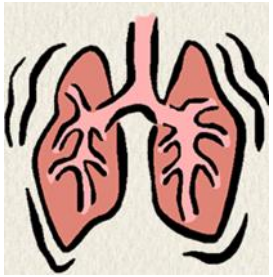
Bronchial Asthma in Children

Enas Al Zayadneh

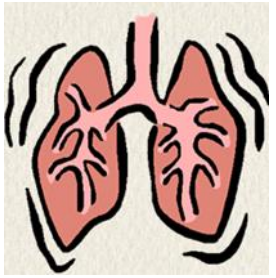
Pediatric Pulmonologist ,JUH



Introduction

Bronchial asthma is the most common inflammatory condition in children and adults with significant morbidity world wide.

In Jordan, MOH estimates 10% of population are diagnosed with bronchial Asthma .

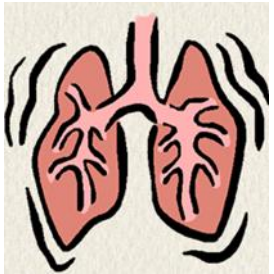


Definition

- Chronic condition characterized by :
- Airway inflammation airway inflammation cause recurrent or persistent bronchospasm, which causes symptoms including wheezing, breathlessness, chest tightness, and cough, particularly at night or after exercise.
- Infiltration of inflammatory cells, including mast cells, and eosinophilic and neutrophilic granulocytes .
- .

Hyperresponsiveness (BHR),

- Airway inflammation is associated with airway hyperreactivity or bronchial hyperresponsiveness (BHR), which is defined as the inherent tendency of the airways to narrow in response to a variety of stimuli (eg, environmental allergens and irritants).
- Chronic inflammation, persistent changes , i.e. airway remodelling



Pathophysiology :

- **Inflammation** :

Interactions between environmental and genetic factors →

- **-(EARLY PHASE 15-30m) :, o functional and structural changes (IgE mediated from mast cells)** –>

  Bronchospasm :

  -**(LATE PHASE 4-12hr) : inflammation,cell infiltration ->mucosal edema, and mucus plugs**

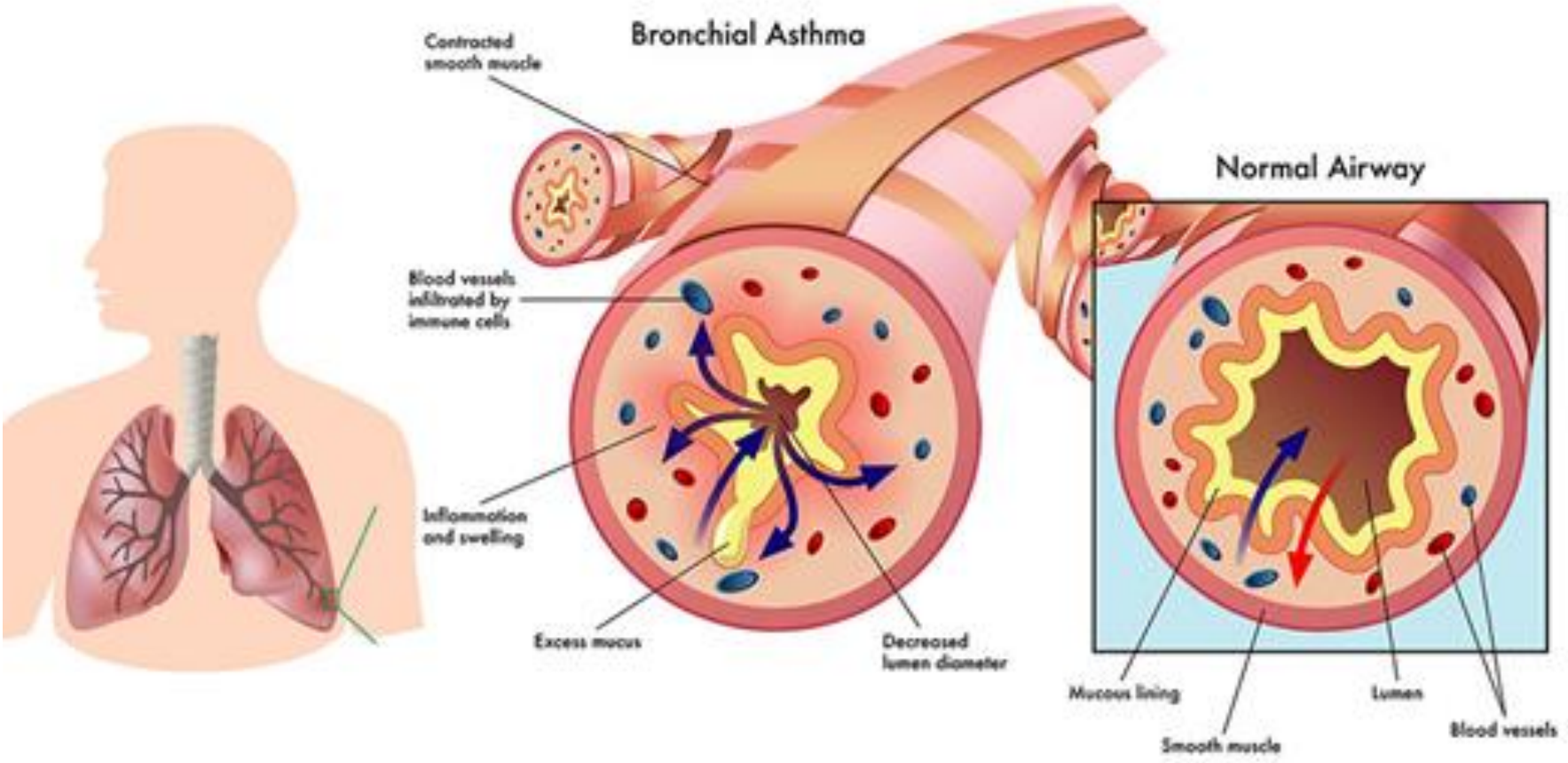
- **Hyperinflation** :overdistention helps maintain airway patency, improving expiratory flow-→
- Increases work of breathing

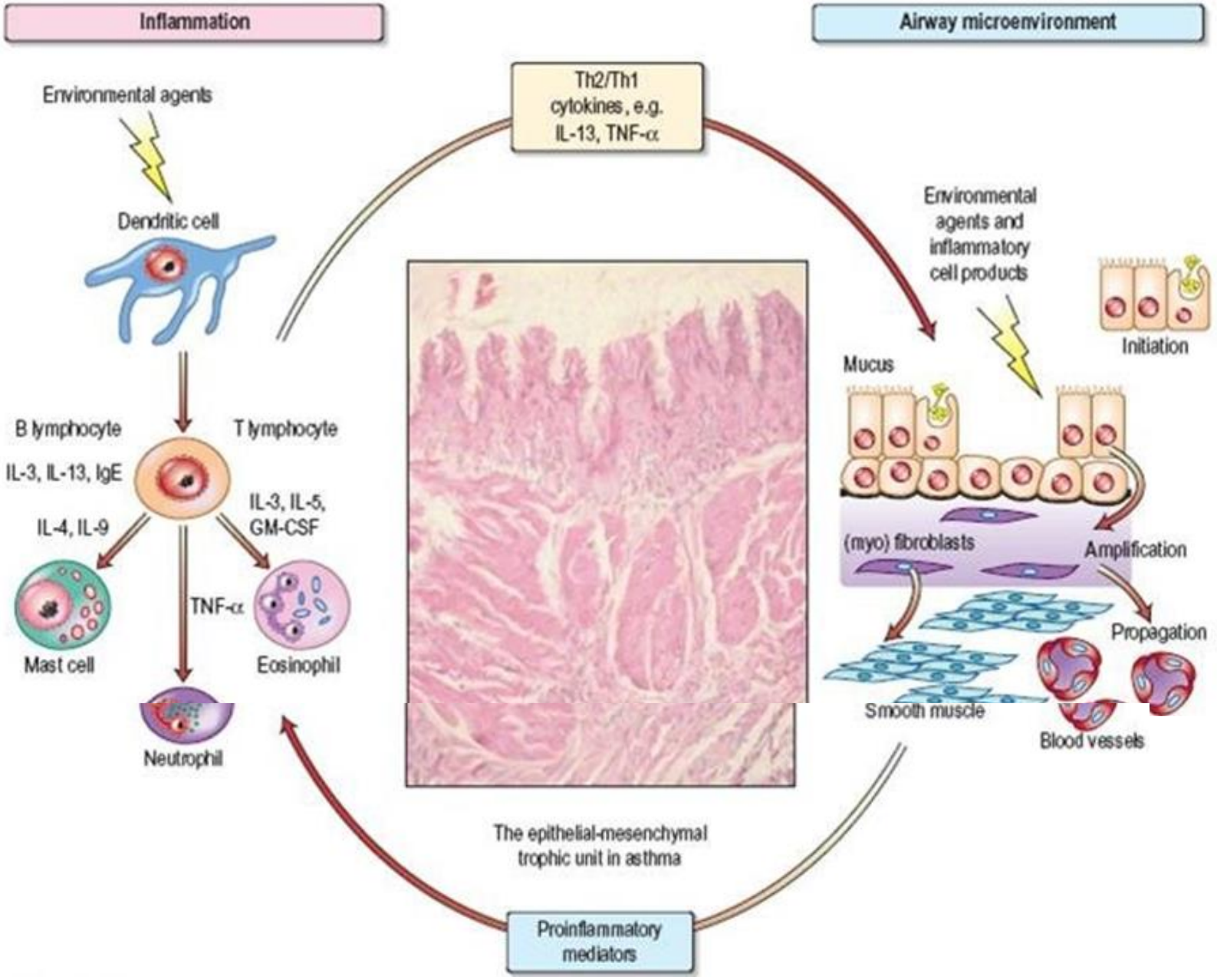
- Hyperinflation ---> compensates for the airflow obstruction, but this later on causes alveolar hypoventilation V/Q mismatch -→ HYPOXIA

- Hyperventilation triggered by the hypoxic drive also causes a decrease in PaCO2 hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar capillary membranes.Respiratory alkalosis

- e in the early stages of an acute episode have hypoxemia in the absence of carbon dioxide retention..

- With worsening obstruction and increasing ventilation-perfusion mismatch, carbon dioxide retention occurs.
- Later, the increased work of breathing, increased oxygen consumption, and increased cardiac output result in metabolic acidosis. Respiratory failure leads to Respiratory Acidosis.
- Chronic inflammation of the airways is associated with increased BHR,. In some patients with chronic asthma, airflow limitation may be only partially reversible because of airway remodeling (hypertrophy and hyperplasia of smooth muscle, subepithelial fibrosis) that occurs with chronic untreated disease.


Bronchial Asthma
Contracted smooth muscle
Blood vessels infiltrated by immune cells
Inflammation and swelling
Excess mucus
Decreased lumen diameter
Normal Airway
Mucous lining
Smooth muscle
Lumen
Blood vessels



The epithelial-mesenchymal trophic unit in asthma

Update in airway inflammation in children

- *Aetiology of airway inflammation in asthmatic children varies depending on age :*

- Viral infections (RV and RSV) linked to obstructive bronchitis in infancy and early childhood and considered controversially a combined risk factor with allergen sensitization .

Viruses and Asthma !

- Rhinovirus and respiratory syncytial virus damage the respiratory epithelium → less resistant to inhaled allergens → enhanced T-helper (Th)2 responses in predisposed children and the development of allergic inflammation .

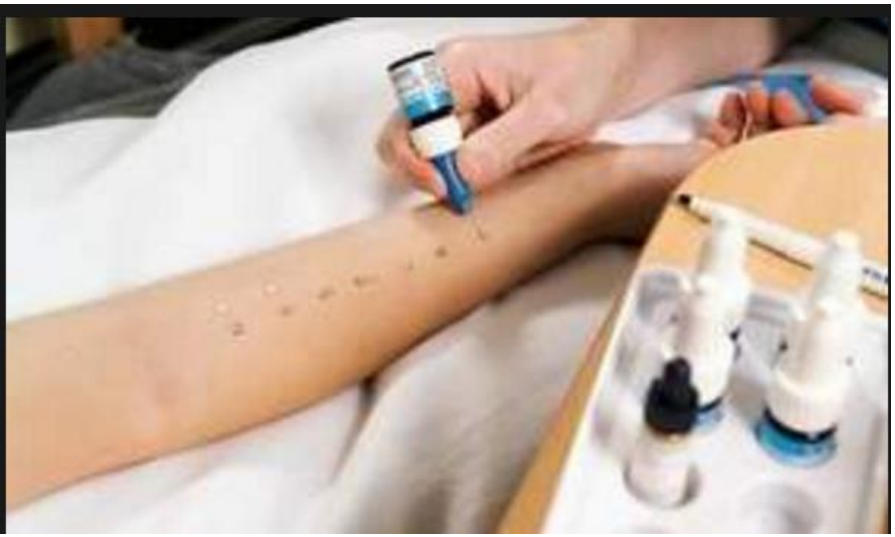
- Other RT infections :
- fungi (ABPA,), bacteria(Mycoplasma,Pertussis), parasites.
- Most children who have persistent wheeze and asthma have high IgE and Eosinophildic response (airways and circulation) at the time of the fisrt URTI.

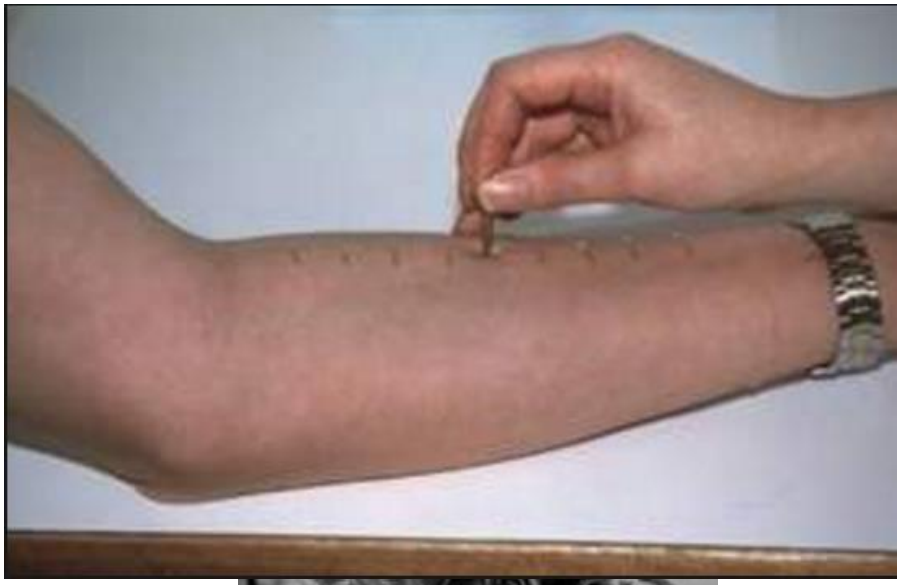
Aerosensitizatio

- Sensitisation and exposure to allergens is the major cause of allergic airway inflammation in older children.

- Immunoglobulin (Ig)E-mediated allergy leading to allergic inflammation is common among children with persistent asthma.

SPT





Aresosensitizatio + Viruses

- Synergistic effect between viral infections and aeroallergen exposure, and subsequent sensitisation in genetically predisposed children .
- Viral infections are the most important cause of asthma exacerbations in all age groups

- Gene-by-environment interaction ; genetic background of the child, with a cytokine imbalance toward Th2, will promote the production of IgE antibody to environmental antigens (eg, dust mites, cockroaches, *Alternaria,* and possibly cats).

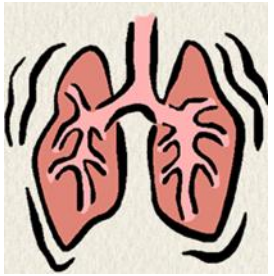
Genetics

- 2 new loci with asthma risk:

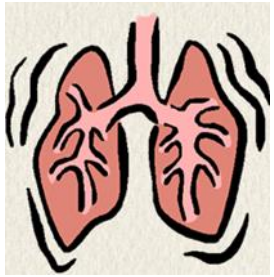
  rs4129267 in IL6R and rs7130588 on band 11q13.5.

  IL6R association → cytokine dysregulation affects asthma risk

  11q13.5 locus → allergic sensitization and subsequent development of asthma.



- Main types of childhood asthma;
- 1-recurrent wheezing/early childhood,triggered by common viral infx. Of respiratory tract.
- 2-chronic astma ass. With allergy persist into later childhood and often adulthood (most common)
- -asthma in female,obese,early puberty
- -Occupational exposure-mediated astma
- Triad Astma ,onset rare in children .
- Male:female 2:1 till puberty (equal) then female pred. after puberty



Risk Factors:

(1) Parental history of asthma, a physician diagnosis of atopic dermatitis, or evidence of sensitization to aeroallergens

- **OR (2) two of the following:**

  evidence of sensitization to foods, ≥4 percent peripheral blood eosinophilia, or wheezing apart from colds .

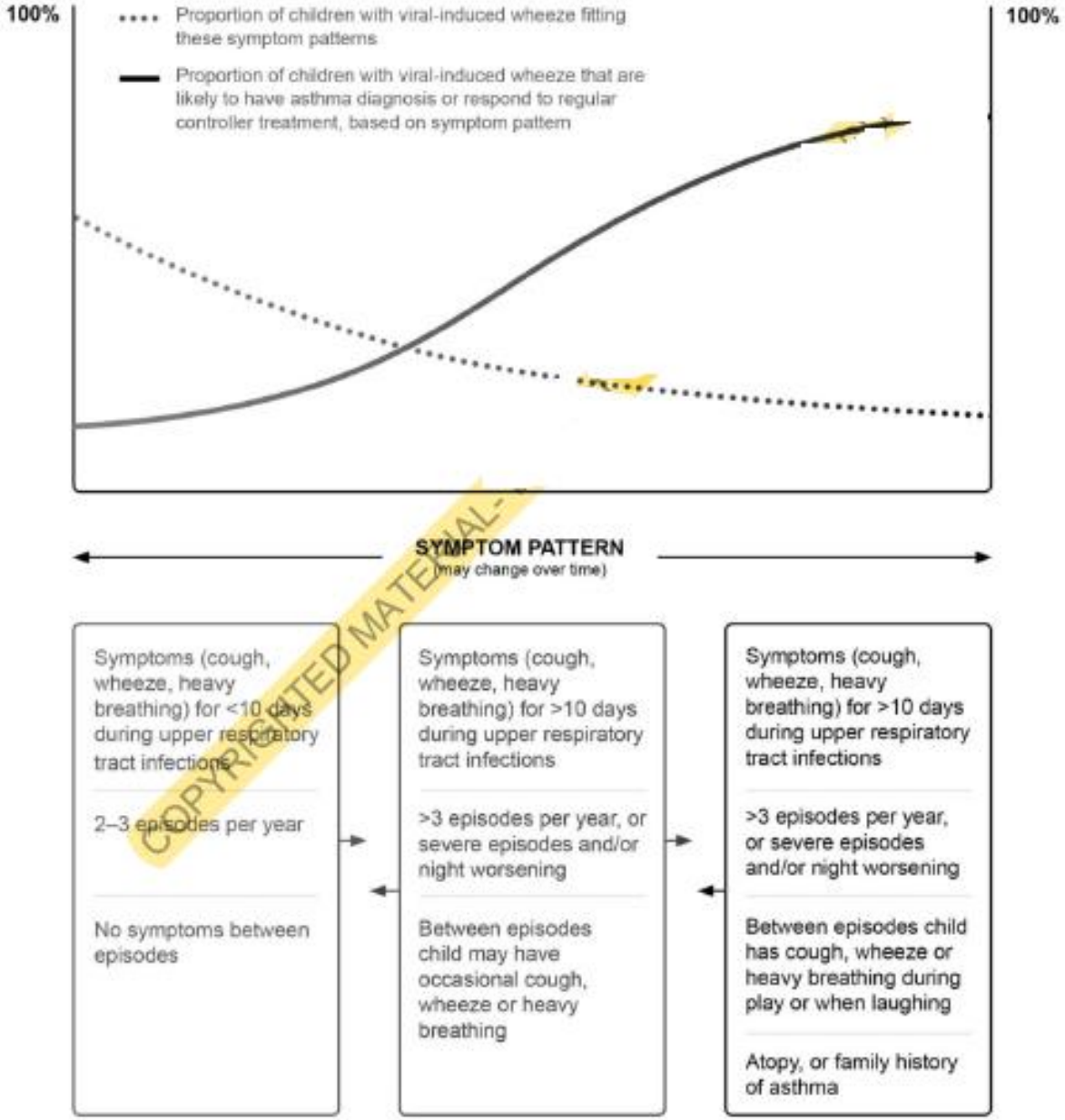
Asthma Predictor Index

Box 16: Modified asthma predicative index

History of ≥4 wheezing episodes with at least one physician diagnosed and either

One (or more) of the major criteria	Or	Two (or more) of the minor criteria
• Parental history of asthma		• Eosinophilia (≥4%)
• Skin test positive to aero-allergens		• Wheezing unrelated to colds
• Eczema (physician-diagnosed atopic dermatitis)		• Allergic sensitization to milk, egg, or peanuts

Box 6-1. Probability of asthma diagnosis or response to asthma treatment in children 5 years and younger

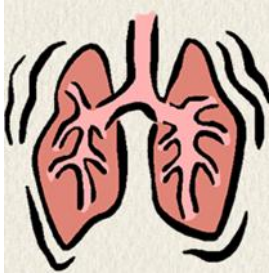


Box 6-3. Common differential diagnoses of asthma in children 5 years and younger

Condition	Typical features
Recurrent viral respiratory tract 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	Noisy breathing when crying or eating, or during upper airway infections (noisy inspiration if extrathoracic or expiration if intrathoracic); harsh cough; inspiratory or expiratory retraction; symptoms often present since birth; poor response to asthma medications
Tuberculosis	Persistent noisy respirations and cough; fever unresponsive to normal antibiotics; enlarged lymph nodes; poor response to bronchodilators or inhaled corticosteroids; contact with someone who has tuberculosis
Congenital heart disease	Cardiac murmur; cyanosis when eating; failure to thrive; tachycardia; tachypnea or hepatomegaly; poor response to asthma medications
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 occurs in about 50% of 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

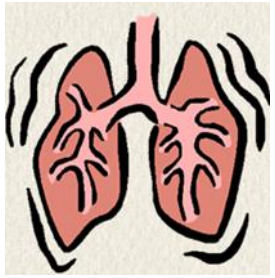
Epidemiology

- In USA most common pediatric emergency department visits-admissions.
- Increasing prevalence in childhood astma ,despite improvement in mx.
- 80% onset before 6 yr , but most children with recurrent wheesing in early childhood will not have persistant asthma in later childhoo.
- Two thirds of all asthma cases are diagnosed <18 yr.
- Approximately half of all children diagnosed with asthma have a decrease or disappearance of symptoms by early adulthood.



Asthma triggers

- Aeroallergens in sensitized asthmatics:
- Common viral infx of resp. tract
- Animal dander
- Indoor allergens (dust mites, cockroaches,molds)
- Seasonal aeroallergens: pollens(trees,grasses,weeds)-seasonal molds
- Environmental tobacco smoke
- Air pollutants (ozone ,sulfer dioxide,particulate matter .wood-coal-burning smoke ,endotoxins ,mycotoxins ,dust)
- Strong/noxious odors/fumes(perfumes ,hairsprays,cleaning agents)
- Occupational exposure (farm/barn exposure, formaldehydes,paint fumes,cedar)
- Cold air , dry air
- Exercise
- Crying ,laughter ,hyperventillation)

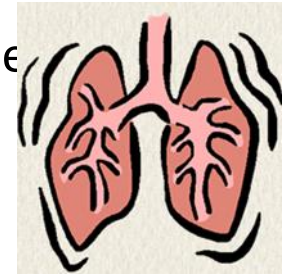


Clinical manifestations

- HISTORY :A detailed medical history should address (1) whether symptoms are attributable to asthma, (2) whether findings support the likelihood of asthma (eg, family history), (3) asthma severity, and (4) the identification of possible precipitating factors.

  Symptoms may include the following:
- Cough
- Wheezing
- Shortness of breath
- Chest tightness
- Sputum production
- Symptom patterns can vary as follows:
  Perennial versus seasonal /Continual versus episodic/ Duration, se
  and frequency

Diurnal variations (nocturnal and early-morning awakenings)



- Acute severe episode :
- breathlessness at rest
- Not interested in feeding
- Sits upright
- Talks in words not sentences
- Usually agitated
- Imminent respiratory arrest :drowsy,confused(not necessary in adolescents)

PHYSICAL EXAMINATION

- General
- Evidence of respiratory distress ;increased respiratory rate, increased heart rate, diaphoresis, and use of accessory muscles of respiration.
- Marked weight loss or severe wasting may indicate severe emphysema.
- Pulsus paradoxus: This is an exaggerated fall in systolic blood pressure during inspiration and may occur during an acute asthma exacerbation.
- Depressed sensorium: This finding suggests a more severe asthma exacerbation with impending respiratory failure.

- End-expiratory wheezing or a prolonged expiratory phase /most commonly, although inspiratory wheezing can be heard.
- Diminished breath sounds and chest hyperinflation may be observed during acute exacerbations.
- The presence of inspiratory wheezing or stridor may prompt an evaluation for an upper airway obstruction such as vocal cord dysfunction, vocal cord paralysis, thyroid enlargement, or a soft tissue mass (eg, malignant tumor).

» Upper airway exam. :

Erythematous or boggy turbinates or the presence of polyps from sinusitis, allergic rhinitis, or upper respiratory infection.

Any type of nasal obstruction may result in worsening of asthma or symptoms of EIA.

- Skin: Observe for the presence of atopic dermatitis, eczema, or other manifestations of allergic skin conditions.

P/E in severe episode:

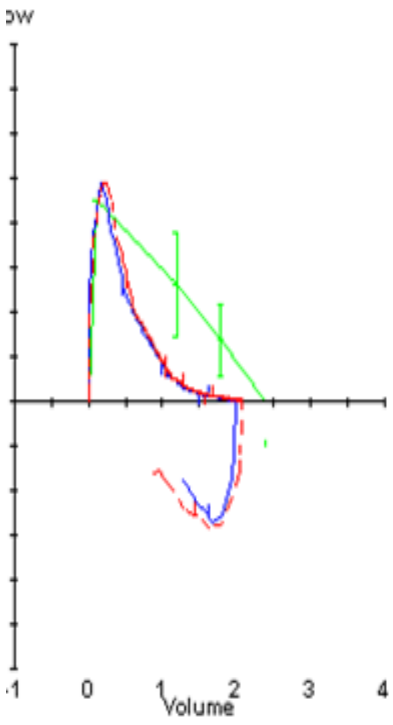
- RR > 30
- Use of accessory muscles
- Suprasternal retractions
- HR > 120/minute
- Loud biphasic (expiratory and inspiratory) wheeze
- Pulsus paradoxus present(20-40 mmHg)
- Po2 sat RA <91%

P/E in status asthmaticus with pending respiratory arrest :

- Paradoxical thoracoabdominal movements
- Wheeze may be absent
- Severe hypoxemia may manifist as bradycardia
- Pulsus paradoxus may disappear

Laboratory Findings

- Lung Function Tests
- SPIROMETRY; measures lung volumes and airflow during forced expiration(gold standard in asthma) :
- Airflow limitation (low FEV 1 ,FEV 1/FVC < 0.8
- Bronchodilator response : improvement in FEV1> = 12%
- Exercise challenge : worsening in FEV1 >=15%
- Peak flow morning-to-afternoon variation>=20% (PEF):monitor severity -zones



Spirometry

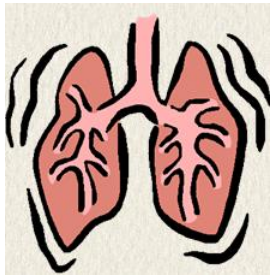
		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.40	1.99	83	2.09	87	5
FEV1	Liters	2.25	1.28	57	1.31	58	3
FEV1/FVC	%	86	64		63		
FEF25-75%	L/sec	2.64	0.57	22	0.54	20	-5
FEF50%	L/sec	2.58	0.87	34	0.79	31	-9
PEF	L/sec	4.50	4.87	108	4.90	109	1

- Exercise challenge test

- Histologic evaluation
- Challenge test :methacoline challenge test PC 20 < 4 mg/ml is positive .

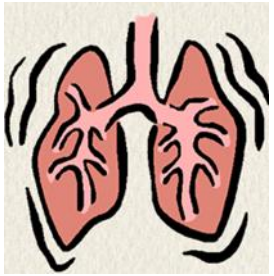
Radiology

- CXR (AP and LATERAL)
- Often normal
- Subtle nonspecific findings of hyperinflation and peribronchial thickening.
- Helpful to exclude major DDx(aspiration pneumonitis ,bronchiolitis obliterans)
- Complications of asthma (atelectasis,pneumothorax)
- CT ,high resolution ,thin cuts (bronchiectasis in CF,ABPA,ID..etc)



- Allergy testing to assess sensitization(inhalant allergen sens. By prick skin testing)

- Fraction of Exhaled Nitric Oxide Testing



Diagnostic Challenge

- DDx :

- **Airway Foreign Body**
- Allergic Rhinitis
- Aspergillosis
- Aspiration Syndromes
- **Bronchiectasis**
- **Bronchiolitis**
- Bronchopulmonary Dysplasia
- **Cystic Fibrosis**
- **Gastroesophageal Reflux**
- Primary Ciliary Dyskinesia

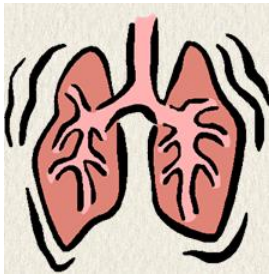
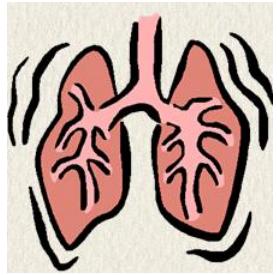


TABLE 1 Possible differential diagnosis in a child presenting with severe asthma

Tracheomalacia
Congenital disorders
Primary ciliary dyskinesia
Oesophageal fistula
Foreign body
Bronchiolitis
Immunodeficiency
Cardiac disease



Considerations for Treatment

- **Control asthma** by reducing impairment through prevention of chronic and troublesome symptoms (eg, coughing or breathlessness in the daytime, in the night, or after exertion)
- **Reduce the need for a short-acting beta2-agonist (**SABA) for quick relief of symptoms (not including prevention of exercise-induced bronchospasm)
- **Maintain near-normal pulmonary function**
- **Maintain normal activity levels (including exercise and** other physical activity and attendance at work or school)
- Satisfy patients' and families' expectations for asthma care

Components of Asthma Care

- Assessment and monitoring
- Education
- Control of environmental factors and comorbid conditions
- Pharmacologic treatment

Assessment and monitoring

Components of Severity		Classification of Asthma Control (0-4 Years of Age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
IMPAIRMENT	Symptoms	≤2 days/week	>2 days/ week	Throughout the day
	Nighttime awakenings	≤1x/month	>1x/month	>1x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short acting beta2-agonist use for symptom control**	≤2 days/week	>2 days/week	Several times per day
RISK	Exacerbations requiring oral systemic corticosteroids	0-1 per year	2-3 per year	>3 per year
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		■ Maintain current treatment. ■ Regular follow-up every 1-6 months. ■ Consider step down if well controlled for at least 3 months.	■ Step up 1 step and reevaluate in 2-6 weeks. ■ If no clear benefit in 4-6 weeks, consider alternative diagnoses or adjust therapy. ■ For side effects, consider alternative treatment options.	■ Consider short course of oral systemic corticosteroids. ■ Step up 1-2 steps, and reevaluate in 2 weeks. ■ If no clear benefit in 4-6 weeks, consider alternative diagnosis or adjusting therapy. ■ For side effects, consider alternative treatment options.

Adapted from the 2007 NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. To access the complete report, go to: www.nhlbi.nih.gov/guidelines/asthma/asthgdin.pdf.

Assessment and monitoring

Components of Severity		Classification of Asthma Control (5-11 Years of Age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
IMPAIRMENT	Symptoms	≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the day
	Nighttime awakenings	≤1x/month	>2x/month	≥2x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short acting beta2-agonist use for symptom control**	≤2 days/week	>2 days/week	Several times per day
	■ FEV_1 or peak flow	>80% predicted/ personal best	60-80% predicted personal best	<60% predicted/ personal best
	■ FEV_1/FVC	>80%	75-80%	<75% predicted
RISK	Exacerbations requiring oral systemic corticosteroids	0-1 per year	≥2 per year	
		Consider severity and interval since last exacerbation.		
	Reaction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		■ Maintain current step. . ■ Regular follow-up every 1-6 months. ■ Consider step down if well controlled for at least 3 months.	■ Step up 1 step and reevaluate in 2-6 weeks. ■ For side effects, consider alternative treatment options.	■ Consider short course of oral systemic corticosteroids. ■ Step up 1-2 steps, and reevaluate in 2 weeks. ■ For side effects, consider alternative treatment options.

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Assessment and monitoring

Components of Severity		Classification of Asthma Control (12 Years of Age and Older)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
IMPAIRMENT	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1-3x/month	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short acting beta2-agonist use for symptom control**	≤2 days/week	>2 days/week	Several times per day
	▪ FEV_1 or peak flow	>80% predicted/ personal best	60-80% predicted personal best	<60% predicted/ personal best
	Validated questionnaires			
	▪ ATAQ* ▪ ACQ** ▪ ACT***	0 ≤0.75 ≥20	1-2 ≥1.5 16-19	3-4 N/A ≤15
RISK	Exacerbations requiring oral systemic corticosteroids	0-1 per year	≥2 per year	
		Consider severity and interval since last exacerbation.		
	Reaction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
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Have your child complete these questions.

1. How is your asthma today?

 0 Very bad	 1 Bad	 2 Good	 3 Very good

SCORE

2. How much of a problem is your asthma when you run, exercise or play sports?

 0 It's a big problem, I can't do what I want to do.	 1 It's a problem and I don't like it.	 2 It's a little problem but it's okay.	 3 It's not a problem.

3. Do you cough because of your asthma?

 0 Yes, all of the time.	 1 Yes, most of the time.	 2 Yes, some of the time.	 3 No, none of the time.

4. Do you wake up during the night because of your asthma?

 0 Yes, all of the time.	 1 Yes, most of the time.	 2 Yes, some of the time.	 3 No, none of the time.

Please complete the following questions on your own.

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

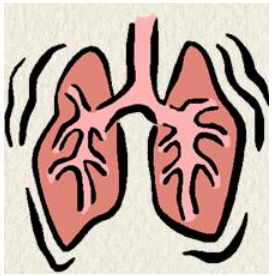
7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday

TOTAL

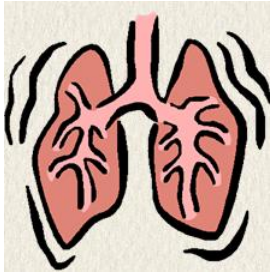
Assessment/Biomarkers for Asthma

- Pulmonary function and BHR
- Eosinophil in sputum and blood
- Exhaled NO (FeNO)
- urinary leukotrienes
- Total and specific IGE



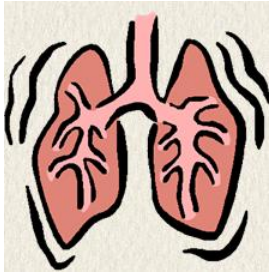
Consultations

- Refer High risk patients to specialist :
- *History of sudden severe exacerbations*
- *History of prior intubation for asthma*
- *Admission to an ICU because of asthma*
- *Two or more hospitalizations for asthma in the past year*
- *Three or more emergency department visits for asthma in the past year*
- *Use of 2 or more canisters of inhaled short-acting beta2-agonists per month*
- *Current use of systemic corticosteroids or recent withdrawal from systemic corticosteroids*



Consultations

- Pulmonolosit ,Allergist
- ENT specialist ,chronic rhinosinusitis
- Gastroenterologist ,to exclude and/or treating gastroesophageal reflux.



Components of Severity		Classification of Asthma Severity (5–11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60–80% predicted • FEV_1/FVC = 75–80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option	Step 3, medium-dose ICS option, or step 4
				and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

Key: EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids

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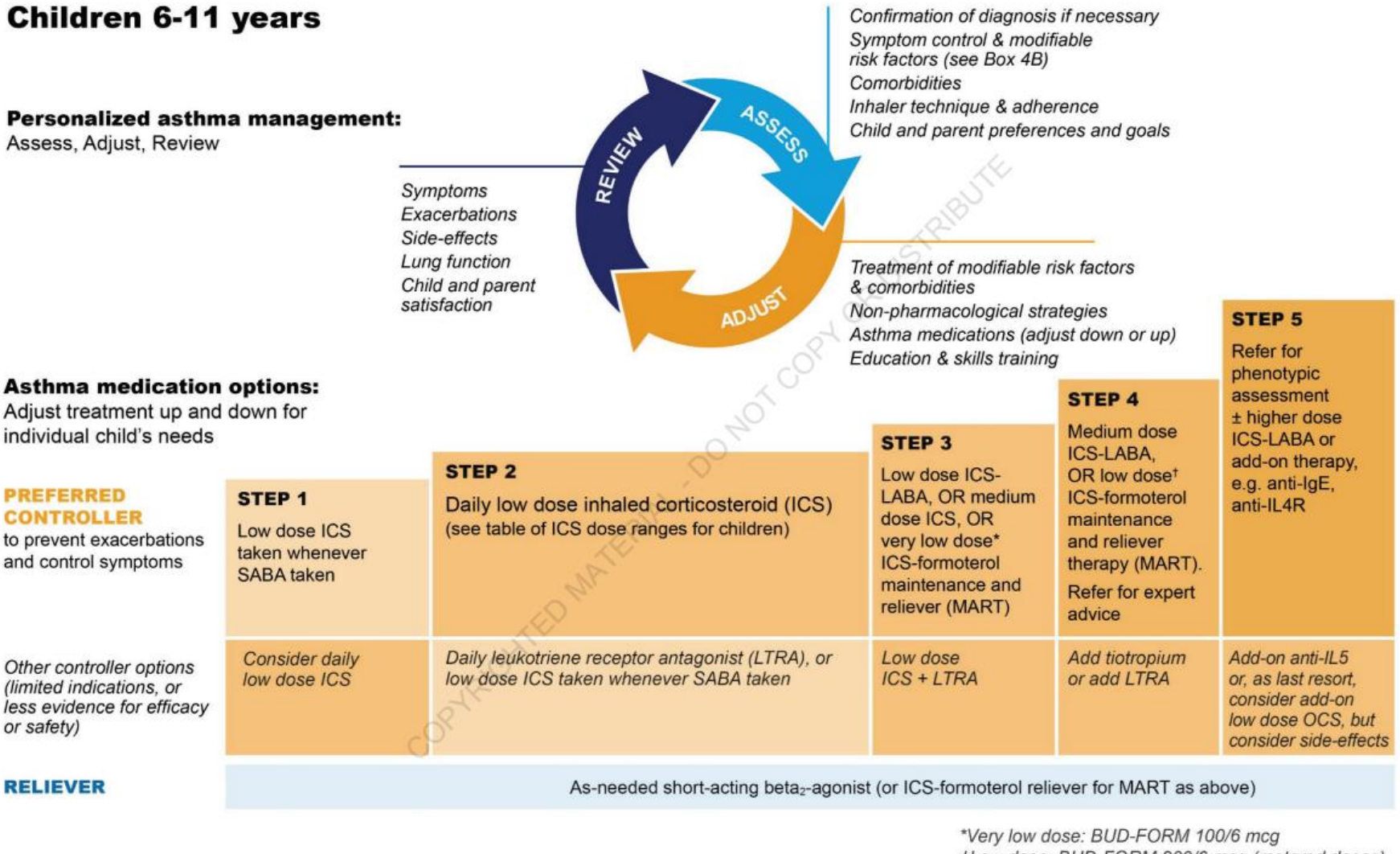
Children 6-11 years
Personalized asthma management:
Assess, Adjust, Review
Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 4B)
Comorbidities
Inhaler technique & adherence
Child and parent preferences and goals
ASSESS
ADJUST
REVIEW
Symptoms
Exacerbations
Side-effects
Lung function
Child and parent satisfaction
Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training
Asthma medication options:
Adjust treatment up and down for individual child's needs
PREFERRED CONTROLLER
to prevent exacerbations and control symptoms
STEP 1
Low dose ICS taken whenever SABA taken
STEP 2
Daily low dose inhaled corticosteroid (ICS)
(see table of ICS dose ranges for children)
STEP 3
Low dose ICS-LABA, OR medium dose ICS, OR very low dose* ICS-formoterol maintenance and reliever (MART)
STEP 4
Medium dose ICS-LABA, OR low dose† ICS-formoterol maintenance and reliever therapy (MART).
Refer for expert advice
STEP 5
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 beta2-agonist (or ICS-formoterol reliever for MART as above)
*Very low dose: BUD-FORM 100/6 mcg

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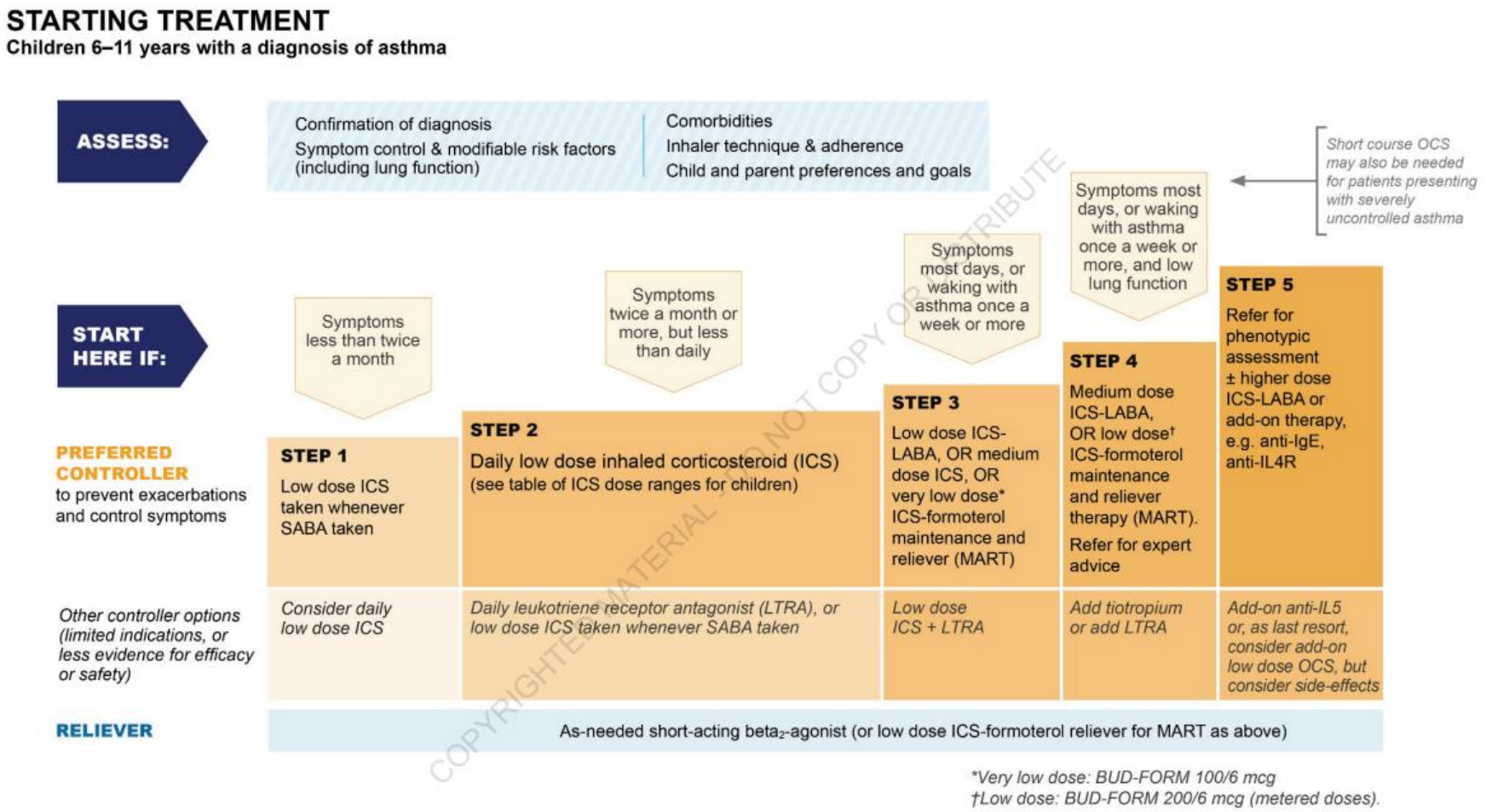
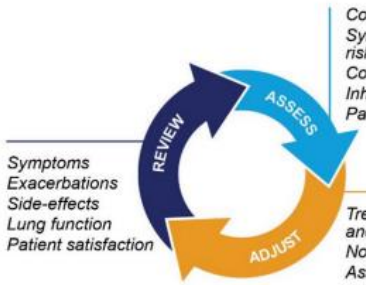


ICS: inhaled corticosteroid; LABA: long-acting beta2-agonist; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroid; SABA: short-acting beta2-agonist.
For initial asthma treatment in adults and adolescents, see Box 7B (p.24). For more details about treatment recommendations including supporting evidence, and clinical advice about implementation in different populations see the full GINA 2022 report (www.ginasthma.org). Check eligibility criteria with local payers.

Box 7A. The GINA asthma treatment strategy – adults and adolescents

Adults & adolescents 12+ years

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



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 4B)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

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			

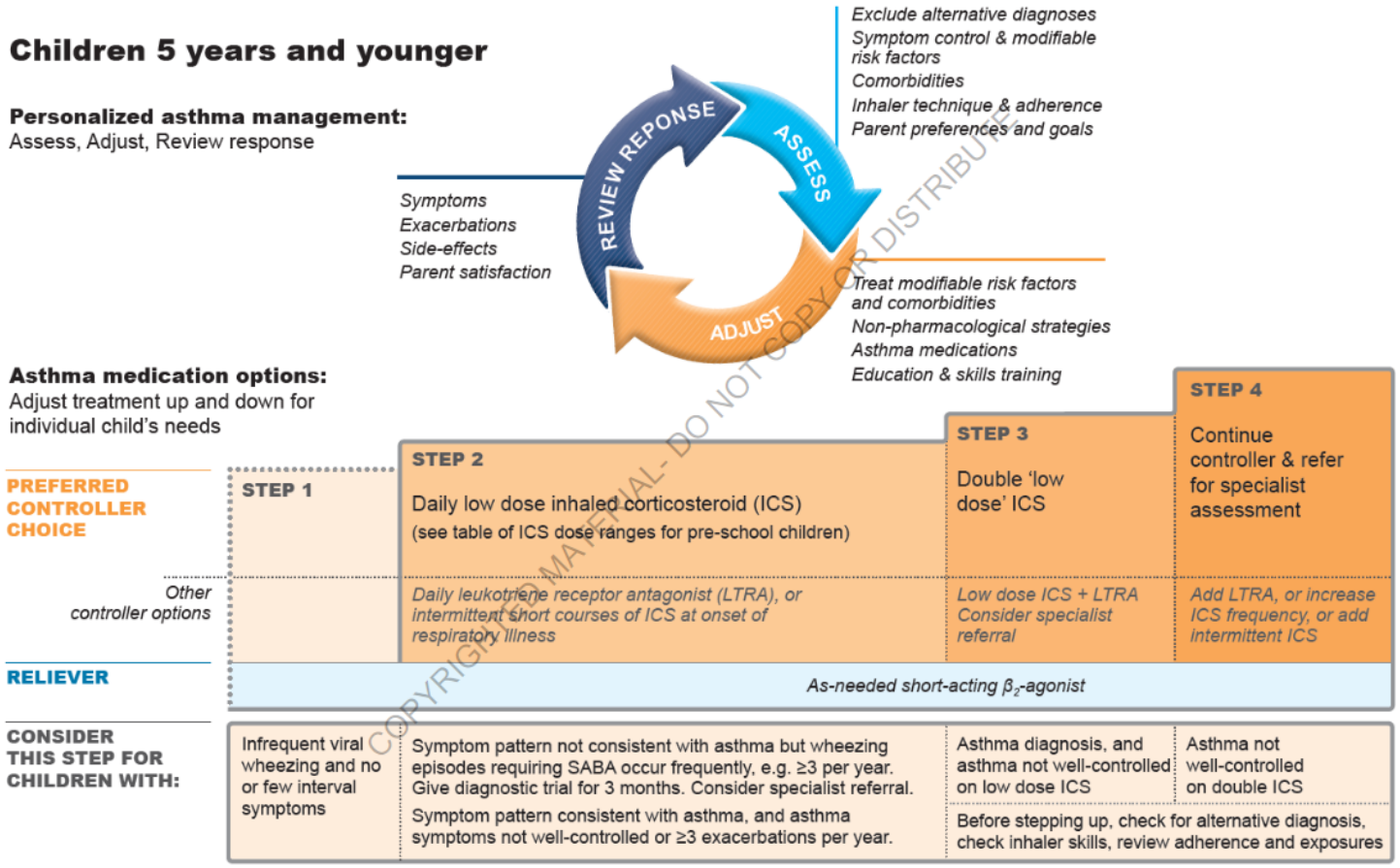
See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER** (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	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	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*

Box 6-5. Personalized management of asthma in children 5 years and younger



ICS: inhaled corticosteroids; LTRA: leukotriene receptor antagonist; SABA: short-acting beta2-agonist

Delivery devices and best route of administration

1. Pressurized metered dose inhaler (pMDI) - Propellant used to dispense steroid when canister is pressed manually
2. •Dry powder inhaler (DPI) - Does not require hand-breath coordination to operate
3. •Breath-actuated pMDI - Propellant used to dispense steroid when patient inhales
4. •Nebulized solution devices

Technique /preferred devices

- 1-Children < 4 years : pMDI with a valved holding chamber + age-appropriate mask.
- 2-Children 4-6 years : a pMDI plus a valved holding chamber.
- 3-Children > 6 years : a pMDI, a DPI, or a breath-actuated pMDI.
- 4-For all 3 groups, a nebulizer with a valved holding chamber ,is recommended as alternate therapy

Technique :
MDI + Spacer

DPI

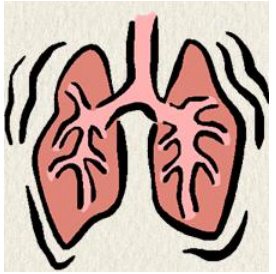

Breathe in


wiseGEEK


Multidose dry powder inhalers
Accuhaler®
Turbuhaler®
Genuair®
Easyhaler®
Twisthaler®
Nexthaler®

Quick-relief medications

- Rapid-acting beta2-agonists as needed for symptoms
- Short course of systemic steroids
- Ipratropium Bromide



SABA

- Used to treat bronchospasm in acute episodes
- Prevent bronchospasm associated with EIA and nocturnal asthma.
- Albuterol (MDI,solution for neb,oral)

Pirbuterol,levalbuterol,terbutaline

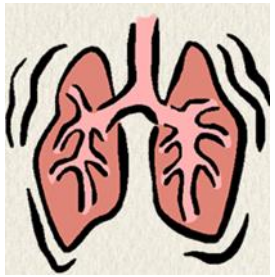
- Prolonged use may produce tachyphylaxis (downregulation and receptor hyposensitivity)

SABA receptors

- SABA may produce adverse effects (decreased PF and increased risk of exacerbations in pts homozygous for (Arg/Arg) att 16^{th} aaposition of b-adrenergic receptor gene vs (Gly-Gly).

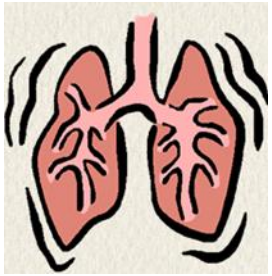
Control /Long term medications

- ICS: fluticasone,budesonide, beclomethasone
- LABA: salmetrol ,formoterol
- LTRA : montelukast
- Combination LABA/ICS
- Cromolyn/Nedocromil
- Methylxanthines: Theophylline
- Systemic steroids :dexamethasone,hydrocortisone,methylpredinisolone, prednisolone
- LAMA (Long acting muscarinic antagonists): Tiotropium bromide
- Biological therapy



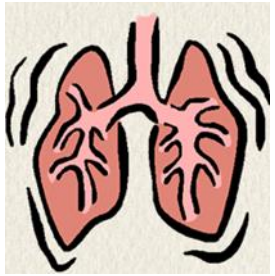
ICS

- Topically active, poorly absorbed, and least likely to cause adverse effects.
- Inhaled forms reduce the need for systemic corticosteroids.
- -Block late asthmatic response to allergens
- -Reduce airway hyperresponsiveness
- -Inhibit cytokine production, adhesion protein activation, and inflammatory cell migration and activation
- -Reverse beta2-receptor downregulation



ICS

- Ciclesonode(Alvesco)
- Fluticasone
- Beclomethasone
- Budesonide
- Mometasone furate

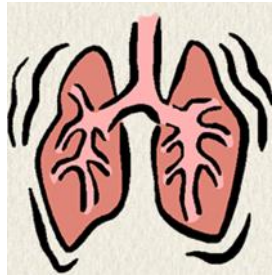


LABA

- Not for acute episodes
- Preventive treatment of nocturnal and EIA
- Should not be used as single agent (combination) if it other plans not successful.
- Studies : may increase risk of severe asthma episodes and death with severe episodes.
- Salmetrol,formoterol

Systemic steroids

- Relief : (3-10 d) to gain prompt control of inadequately controlled acute asthmatic episodes.
- Long-term :sevre persistent asthma .
- Reverse beta2-receptor subsensitivity and downregulation
- Higher-dose GCS no advantage in severe asthma exacerbations.
- IV route no advantage over oral therapy



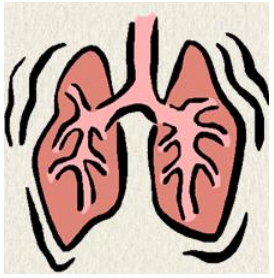
Leukotrienes Modifiers

- Counteract leukotrienes action(bronchospasm, increased vascular permeability, mucosal edema)

- 5-lipoxygenase inhibitors: Zileuton

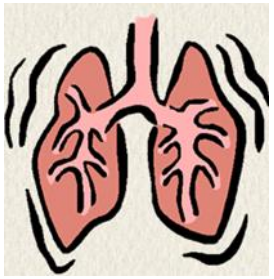
-Leukotriene-receptor antagonists :

Zafrilukast ,Montelukast



Co-morbidities

- Bronchopulmonary aspergillosis
- Gastroesophageal reflux disease (GERD)
- Obesity
- Obstructive sleep apnea
- Rhinitis
- Sinusitis
- Depression
- Stress
- Low vitamin D levels



Biological treatment

- Mepolizumab and benralizumab (inhibit IL-5 binding to eosinophils)
- Omalizumab : (IgE antagonist)
- Reslizumab (IL5 antagonist ,adults)
- Pitrakinra (IL4-/IL-13 antagonist)
- Lebrikizumab (IL-13 antagonist)

Conclusion

- A number of recent advances in treating asthma exist, HOWEVER
- Importance of adhering to essentials in Treating childhood asthma.
- Childhood asthma can be treated at community level.
- Healthworkers should try to focus on improving quality of indoor and outdoor aie quality.

Box 7-1. Advice about primary prevention of asthma in children 5 years and younger

Parents enquiring about how to reduce the risk of their child developing asthma can be provided with the following advice:

- Children should not be exposed to environmental tobacco smoke during pregnancy or after birth
- Vaginal delivery should be encouraged where possible
- Breast-feeding is advised, for reasons other than prevention of allergy and asthma
- The use of broad-spectrum antibiotics during the first year of life should be discouraged.

Management: Acute severe Asthma

Severe asthma is indicated by:

- Apprehensiveness
- Unable to complete sentences in one breath
- SaO2<92% in room air after three appropriate doses of inhaled salbutamol within 60 mins.
- Tachycardia >120 in children aged >5 yr >130 in children aged 2-5

- **Increasing tachycardia denotes worsening asthma or increasing doses of salbutamol. Tachycardia is universal in the setting of a salbutamol infusion. (? SVT)**
- **Tachypnoea >30 in children aged >5 yr >50 in children aged 2-5 yr**
- **Palpable pulsus paradoxus (equates to ≥15 mm Hg) – NB all asthmatics have some degree of pulsus paradoxus at rest.**

Progressive worsening:

- Agitation and Confusion
- Exhaustion
- Cyanosis
- Increasing tachycardia. NB Decreasing heart rate is pre-terminal
- Poor respiratory effort

Important Notes

- **1.Wheezing may be less apparent with increasing airway obstruction, with a silent chest occurring in life threatening asthma.**

- **2. Clinical signs correlate poorly with severity of airway obstruction. Thus objective measurements with SaO2 are essential.**

Important Notes

- **3. CXR may be abnormal but does not usually guide management. A pneumothorax may be revealed in severe respiratory failure.**
- **4. Blood gases rarely guide therapy. A rising pCO2 may be indicative of worsening respiratory failure, but the decision to intubate is still a clinical one. Metabolic acidosis may be caused by salbutamol, particularly intravenous**

Status asthmaticus

- an acute exacerbation of asthma that remains unresponsive to initial treatment with bronchodilators.
- varies from a mild form to a severe form with bronchospasm, airway inflammation, and mucus plugging that can cause difficulty breathing, carbon dioxide retention, hypoxemia, and respiratory failure.

Indications for consideration of admission to PICU

- **Severe acute asthma which has not responded adequately to continuous inhaled bronchodilators for one hour . and a single bolus of IV salbutamol (epinephrine) and IV bolus of steroids**

Aims of therapy in severe episode

- **Maintenance of adequate oxygenation (SaO2 ≥ 93%).**
- **Maintenance of haemodynamic stability**
- **Rapid bronchodilation**

Maintenance of adequate oxygenation

- **Oxygen delivery is best by high flow oxygen via reservoir fitted facial mask (thereby increasing FiO2), with the aim of maintaining SaO2 ≥ 92%.**

- .

Why is there hypoxaemia?

- **Bronchial obstruction leading to ventilation-perfusion mismatch**
- **+ hypoventilation**
- **+ alveolar hypercarbia**
- **+ acidotic pulmonary vasoconstriction.**

What is hypoxaemia?

- **SaO2 <93% (PaO2 <80 mmHg).**

- **Bronchodilators may paradoxically worsen the ventilation-perfusion mismatch, via preferential distribution of pulmonary blood flow to atelectatic areas.**

Maintenance of haemodynamic stability

Haemodynamic compromise could result from :

- **Hypoxia – directly myocardial depressant**
- **Arrhythmia related to hypoxia or therapy**
- **Impaired venous return (dynamic overinflation)**
- **Adrenal suppression due to prior outpatient use of high doses of inhaled corticosteroid.**
- **Allergies (food, drug induced**)

- **Management is via appropriate intravascular filling, attention to appropriate ventilation and consideration of inotropy.**
- **Maintain electrolyte balance (K glucose PO4)**

Bronchodilation

- **Receiving beta-2 agonists continuously via a nebuliser is the preferred option in severe asthma.**
- **Use 2.5 mg for infants, 5 mg for older children, diluted to 3-4mL with 0.9% saline. Some children become quite distressed with nebulisers and may prefer spacer administration – delivery is equivalent.**

Bronchodilation

- **In between nebulisations change to a Hudson mask with reservoir bag.**

- **Receiving beta-2 agonists via a spacer is the preferred option in mild to moderate asthma and is less likely to be associated with the adverse effects of tachycardia and hypoxia, give 6-10 puffs.**

Bronchodilatation

- **The recommended dose of salbutamol via the spacer is 6 puffs (600mcg) for children under 6 years and 12 puffs (1200mcg) for children 6 years and over. These doses should be administered one puff at a time.**
-
- **Frequent beta-2 agonist use can lead to the side effects that include tachycardia, tremors, agitation, paradoxical bronchospasm, hyperglycaemia and hypokalaemia.**

Nonselective beta2-agonists

- epinephrine [0.3-0.5 mg] or terbutaline [0.25 mg]) administered subcutaneously.
- Caution in patients with complicating factors (eg, (CHF), history of cardiac arrhythmia).
- !? cardiac enzyme levels monitoring . (troponin I)

IV adrenaline/salbutamol infusion

- **IV adrenaline infusion should be used in prepubertal children only in life threatening acute attacks or in the presence of anaphylactic shock.**
- **In older children IV adrenaline is a (cheaper) alternative to IV salbutamol. Discuss with Intensivist. Starting dose is 0.1 micrograms/kg/min.**

Anticholinergic agents

- **There is evidence for the efficacy of frequent doses of ipratropium bromide in addition to inhaled beta-2 agonist,**

- **If ipratropium has been started it is reasonable to stop in the recovery phase.**

Ipratropium bromide

- Antisecretory properties, when applied locally, inhibits secretions from serous and seromucous glands lining the nasal mucosa.
- Inhibits acetylcholine at parasympathetic sites in bronchial smooth muscle, resulting in bronchodilation.

Magnesium Sulfate

- Intravenous Magnesium can relax smooth muscle and cause bronchodilation by competing with calcium at calcium-mediated smooth muscle–binding sites.
- Dosing regimen recommended is between 25 and 75 mg/kg with a maximum of 2 g/dose over 20 min .
- Proper monitoring in PICU during infusion for cardiovascular vital signs .

mechanical ventilation/considerations

- Controlled hypoventilation (toleration of higher levels of $PCO_{2)}$
- Minimize tidal volume and peak inspiratory pressures.
- Permissive hypercapnia can be tolerated as long as the patient remains adequately oxygenated.
- A longer (I/E) ratio, often greater than 1:3-4, [auto-PEEP]).

ECG monitoring and oximetry are mandatory for all asthmatic patients