# **Bronchial Asthma**

Haneen Abu Al-Rous

Asthma is a serious global health problem affecting all age groups. Its prevalence is increasing in many countries, especially among children.

Asthma is the most common chronic disease of childhood.

The prevalence in different countries ranges from 1 to 18 percent.

Before the onset of puberty, boys have a higher prevalence of asthma than girls. This trend reverses in adolescence.

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

It is defined by the history of respiratory symptoms, such as wheeze, shortness of breath, chest tightness and cough, that vary over time and in intensity, together with variable expiratory airflow limitation.

These variations are often triggered by factors such as exercise, allergen or irritant exposure, change in weather, or viral respiratory infections.

Asthma is usually associated with airway hyperresponsiveness and airway inflammation, but these are not necessary or sufficient to make the diagnosis.

### **Asthma Phenotypes**

Allergic asthma: This is the most easily recognized asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. Examination of the induced sputum of these patients before treatment often reveals eosinophilic airway inflammation.

Non-allergic asthma: Some patients have asthma that is not associated with allergy.

Adult-onset (late-onset) asthma: These patients tend to be non-allergic, and often require higher doses of ICS or are relatively refractory to corticosteroid treatment.

Asthma with persistent airflow limitation: Some patients with long-standing asthma develop airflow limitation that is persistent or incompletely reversible.

### Pathophysiology

Interactions between environmental and genetic factors result in airway inflammation, limits airflow and leads to functional and structural changes in the airways in the form of Bronchospasm, mucosal edema, and mucus plugs, basement membrane thickening, subepithelial collagen deposition, smooth muscle and mucous gland hypertrophy and mucus hypersecretion.

A cellular inflammatory infiltrate and exudates distinguished by eosinophil, but also including other inflammatory cell types can fill and obstruct the airways and induce epithelial damage.

Airway obstruction causes increased resistance to airflow and decreased expiratory flow rates. These changes lead to a decreased ability to expel air and may result in hyperinflation, which helps maintain airway patency, improving expiratory flow; but also alters pulmonary mechanics and increases work of breathing.

Uneven changes in airflow resistance, the resulting uneven distribution of air, and alterations in circulation from increased intraalveolar pressure due to hyperinflation all lead to ventilation-perfusion mismatch.

In the early stages, when ventilation-perfusion mismatch results in hypoxia, hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar capillary membranes.

Thus, asthmatic patients who are 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.

In the early stages of an acute episode, respiratory alkalosis results from hyperventilation.

Later, the increased work of breathing, increased oxygen consumption, and increased cardiac output result in metabolic acidosis. Respiratory failure leads to respiratory acidosis.

### **Clininal Manifestations and Diagnosis**

Establishing a diagnosis of asthma involves a careful process of history taking, physical examination, and diagnostic studies.

Based on identifying both a characteristic pattern of respiratory symptoms such as wheezing, shortness of breath (dyspnea), chest tightness or cough, and variable expiratory airflow limitation.

### Symptoms

Approximately 80 percent of children with asthma develop symptoms before five years of age.

Cough: Typically dry, nocturnal cough, a cough that recurs seasonally, a cough in response to specific exposures, or a cough that lasts more than three weeks should raise the suspicion for asthma.

Wheeze: Usually polyphonic. When airflow obstruction becomes severe, wheezing can be heard on both inspiration and expiration.

Older children and adults report associated shortness of breath and chest congestion and tightness; younger children are more likely to report intermittent, nonfocal chest pain.

Respiratory symptoms can be worse at night.

Self-imposed limitation of physical activities, general fatigue (possibly resulting from sleep disturbance), and difficulty keeping up with peers in physical activities.

## **Precipitating Factors**

- Respiratory tract infections: Viral upper respiratory infections (URIs) are the most important triggering factor for patients with asthma of all ages, including infants and young children.
- Exercise: Exercise-triggered symptoms typically develop several minutes into prolonged exercise. Symptoms usually resolve with rest over 30 to 60 minutes.
- Weather.
- Tobacco smoke: Exposure to second-hand cigarette smoke is the single, most common, external risk factor for the development and progression of asthma symptoms in children.
- Allergens: House dust mites, pet exposures, Pollens , Molds.

### Symptom Patterns

Intermittent exacerbations superimposed upon an asymptomatic baseline.

Chronic symptoms punctuated by periods of worsening symptoms.

Morning "dipping" (an accentuation of the physiologic cycle of pulmonary function in normal individuals, characterized by worsening of symptoms and decreased peak flow in the early morning, with improvement as the day progresses).

### **Allergic History**

Allergic disease is associated with the development, severity, and persistence of asthma.

Patients with allergic rhinitis or atopic dermatitis should be asked specifically about respiratory symptoms.

### **Family History**

A family history of asthma or other atopic disease (ie, allergic rhinitis, atopic dermatitis, or food allergy) certainly strengthens the likelihood that a child with a compatible history has asthma.

Maternal asthma appears to make a bigger contribution than paternal asthma to asthma in offspring, although this finding is inconsistent .

### **Past Medical History**

Preterm .

Low birth weight.

Bronchiolitis required hospitalization.



### **Physical Examination**

Physical examination of a child with asthma is generally normal if performed when the patient does not have an acute exacerbation.

Abnormalities that may be observed include:

- Decreased air entry or wheezing on auscultation.
- •A prolonged expiratory phase on auscultation.

•An increased anterior-posterior diameter of the chest due to air trapping.

Examination findings during an acute exacerbation include tachypnea, hypoxia, wheezing, accessory muscle use, retractions, and prolonged expiratory phase.

### **Pulmonary Function Testing**

Demonstration of reversible airflow obstruction establishes the diagnosis of asthma and facilitates the assessment of severity.

Spirometry is the preferred method of diagnosis of airflow obstruction.

A reduced FEV1 may be found with many other lung diseases (or poor spirometric technique), but a reduced ratio of FEV1 to forced vital capacity (FEV1/FVC), compared with the lower limit of normal, indicates expiratory airflow limitation.

Reversibility: An increase in lung function after administration of a bronchodilator, or after a trial of controller treatment. Generally, with respiratory symptoms typical of asthma, an increase in FEV1 of >12% from baseline, or (if spirometry is not available) a change in PEF of at least 20%, is accepted as being consistent with asthma.

A decrease in lung function after exercise or during a bronchial provocation test with methacholine, cold air, or exercise.

Variability: Variation in lung function beyond the normal range when it is repeated over time, either on separate visits, or on home monitoring over at least 1–2 weeks.so in general, diurnal variability >13% for children.

### **Chest Radiograph**

Only in children who do not respond to initial therapy.

In those children, the chest radiograph may display findings suggestive of causes for wheezing other than asthma including congenital malformations, evidence of airspace disease consistent with aspiration or cystic fibrosis, or findings consistent with asthma, such as hyperinflation, peribronchial thickening, and mucoid impaction with atelectasis.

### **Exhaled Nnitric Oxide**

The fractional concentration of exhaled nitric oxide (FeNO) is modestly associated with levels of sputum and blood eosinophils.

FeNO has not been established as useful for ruling in or ruling out a diagnosis of asthma.

### **Allergy Testing**

- The presence of atopy increases the probability that a patient with respiratory symptoms has allergic asthma, but this is not specific for asthma nor is it present in all asthma phenotypes.
- Atopic status can be identified by skin prick testing or by measuring the level of specific immunoglobulin E (slgE) in serum.
- The presence of a positive skin test or positive slgE, however, does not mean that the allergen is causing symptoms – the relevance of allergen exposure and its relation to symptoms must be confirmed by the patient's history.

**Children <5 years** — In infants and children younger than five years of age, the diagnostic steps should remain the same as described above, except that spirometry often cannot be performed in this age group. A trial of asthma medications may help to establish the diagnosis in these children . Reversal of symptoms and signs in the time expected for albuterol to work is suggestive of the diagnosis of asthma.

# Diagnostic criteria for asthma in children 6–11 years

1. History of variable respiratory symptoms.

2. Confirmed variable expiratory airflow limitation:

#At a time when FEV1 is reduced, confirm that FEV1/FVC is reduced compared with the lower limit of normal (less than 0.80).

And

#Documented excessive variability in lung function: one of the following:

1)Positive bronchodilator (BD) responsiveness (reversibility) test: increase in FEV1 of >12% predicted.

2)Excessive variability in twice daily PEF over 2 weeks: average daily diurnal PEF variability >13%.

3)Positive exercise challenge test: fall in FEV1 of >12% predicted.

4)Excessive variation in lung function between visits: variation in FEV1 of >12% in FEV1 between visits.

Box 6-2. Features suggesting a	a diagnosis of asthma in children 5 years and younger

Feature	Characteristics suggesting asthma		
Cough	<ul> <li>Recurrent or persistent non-productive cough that may be worse at night or accompanied by wheezing and breathing difficulties</li> <li>Cough occurring with exercise, laughing, crying or exposure to tobacco smoke, particularly in the absence of an apparent respiratory infection</li> </ul>		
Wheezing	<ul> <li>Recurrent wheezing, including during sleep or with triggers such as activity laughing, crying or exposure to tobacco smoke or air pollution</li> </ul>		
Difficult or heavy breathing or shortness of breath	<ul> <li>Occurring with exercise, laughing, or crying</li> </ul>		
Reduced activity	<ul> <li>Not running, playing or laughing at the same intensity as other children; tires earlier during walks (wants to be carried)</li> </ul>		
Past or family history	• Other allergic disease (atopic dermatitis or allergic rhinitis, food allergy). Asthma in first-degree relative(s)		
Therapeutic trial with low dose ICS (Box 6-5, p. <u>165</u> ), and as-needed SABA	<ul> <li>Clinical improvement during 2–3 months of controller treatment and worsening when treatment is stopped</li> </ul>		

### Assessment of Severity in Patients not on Daily Therapy

Initial assessment of patients who have confirmed asthma begins with a severity classification because selection of the type, amount, and scheduling of therapy corresponds to the level of asthma severity.

Assessment of asthma severity is made on the basis of components of current impairment and future risk .

Impairment:

•The frequency of symptoms, night time awakenings, and use of short-acting beta agonists for symptom control in the past four weeks, based upon patient/caregiver recall.

•The degree to which symptoms have interfered with normal activity in the past four weeks, based upon patient/caregiver recall.

•Spirometry results in children that are able to perform the test.

Risk: Risk assessment is primarily based upon the patient/caregiver recall of the number of exacerbations in the past year that have required treatment with oral glucocorticoids.

Table 169.7	Assessing Asthma Severity Control Medications*	and Initiating Treatment f	or Patients Who Are No	t Currently Taking Long-Term
		CLASSIFICAT	ION OF ASTHMA SEVERIT	ΓY
		PERSISTENT		
	INTERMITTENT	Mild	Moderate	Severe
COMPONENTS C Impairment	DF SEVERITY			
Daytime symptom Nighttime awaken	is ≤2 days/wk ings:	>2 days/wk but not daily	Daily	Throughout the day
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Age 0-4 yr	0	1-2×/mo	3-4×/mo	>1×/wk
Age ≥5 yr	≤2×/mo	3-4×/mo	>1×/wk but not nightly	Often 7×/wk
Short-acting β <sub>2</sub> -agonist use for symptoms (not for EIB prevention)	≤2 days/wk	>2 days/wk but not daily, and not more than 1× on any day	Daily	Several times per day
Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation
Lung function:				
FĒV₁ % predicted, age ≥5 yr	Normal FEV <sub>1</sub> between exacerbations >80% predicted	≥80% predicted	60–80% predicted	<60% predicted
FEV <sub>1</sub> /FVC ratio <sup>†</sup> :				
Age 5-11 yr	>85%	>80%	75-80%	<75%
Age ≥12 yr	Normal	Normal	Reduced 5%	Reduced >5%
Risk				

Exacerbations requiring systemic corticosteroids:

≥2 exacerbations in 6 mo requiring systemic CS Age 0-4 yr 0-1/yr (see notes) or ≥4 wheezing episodes/yr lasting >1 day *and* risk factors for persistent asthma ≥2/yr (see notes) ≥2/yr (see notes) ≥2/yr (see notes) Age ≥ 5 yr 0-1/yr (see notes) 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<sub>1</sub>.

#### RECOMMENDED STEP FOR INITIATING THERAPY

(See Table 169.11 fc	or treatment steps.)			
The stepwise appro	ach is meant to assist,	not replace, the clinical de	cision-making required to meet individua	l patient needs.
All ages	Step 1	Step 2	5 1	
Age 0-4 yr			Step 3 and consider a short course of systemic CS	Step 3 and consider a short course of systemic CS
Age 5-11 yr			Step 3: medium-dose ICS option and consider a short course of systemic CS	Step 3: medium-dose ICS option <i>or</i> Step 4 and consider a short course of CS
	In 2-6 wk, depe	ending on severity, evaluate	level of asthma control that is achieved.	
	<ul> <li>Children 0-4 adjusting the</li> <li>Children 5-1</li> </ul>	yr old: If no clear benefit is erapy accordingly. 1 yr old: Adjust therapy acc	observed in 4-6 wk, stop treatment and o ordinaly.	consider alternative diagnoses or

### Assessment of Severity in Patients on Daily Therapy

Asthma control rather than severity in patients who are already on daily controller treatment.

The level of asthma control is the extent to which the features of asthma can be observed in the patient, or have been reduced or removed by treatment.

Asthma control is assessed in two domains: symptom control and risk of adverse outcomes.

In the past 4 weeks, has the child had:	Well	Partly	Uncontrolled
<ul> <li>Daytime asthma symptoms for more than a few minutes, Yes No</li> <li>More than once a week?</li> <li>Any activity limitation due to asthma? (Runs/plays less Yes No</li> <li>than other children, tires easily during walks/playing?)</li> <li>Reliever medication needed* more than once a week? Yes No</li> <li>Any night waking or night coughing due to asthma? Yes No</li> </ul>	None of these	1–2 of these	3–4 of these
3. Future risk for poor asthma outcomes			•
<ul> <li>Uncontrolled asthma symptoms</li> <li>One or more severe exacerbation in previous year</li> <li>The start of the child's usual 'flare-up' season (especially if autumn/fall)</li> <li>Exposures: tobacco smoke; indoor or outdoor air pollution; indoor allerg pets, mold), especially in combination with viral infection<sup>509</sup></li> <li>Major psychological or socio-economic problems for child or family</li> <li>Poor adherence with controller medication, or incorrect inhaler technique</li> </ul>	gens (e.g. hous ue	se dust mite, c	ockroach,
<ul> <li>Risk factors for fixed airflow limitation</li> <li>Severe asthma with several hospitalizations</li> <li>History of bronchiolitis</li> </ul>			
<ul> <li>Risk factors for medication side-effects</li> <li>Systemic: Frequent courses of OCS; high-dose and/or potent ICS</li> <li>Local: moderate/high-dose or potent ICS; incorrect inhaler technique; for spacer with face mask</li> </ul>	ailure to protec	t skin or eyes	when using

CS = inhaled corticosteroids; OCS = oral corticosteroids \* Excludes reliever taken before exercise

<sup>&#</sup>x27;his GINA asthma symptom control classification corresponds to 'current control' in GINA pediatric report 2009.510 Before stepping up treatment, ensure

Asthma severity can be assessed when the patient has been on controller treatment for several months:

Mild asthma is asthma that is well controlled with Step 1 or Step 2 treatment.

Moderate asthma is asthma that is well controlled with Step 3 treatment .

Severe asthma is asthma that requires Step 4 or 5 treatment .

### Treatment

Goals of treatment: Maintain control of asthma symptoms and reduce exacerbations with the least amount of medications and fewest side effects.

Quick-relief (rescue) medications.

Long-term controller medications.

### Quick-relief (rescue) Medications

Primarily taken to relieve the bronchoconstriction that occurs with acute asthma symptom.

Quick-relief agents include:

- 1- Short-acting Beta Agonists (SABAs)
- 2- Anticholinergic Agents
- 3- Injectable Sympathomimetic Epinephrine

Short-Acting Inhaled β-Agonists:

Drugs of choice for acute asthma symptoms given their rapid onset of action, effectiveness.

Ex. Salbutamol, albuterol, levalbuterol, terbutaline.

The most common side effects are: tremor, tachycardia, palpitations hypokalemia, hypomagnesemia, hyperglycaemia.

Anticholinergic Agents:

Bronchodilators.

Ex. Ipratropium bromide.

When used in combination with albuterol, ipratropium can improve lung function and reduce the rate of hospitalization.

Potential adverse effects include: drying of the mouth, blurred vision, urinary retention, tachycardia.

Injectable sympathomimetic epinephrine:

Bronchodilator

For extreme circumstances (e.g., impending respiratory failure despite highdose inhaled SABA, respiratory failure).

### Long-term Controller Medications

Include:

- 1- Inhaled glucocorticoids
- 2- Systemic Corticosteroids
- 3- Inhaled long-acting beta agonists (LABA)
- 4- Oral leukotriene receptor antagonists (LTRAs)
- 5- Long-acting muscarinic antagonists [LAMAs]
- 6- Theophylline
- 7- Biologic agents

Inhaled glucocorticoids:

Ex. Budesonide, Fluticasone.

The most effective antiinflammatory agents available for the treatment of asthma.

The guidelines recommend daily ICS therapy as the treatment of choice for all patients with persistent asthma.

The most commonly encountered adverse effects of ICSs are local: oral candidiasis (thrush) and dysphonia (hoarse voice). The incidence of these local effects can be greatly minimized by using a spacer with an MDI ICS, because spacers reduce oropharyngeal deposition of the drug and propellant. Mouth rinsing. Hoarsness of voice The potential for growth suppression and osteoporosis with long term ICS use has been a concern. Systemic Corticosteroids:

Oral corticosteroids are used primarily to treat asthma exacerbations and, rarely, in patients with severe disease who remain symptomatic despite optimal use of other asthma medications.

Children who require long-term oral corticosteroid therapy are at risk for development of associated adverse effects over time.

Long-Acting Inhaled β-Agonists:

Ex. salmeterol, formoterol.

Not intended for use as rescue medication for acute asthma symptoms or exacerbations, nor as mono therapy for persistent asthma.

Controller formulations combines an ICS.

Both have a prolonged duration of effect.

For patients with nocturnal asthma and for individuals who require frequent SABA use during the day to prevent exercise-induced bronchospasm.

Leukotriene-Modifying Agents:

LTRAs have bronchodilator and targeted antiinflammatory properties and reduce exercise-, aspirin-, and allergen-induced bronchoconstriction.

LTRAs are recommended as alternative treatment for mild persistent asthma and as add-on medication with ICS for moderate persistent asthma.

Montelukast is approved for children (6 months -  $\geq$ 1 yr) of age and is administered once daily.

Zafirlukast is approved for children  $\geq 5$  yr of age and is administered twice daily.

Long-acting muscarinic antagonists [LAMAs]:

Ex. Tiotropium.

Approved by the US FDA for long-term maintenance treatment in patients  $\geq 6$  years of age with severe symptomatic asthma not well controlled on inhaled glucocorticoids and other maintenance therapies.

Tiotropium should not be used for initial treatment nor as sole therapy for persistent asthma.

Theophylline:

In addition to its bronchodilator effects, theophylline has antiinflammatory properties as a phosphodiesterase inhibitor.

When used long-term, theophylline can reduce asthma symptoms and the need for rescue SABA use.

Theophylline has a narrow therapeutic window; therefore, when it is used, serum theophylline levels need to be routinely monitored.

Theophylline overdosage and elevated theophylline levels have been associated with headaches, vomiting, cardiac arrhythmias, seizures, and death. Biologic agents :

Monoclonal antibodies against immunoglobulin E [IgE] and interleukin [IL] 5 for children  $\geq$ 6 years of age who have not responded to usual therapy include omalizumab (anti-IgE), dupilumab (anti-IL5).





If a patient has persisting uncontrolled symptoms and/or exacerbations despite 2–3 months of controller treatment, assess and correct the following common problems before considering any step up in treatment:

- 1- Incorrect inhaler technique.
- 2- Poor adherence .
- 3- Persistent exposure.

4- Comorbidities that may contribute to respiratory symptoms and poor quality of life .

5- Incorrect diagnosis.

### Managemet of Worsening Asthma and Exacerbations

Early symptoms of an exacerbation may include any of the following:

- An acute or sub-acute increase in wheeze and shortness of breath
- An increase in coughing, especially while the child is asleep
- Lethargy or reduced exercise tolerance
- Impairment of daily activities, including feeding
- A poor response to reliever medication.

Upper respiratory symptoms frequently precede the onset of an asthma exacerbation.

#### Box 6-9. Initial assessment of acute asthma exacerbations in children 5 years and younger

Symptoms	Mild	Severe*
Altered consciousness	No	Agitated, confused or drowsy
Oximetry on presentation (SaO <sub>2</sub> )**	>95%	<92%
Speech <sup>†</sup>	Sentences	Words
Pulse rate	<100 beats/minute	>180 beats/minute (0–3 years)
	0 12	>150 beats/minute (4–5 years)
Respiratory rate	≤40/minute	>40/minute
Central cyanosis	Absent	Likely to be present
Wheeze intensity	Variable	Chest may be quiet

\*Any of these features indicates a severe asthma exacerbation. \*\*Oximetry before treatment with oxygen or bronchodilator.

<sup>†</sup> The normal developmental capability of the child must be taken into account.

### Treatment in Acute Care Settings

The main initial therapies include repetitive administration of short-acting inhaled bronchodilators, early introduction of systemic corticosteroids, and controlled flow oxygen supplementation.

The aim is to rapidly relieve airflow obstruction and hypoxemia, address the underlying inflammatory pathophysiology, and prevent relapse.

#### Inhaled short-acting beta2 -agonists

Repeated administration of inhaled SABA (up to 4–10 puffs) every 20 minutes for the first hour.

For children with moderate-severe exacerbations and a poor response to initial SABA, nebulized ipratropium bromide may be added every 20 minutes for 1 hour only.

#### Controlled oxygen therapy

Oxygen therapy should be titrated against pulse oximetry to maintain oxygen saturation at 93-95%

#### Systemic corticosteroids

OCS should be given promptly, especially if the patient is deteriorating, or had already increased their reliever and controller medications before presenting.

Should be administered to the patient within 1 hour of presentation. The recommended dose is 1–2 mg/kg/day for children 6–11 years up to a maximum of 40 mg/day).

OCS should usually be continued for 3-5 days in children.

#### Inhaled corticosteroids

high dose ICS given within the first hour after presentation reduces the need for hospitalization in patients not receiving systemic corticosteroids.

#### Magnesium sulfate

When administered as a single 2 g infusion over 20 minutes, it reduces hospital admissions in some patients, including adults and children who fail to respond to initial treatment and have persistent hypoxemia; and children whose FEV1 fails to reach 60% predicted after 1 hour of care .

### **Reviewing Response**

Clinical status and oxygen saturation should be re-assessed frequently, with further treatment titrated according to the patient's response .

Lung function should be measured after one hour, i.e. after the first three bronchodilator treatments, and patients who deteriorate despite intensive bronchodilator and corticosteroid treatment should be re-evaluated for transfer to the intensive care unit.

# Thank You