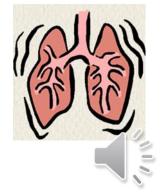
# Bronchial Asthma in Children part I

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- Introduction
- Pathophysiology
- Epidemiology
- Clinical presentation
- DDX
- Investigations
- Treatment



#### 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 :
- <u>Airway inflammation</u> airway inflammation cause recurrent or persistent <u>bronchospasm</u>, 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 ightarrow

 -(EARLY PHASE 15-30m) :, o functional and structural changes: Bronchospasm :

-(LATE PHASE4-12hr) : mucosal edema, and mucus plugs

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

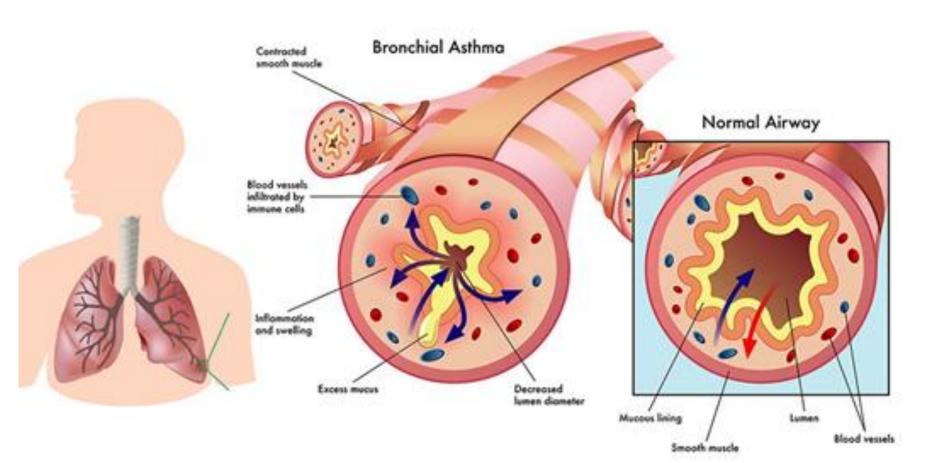


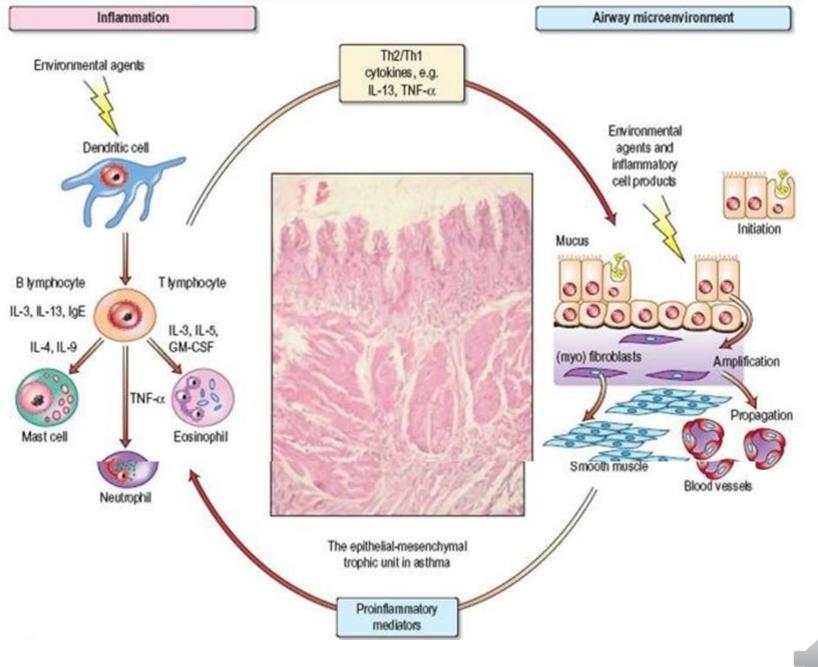
- Hyperinflation ---> compensates for the airflow obstruction, but this later on causes alveolar hypoventilation V/Q mismatch -→ HYPOXIA
- Hyperventilation triggered by the hypoxic drive also causes a decrease in PaCO2 hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar 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 ventilationperfusion 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.







# Update in airway inflammation in children

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

 <u>Viral infections</u> (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 Thelper (Th)2 responses in predisposed children and the development of allergic inflammation.



#### Aerosensitizatio

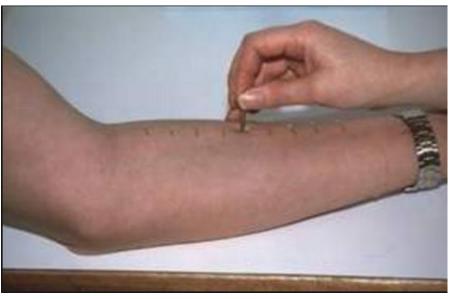
 <u>Sensitisation and exposure to allergens</u> is the major cause of allergic airway inflammation in older children.

 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).



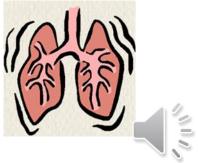
#### Genetics

• 2 new loci with asthma risk:

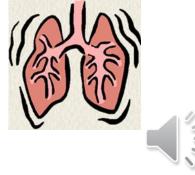
rs4129267 in IL6R and rs7130588 on band 11q13.5.

IL6R association  $\rightarrow$  cytokine dysregulation affects asthma risk

11q13.5 locus  $\rightarrow$  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.



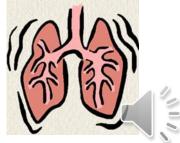
## Asthma Predictor Index

History of $\geq$ 4 wheezing episodes with at least one physician diagnosed and either					
One (or more) of the major criteria	Two (or more) of the minor criteria				
<ul> <li>Parental history of asthma</li> </ul>		<ul> <li>Eosinophilia (≥4%)</li> </ul>			
<ul> <li>Skin test positive to aero-allergens</li> </ul>		<ul> <li>Wheezing unrelated to colds</li> </ul>			
<ul> <li>Eczema (physician-diagnosed atopic dermatitis)</li> </ul>		<ul> <li>Allergic sensitization to milk, egg, or peanuts</li> </ul>			



# 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 .woodcoal-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 )





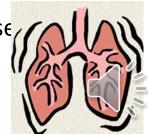
# **Clinical manifestations**

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)



# 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).

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» Upper airway exam. :
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- 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.



• Please turn to Bronchial Asthma Part II

#### Bronchial Asthma in children Part II

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#### **WORK UP**

# 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



j I I					Spire	ometry						
	A				FVC FEV1 FEV1/FVC FEF25-75% FEF50% PEF	Liters Liters % L/sec L/sec L/sec	Ref 2.40 2.25 86 2.64 2.58 4.50	Pre Meas 1.99 1.28 64 0.57 0.87 4.87	Pre % Ref 83 57 22 34 108	Post Meas 2.09 1.31 63 0.54 0.79 4.90	Post % Ref 87 58 20 31 109	Post % Chg 5 3 -5 -9 1
- - -1	0	Volume <sup>2</sup>	3	4		% PRED	ICTED	200 T 150 -				



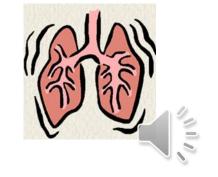
# Radiology

- 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**

- <u>DDx</u> :
- Airway Foreign Body
- <u>Allergic Rhinitis</u>
- <u>Aspergillosis</u>
- <u>Aspiration Syndromes</u>
- **Bronchiectasis**
- **Bronchiolitis**
- Bronchopulmonary Dysplasia
- <u>Cystic Fibrosis</u>
- Gastroesophageal Reflux
- Primary Ciliary Dyskinesia

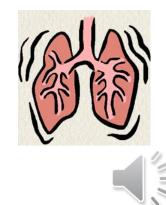


TABLE 1	Possible differential diagnosis in a child presenting with severe asthma
Tracheomala Congenital d Primary cilian Oesophagea Foreign body Bronchiolitis Immunodefic Cardiac disea	isorders ry dyskinesia I fistula



## **Components of Asthma Care**

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



## TREATMENT

## **Considerations for Treatment**

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



## Assessment and monitoring

1		Classification of Asthma Control (0-4 Years of Age)			
Components of Severity		Well Controlled	Not Well Controlled	Very Poorly Controlled	
1	Symptoms	≤2 days/week	>2 days/ week	Throughout the day	
M P	Nighttime awakenings	≤1x/month	>1x/month	>1x/week	
A I R	Interference with normal activity	None	Some limitation	Extremely limited	
M E N T	Short acting beta2- agonist use for symptom control**	≤2 days/week	>2 days/week	Several times per day	
R	Exacerbations requiring oral systemic corticosteroids	0-1 per year	2-3 per year	>3 per year	
S K	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		<ul> <li>Maintain current treatment.</li> <li>Regular follow-up every 1-6 months.</li> <li>Consider step down if well controlled for at least 3 months.</li> </ul>	<ul> <li>Step up 1 step and reevaluate in 2-6 weeks.</li> <li>If no clear benefit in 4-6 weeks, consider alternative diagnoses or adjust therapy.</li> <li>For side effects, consider alternative treatment options.</li> </ul>	<ul> <li>Consider short course of oral systemic corticosteroids.</li> <li>Step up 1-2 steps, and reevaluate in 2 weeks.</li> <li>If no clear benefit in 4-6 weeks, consider alternative diagnosis or adjusting therapy.</li> <li>For side effects, consider alternative treatment options.</li> </ul>	
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.					

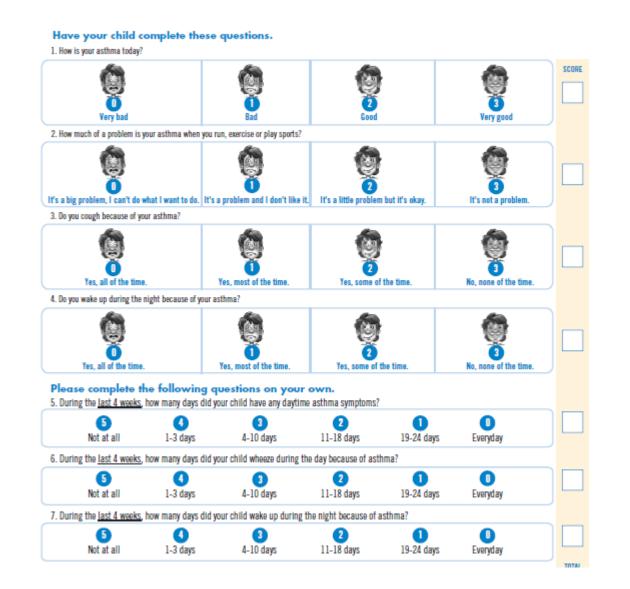
## Assessment and monitoring

		Classific	cation of Asthma Control (5-1	1 Years of Age)
Components of Severity		Well Controlled	Not Well Controlled	Very Poorly Controlled
	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
N T	■ FEV <sub>1</sub> or peak flow	>80% predicted/ personal best	60-80% predicted personal best	<60% predicted/ personal best
-	■ FEV <sub>1</sub> /FVC	>80%	75-80%	<75% predicted
	Exacerbations requiring	0-1 per year	0-1 per year ≥2 per year	
R	oral systemic corticosteroids	Consider severity and interval since last exacerbation.		
I S	Reaction in lung growth	Evaluation requires long-term follow-up care.		
ĸ	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		<ul> <li>Maintain current step</li> <li>Regular follow-up every 1-6 months.</li> <li>Consider step down if well controlled for at least 3 months.</li> </ul>	<ul> <li>Step up 1 step and reevaluate in 2-6 weeks.</li> <li>For side effects, consider alternative treatment options.</li> </ul>	<ul> <li>Consider short course of oral systemic corticosteroids.</li> <li>Step up 1-2 steps, and reevaluate in 2 weeks.</li> <li>For side effects, consider alternative treatment options.</li> </ul>
	nted from the 2007 NAEPP Exp rt, go to: www.nhlbi.nih.gov/gui		or the Diagnosis and Management (	of Asthma. To access the complete

## Assessment and monitoring

			n of Asthma Control (12 Year	s of Age and Older)
Components of Severity		Well Controlled	Not Well Controlled	Very Poorly Controlled
I	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1-3x/month	≥4x/week
M P	Interference with normal activity	None	Some limitation	Extremely limited
A I R	Short acting beta2- agonist use for symptom control**	≤2 days/week	>2 days/week	Several times per day
M	FEV <sub>1</sub> or peak flow	>80% predicted/	60-80% predicted	<60% predicted/ personal bes
E		personal best	personal best	
Ν		Valida	ated questionnaires	-
т	■ ATAQ* ■ ACQ**	0 <0.75	1-2 ≥1.5	3-4 N/A
	ACT***	>20	≥1.5 16-19	< <u>15</u>
	Exacerbations requiring	0-1 per year		per year
R	oral systemic corticosteroids	Consider severity and interval since last exacerbation.		
I S	Reaction in lung growth	Evaluation requires long-term follow-up care.		
K	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		<ul> <li>Maintain current step</li> <li>Regular follow-up every 1-6 months.</li> <li>Consider step down if well controlled for at least 3 months.</li> </ul>	<ul> <li>Step up 1 step and reevaluate in 2-6 weeks.</li> <li>For side effects, consider alternative treatment options.</li> </ul>	<ul> <li>Consider short course of oral systemic corticosteroids.</li> <li>Step up 1-2 steps, and reevaluate in 2 weeks.</li> <li>For side effects, consider alternative treatment options.</li> </ul>

## ACT test





## Assessment/Biomarkers for Asthma

- Pulmonary function and BHR
- BAL/Sputum
- Exhaled NO
- urinary leukotrienes
- Total and specific IGE
- Chitinases\*



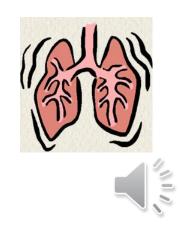
## Consultations

- 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



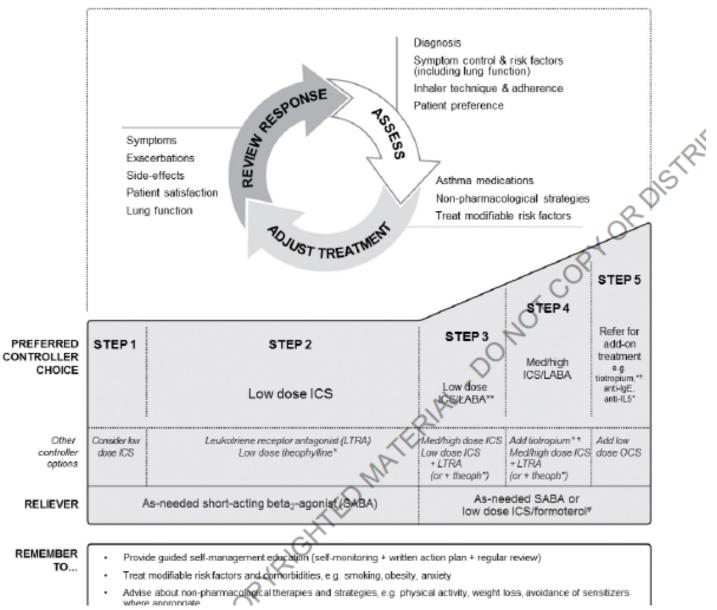
## Consultations

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



#### Children 6 to 12 years sten annroach GINA

Box 3-5. Stepwise approach to control symptoms and minimize future risk





CLASSIFY SEVERITY Clinical Features before Treatment					
	Symptoms	Nocturnal Symptoms	FEV <sub>1</sub> or PEF		
STEP 4 Severe Persistent	Continuous Limited physical activity	Frequent	< 60% predicted Variability > 30%		
STEP 3 Moderate Persistent	Daily Attacks affect activity	> 1 time week	60 to 80% predicted Variability > 30%		
STEP 2 Mild Persistent	> 1 time a week but < 1 time a day	> 2 times a month	> 80% predicted Variability 20 to 30%		
STEP 1 Intermittent	< 1 time a week Asymptomatic and normal PEF between attacks	< 2 times a month	> 80% predicted Variability < 20%		

NIN,

# 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







## Multidose dry powder inhalers



Accubaler"

Easyhaler\*



Turbuhaler\*



#### Twisthalor\*



Genuair\*





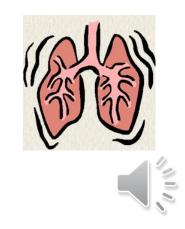






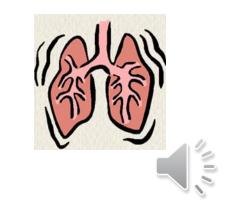
## **Quick-relief medications**

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



# Control /Long term medications

- ICS
- LTRA
- Combination LABA/ICS
- Cromolyn/Nedocromil
- Methylxanthines:Theophylline
- Syetemic steroids



- 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





## 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

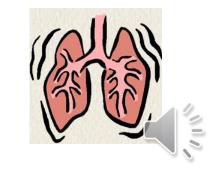


## Leukotrienes Modifiers

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

- 5-lipoxygenase inhibitors: Zileuton

-Leukotriene-receptor antagonists : Zafrilukast ,Montelukast



## ICS Vs LTRA

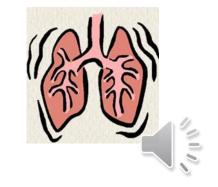
• Oral montelukast, inhaled beclomethasone, and placebo for chronic asthma. A randomized controlled trial.

Both inhaled steroid and a leukotriene inhibitor were better than placebo but Beclomethasone was significantly better than montelukast in reducing exacerbations

Ann Intern Med 1999

# **Co-morbidities**

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



## Omalizumab

 Anti-IgE monoclonal antibody , well-established therapy for asthma with eosinophilia

in childhood

• Two recent studies

6-20 years : (>n= 400 ) less eosinophilia ,less no of exacerbations Busse et al. N Engl J Med 2011

2- 6–12 years : 31% reduction in exacerbation

Lanier et al ,J Allergy Clin Immunol 2009



## Proton pump inhibitors

 400 patients minimal or no reflux symptoms and poorly controlled asthma despite moderate to high dose of inhaled corticosteroids to high-dose esomeprazole:

- *no improvement in asthma control in this population, regardless of the presence of asymptomatic gastroesophageal reflux. Mastronade et al et al. N Engl J Med 2009* 

## Further treatment

- Tiotropium (LAMA): now approved for children 12 years and older as add-on therapy
- Mepolizumb (IL 5 antagonist )
- Reslizumab (antibody against IL-5)
- immune therapy (desensitization )
- Vitamin D supplementation



# 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.
- Health workers should try to focus on improving quality of life for these children

