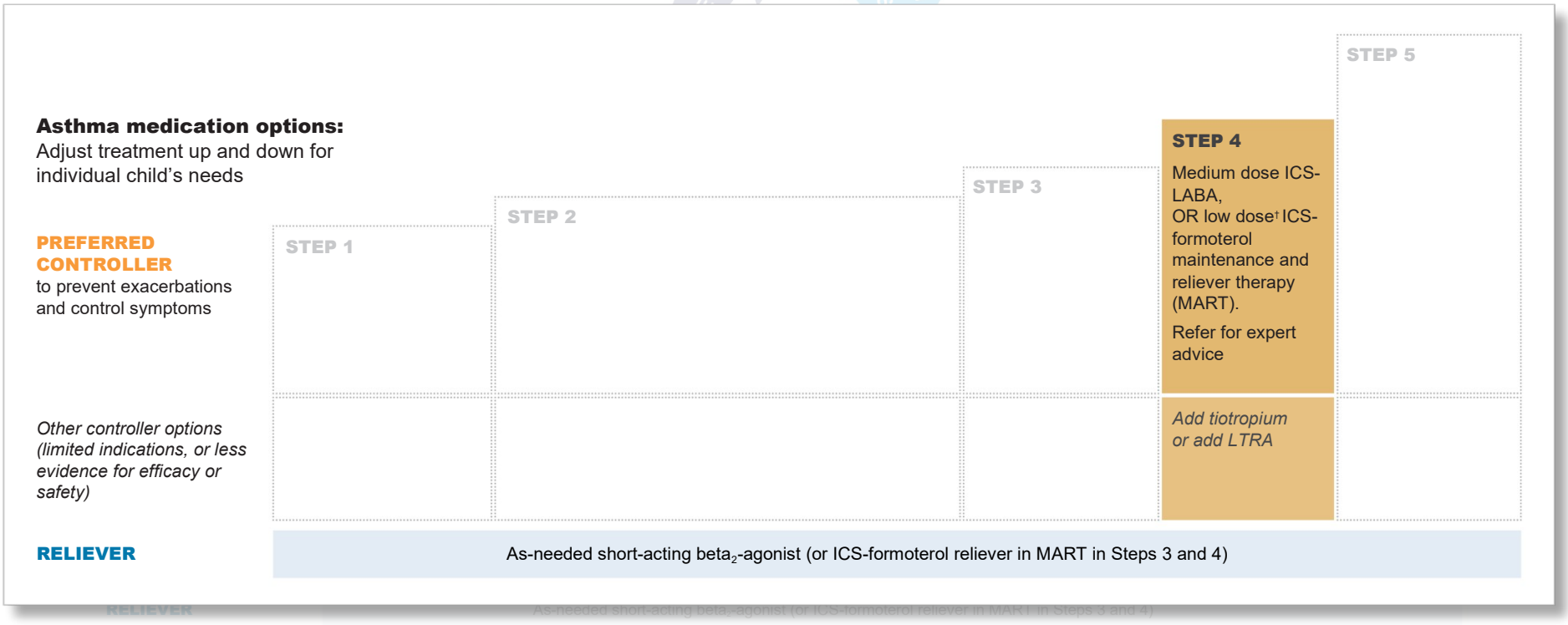
Personalized asthma management:
Assess, Adjust, Review



*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

Children 6-11 years

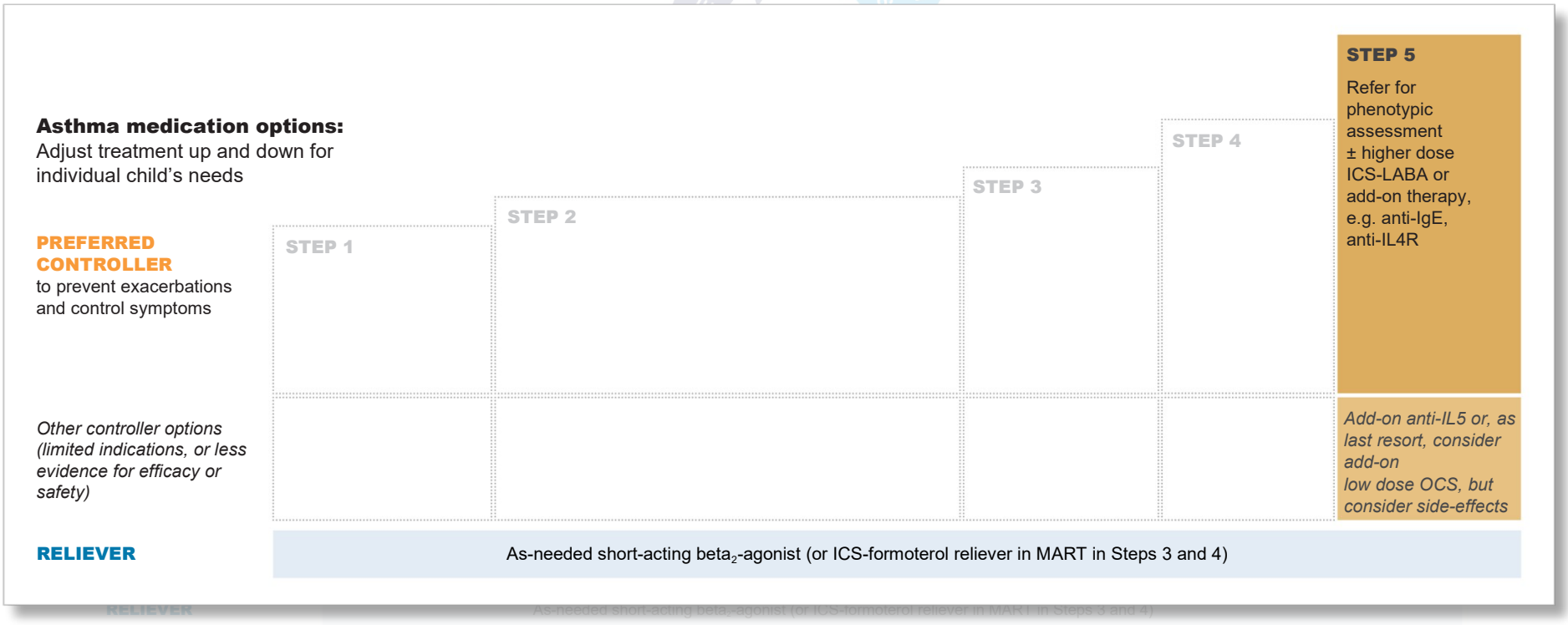
Personalized asthma management:
Assess, Adjust, Review



*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

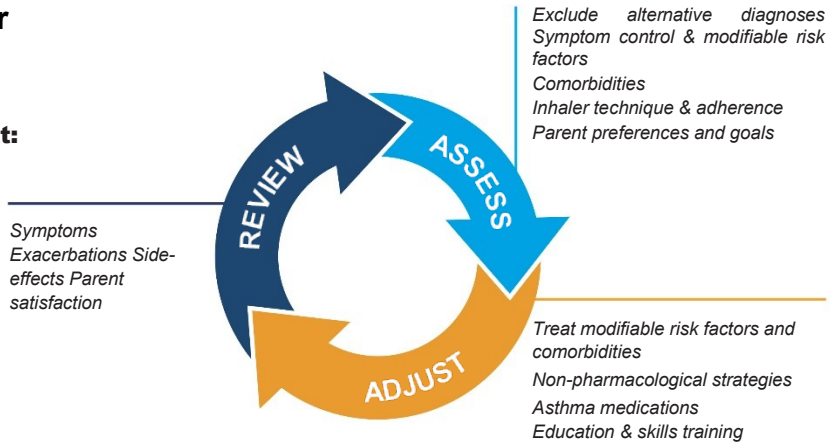
Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review



Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

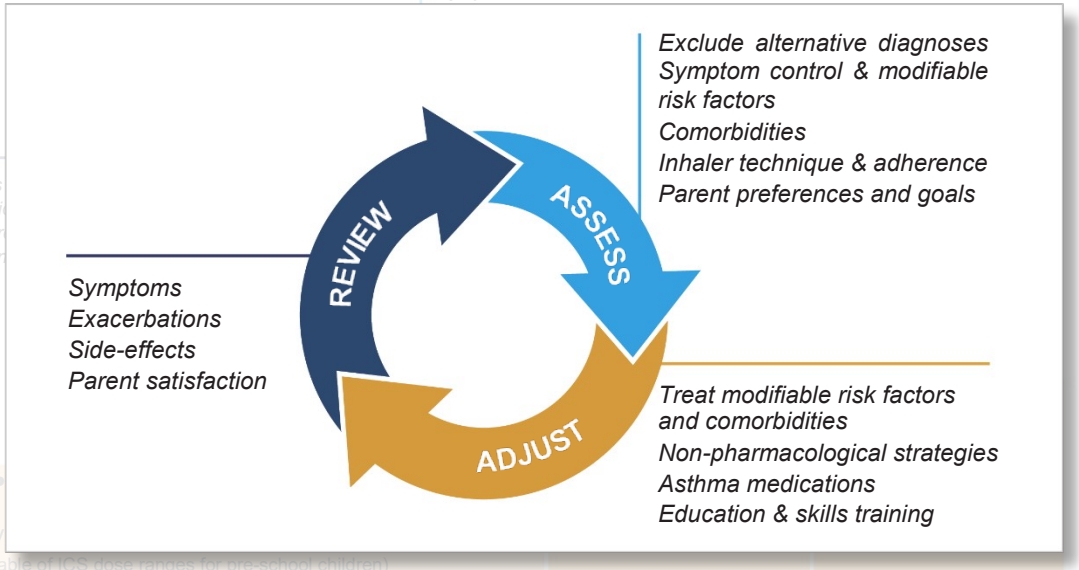


Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Asthma diagnosis, and asthma not well-controlled on low dose ICS Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	Asthma not well-controlled on double ICS

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP		
PREFERRED CONTROLLER CHOICE		Daily (see table of ICS dose ranges for pre-school children)		
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Asthma diagnosis, and asthma not well-controlled on low dose ICS Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	Asthma not well-controlled on double ICS

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE				
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*			
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms			

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)		
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*		
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:		Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral. Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.		

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Parent preferences and goals

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE			Double 'low dose' ICS	
Other controller options (limited indications, or less evidence for efficacy or safety)			*Low dose ICS + LTRA* *Consider specialist referral*	
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:			Asthma diagnosis, and asthma not well-controlled on low dose ICS	
			Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

symptoms

Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.

Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response

Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Parent preferences and goals

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE				Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)				*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:			Asthma not well-controlled on double ICS	
			Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

symptoms

Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.

Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures

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

Asses nt of re Risk

Ris decline

Each exacerbation need reevaluation of "controler" therapy

sed

risk

- Freque
- Ever a cr are fo hma

Low F EV_1, exp e to ette smo e, high dose medicatio

9.3. Allergen Immunotherapy

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

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**

This slide shows examples of interventions with high quality evidence

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 PPARγ (**Peroxisome proliferator-activated receptor gamma) antiinflamatory.
- **Inhibitor of Mastocite 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 (FEV_1), 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

Know your asthma score – ACT now

Asthma Control Test™

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.

					SCORE
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	
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 6 times a week 3	Once or twice a week 4	Not at all 5	
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	
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	
How would you rate your **asthma control** during the **past 4 weeks**?	...ed 1	Poorly controlled 2	Somewhat controlled 3	Well controlled 4	Completely controlled 5	

2: Add up your score to get your total. TOTAL

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

...e: 25 – Congratulations!
...u have **TOTAL CONTROL** of your asthma. ...u have no symptoms and ...sthma-related limitations. ...ntinue your treatment as ...scribed by your doctor and ...our 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.

13. REFERENCES:

1. Global Atlas for Asthma. European Academy of Allergy and Clinical Immunology, 2015, www.eaaci.org
2. Global Initiative for Asthma. GINA Pock Guide for asthma management and prevention (for adults and children < 5 y.0). A Pochet Guietde for physicians and nurses. Updated 2023 www.ginasthma.org
3. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Updated 2023. www.ginasthma.org
4. Global Initiative for Asthma. Difficult – to - treat & severe asthma in adolescents and adult patients. Diagnosis and management. A GINA Pocket Guide for Health Professionals, November 2024. www.ginasthma.org
5. Nelson Textbook of Pediatrics. R. M.Kliegman, W.ST Geme, N.J. Blum, S.S.Shah, R.C Tasker, K.W.Wilson, R.E. Behran 21st Edition. Chapter 169.- 2019 2. Print Book & E-Book. ISBN 9780323529501, *www.elsevier.com*
6. British National Formulary (BNF) for children, September 2021-2022, Publishedjointlyby BMJGroup TavistockSquare,London,WC1H9JP,UK, 1173 pages, www.bnf.org
7. Protocol Clinic National. PCN 54- Astmul bronsic la copil, MSPS, actualizat 2023, www.ms.gov
8. Protocol clinic standartizat pentru unitatea de primiri urgente. Managementul exacerbărilor astmului bronșic la copii - MSPS, 2022
9. Pediatrie. Manual. N. Revenco. Chisinau, 2021
10. WHO Pocket Guide for Hospital Care for Children. Updated, Geneva 2013.
11. WHO Pocket Guide for Primary Care of children and adolescents, Geneva 2022