

# Guidelines

## For The Management Of

### Asthma

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# Asthma

Asthma is a chronic inflammatory disorder of the airways characterized by hyperresponsiveness especially when exposed to various risk factors.

It causes recurring episodes of wheezing, breathlessness, and cough, particularly at night or in the early morning.

The attacks (exacerbations) are episodic & reversible but airway inflammation is chronically present

## ***Differential Diagnosis of Asthma***

*Chronic obstructive pulmonary disease (chronic bronchitis or emphysema)*

*Congestive heart failure*

*Allergic rhinitis and sinusitis*

*Mechanical obstruction of the airways ( foreign body, tumors)*

*Cough secondary to drugs (angiotensin-converting enzyme [ACE] inhibitors)*

*Viral bronchiolitis*

*Gastroesophageal reflux*

*Pulmonary embolism*

*Laryngeal dysfunction*

*Vocal cord dysfunction*

*Cystic fibrosis*

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- Chest Radiography: The value of chest radiography is in revealing complications (pneumonia, pneumothorax or pneumomediastinum) or alternative causes of wheezing
  - Electrocardiography: Sinus tachycardia and ECG evidence of right heart strain are common in patients with acute asthma. Supraventricular tachycardia raises the consideration of theophylline toxicity. Arrhythmias, other than supraventricular tachycardia, are rare.
  - A full blood picture may show peripheral blood eosinophilia, eosinophil count greater than 4% or 300-400/ $\mu$ L supports the diagnosis of asthma, but an absence of this finding is not exclusionary.
  - B.Urea, creatinine, glucose & electrolyte

## **The goals for successful management of asthma**

- Achieve and maintain control of asthma symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications

## **Approach Considerations**

Medical care includes treatment of acute asthmatic episodes and control of chronic symptoms, including nocturnal and exercise-induced asthmatic symptoms.

Relief medications include short-acting bronchodilators, systemic corticosteroids, and ipratropium.

Control agents such as inhaled corticosteroids, inhaled cromolyn or nedocromil, long-acting bronchodilators, theophylline, leukotriene modifiers, and more recent strategies such as the use of anti-immunoglobulin E (IgE) antibodies (omalizumab).

**Management of exacerbations**

Exacerbations of asthma are episodes of progressive increase in shortness of breath, cough, wheezing or chest tightness or combinations of these.

**Do not underestimate the severity of an attack; severe asthma may be life threatening**

**Initial Treatment**

Inhaled rapid-acting  $\beta_2$ -agonist up to three treatments in 1 hour.

Response to Initial Treatment Is....		
Good if.....	Incomplete if.....	Poor if.....
Symptoms subside after initial $\beta_2$ - agonist and relief is sustained for 4 hours	Symptoms decrease but return in less than 3 hours after initial $\beta_2$ - agonist treatment.	Symptoms persist or worsen despite initial $\beta_2$ - agonist treatment.
PEF is greater than 80% predicted	PEF is 60-80% predicted	PEF is less than 60% predicted
<b>ACTIONS:</b>	<b>ACTIONS:</b>	<b>ACTIONS:</b>
Continue $\beta_2$ -agonist every 3-4 hours for 1-2 days.	Add oral glucocorticosteroid Add inhaled anticholinergic Continue $\beta_2$ - agonist.	Add oral glucocorticosteroid Re-repeat $\beta_2$ agonist Add inhaled anticholinergic Transport to hospital emergency department

**Hospital based care**

**Assessment of severity of asthma**

Parameter	Mild	moderate	sever	Respiratory arrest imminent
Breathless	Walking Can lie down	Talking Prefer sitting	At rest Hunched forward	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Often > 30 minutes	
Accessory muscles & suprasternal retractions	Usually not	Usually	Usually	Paradoxical thoraco-abdominal movement
Wheeze	Moderate, often only expiratory	Loud	Loud	Absence of Wheeze
Pulse/min.	< 100	100-120	> 120	Bradycardia
Pulsus paradoxus	Absent < 10 mm Hg	May be present 10- 25 mm Hg	Often present > 25 mm Hg (adult) 20-40 mm Hg (child)	Absence suggests Respirat. muscle Fatigue
PEF after initial bronchodilator % predicted	Over 80%	Approx. 60-80%	< 60% predicted response lasts < 2 hrs	
PaO <sub>2</sub> (on air and/or PaCO <sub>2</sub>	Normal <45 mm Hg	> 60 mm Hg < 45 mm Hg	< 60 mm Hg Possible cyanosis > 45 mm Hg; Possible respiratory failure	
SaO <sub>2</sub> % (on air)	> 95%	91-95%	< 90%	

## **Hospital based care**

### **Initial Assessment**

History, physical examination (heart rate, respiratory rate, dehydration, physical exhaustion), spirometry, pulse oximetry, arterial blood gas analysis

*Patients should immediately seek intensive medical care if:*

1- The attack is severe

- The patient is breathless at rest, is hunched forward, talks in words rather than sentences, is agitated, drowsy, or confused, has bradycardia, or has a respiratory rate greater than 30 per minute

- Wheeze is loud or absent

- Pulse is greater than 120/min

- PEF is less than 60 percent of predicted even after initial treatment

- The patient is exhausted & dehydrated

2-The response to the initial bronchodilator treatment is not prompt and sustained for at least 3 hours

3- There is no improvement within 2 to 6 hours after oral glucocorticosteroids treatment is started

4- There is further deterioration

### Albuterol (Ventolin)

is administered as nebulizer 2.5-5 mg every 20 minutes for 3 doses, then 2.5-10 mg every 1- 4 hours as needed; dilution of 2.5 mg in 3-4 mL of saline.

Oxygen or compressed air delivery of the inhaled beta agonists should be at a rate of 6-8 L/min.

In case nebulizer is not available, use inhaled rapid-acting  $\beta_2$ -agonists in adequate doses.

Begin with 2 to 4 puffs every 20 minutes for the first hour;

mild exacerbations will require 2 to 4 puffs every 3 to 4 hours

moderate exacerbations will require 6 to 10 puffs every 1 to 2 hours.

### Ipratropium bromide (Atrovent)

Ipratropium should be given as nebulizer in combination with Albuterol every 20 minutes for 3 doses, then as needed 6hrly

0.5 mg is recommended in severe exacerbations only

Combination  $\beta_2$ -agonist/anticholinergic therapy is associated with lower hospitalization rates and greater improvement in PEF and FEV<sub>1</sub>

### Corticosteroids

Systemic glucocorticosteroid are indicated if

- no immediate response

- patient is already on glucocorticosteroids

- episode is severe

Oral glucocorticosteroids 0.5 -1 mg of prednisolone/kg as single dose or

i.v methylprednisolone 2 mg/kg or i.v hydrocortisone 200 mg q4 -6h may be given in patients who are vomiting or unable to swallow, until severe symptoms controlled, then reduce the dose.

Introduced early in the course of a moderate or severe attack, it helps to reverse the inflammation, speed the resolution of airway obstruction, prevent a late-phase response and speed recovery.

### Methylxanthines

Theophylline is not recommended if used in addition to high doses of inhaled  $\beta_2$ -agonists, but can be used if inhaled  $\beta_2$ -agonists are not available.

Load: 5mg/kg in 100ml fluid over 20min, then 0.5-1mg/kg/hr (250 mg) in 500 ml. fluid over 6 hrs.

Patients with severe asthma exacerbations unresponsive to bronchodilators and systemic glucocorticosteroids, 2 grams of magnesium sulphate in 50 ml. saline over 20 minutes has been shown to reduce the need for hospitalizations.

Oxygen is given if the patient is hypoxemic to achieve O<sub>2</sub> saturation of 95%.

## **Hospital based care**

**Therapies not recommended** for treating asthma attacks include:

- Sedatives (strictly avoided)
  - Mucolytic drugs (may worsen cough)
  - Chest physical therapy/physiotherapy (may increase patient discomfort)
  - Hydration with large volumes of fluid for adults and older children (maybe necessary for younger children and infants)
  - Antibiotics (do not treat attacks but are indicated for patients who also have pneumonia, sinusitis or any evidence of bacterial infection)
  - Epinephrine/adrenaline is not indicated for asthma attacks unless associated with anaphylaxis and angioedema or fulminating life threatening attack manifested by severe symptoms that is not responding to initial treatment.
- .Avoid the use of NSAID

### **Indications for assisted ventilation in acute severe asthma**

Coma, confusion, drowsiness

Exhaustion

Respiratory arrest

Deterioration of arterial blood gas tensions despite optimal therapy

- $PaO_2 < 8$  kPa (60 mmHg) and falling
- $PaCO_2 > 6$  kPa (45 mmHg) and rising
- pH low and falling (worsening acidosis)

## Hospital based care

**Repeat Assessment** Physical Exam (heart rate, respiratory rate, dehydration, physical exhaustion), PEF or FEV<sub>1</sub>, O<sub>2</sub> saturation:

<b>Moderate Episode</b>	<b>Severe Episode</b>
PEF 60-80 % predicted Physical exam: moderate symptoms, accessory muscle in use  <u>Rx</u> Inhaled $\beta_2$ - agonist and inhaled anticholinergic every 60 minutes. Consider glucocorticosteroids  Continue treatment 1-3 hours, provided there is improvement	PEF < 60% predicted History: high - risk patient Physical exam: severe symptoms at rest, chest retraction. No improvement after initial treatment  <u>Rx</u> Inhaled ( $\beta_2$ - agonist & inhaled anticholinergic) Oxygen Systemic glucocorticosteroid Consider $\beta$ -agonist :0.25 mg terbutaline S.C, salbutamol 3-20 $\mu$ g/min I.V 0.3 mg of 1:1000 concentration of epinephrine S.C . Consider intravenous methylxanthines Consider intravenous magnesium sulphate

### **Monitoring the effects of treatment**

Repeat PEF 15-30min after initiating treatment.  
 Pulse oximetry monitoring: maintain S<sub>a</sub>O<sub>2</sub> >92%.  
 Check blood gases within 2h *if*: initial P<sub>a</sub>O<sub>2</sub> <8kPa (60mmHg) or initial P<sub>a</sub>CO<sub>2</sub> was normal/raised or patient is deteriorating.  
 Record PEF pre- and post  $\beta_2$ -agonist in hospital at least 4 times

*The patient is classified as follows*

<b>Good Response</b>	<b>Incomplete Response Within 1-2 flours</b>	<b>Poor Response within 1 Hr</b>
Response sustained 60 minutes after last treatment Physical exam normal PEF > 70% O <sub>2</sub> saturation >90%	mild to moderate symptoms PEF < 70% O <sub>2</sub> saturation not improving	severe symptoms, drowsiness, confusion PEF <30% PCO <sub>2</sub> > 45 mmHg PO <sub>2</sub> < 60 mmHg
<b>Discharge Home</b> Continue treatment with inhaled $\beta_2$ -agonist Consider. in most cases oral glucocorticosteroid Patient education	<b>Admit to Hospital as in-patient</b> Inhaled $\beta_2$ - agonist $\pm$ inhaled anticholinergic Systemic glucocorticosteroid Oxygen Consider intravenous methylxanthines	<b>Admit to Intensive Care</b> Inhaled $\beta_2$ agonist + anti cholinergic Intravenous glucocorticosteroid Consider subcutaneous, intramuscular, or intravenous $\beta$ -agonists Oxygen Consider intravenous methylxanthines Possible intubations and mechanical ventilation

**.Management of chronic cases**

**Schedule of assessment of management**

Levels of Severity	Daily Controller Medications	Other Treatment Options
Step 1 Intermittent	No need for controller medications The reliever medication is a short-acting $\beta_2$ -agonist as needed for symptoms.	
STEP 2 Mild Persistent	Low -dose inhaled GCST*	Sustained-release theophylline <i>or</i> Cromone <i>or</i> Leukotriene modifier
STEP 3 Moderate Persistent	Low to medium dose GCST + long acting inhaled $\beta_2$ -agonist	Medium-dose inhaled GCST + sustained release theophylline, <i>or</i> Medium-dose inhaled GCST + long acting oral $\beta_2$ -agonist <i>or</i> Medium-dose inhaled GCST + leukotriene modifier <i>or</i> High-dose inhaled GCST
STEP 4 Severe Persistent	High - dose inhaled GCST + long-acting inhaled $\beta_2$ -agonist, + one <i>or</i> more of the following if needed : Sustained release theophylline Leukotriene modifier Long-acting oral $\beta_2$ -agonist Oral GCST Anti-IgE	
<p><b>All steps</b> : Once control of asthma is achieved and maintained for at least 3 months, a gradual reduction of the maintenance therapy should be tried to identify the minimum therapy required</p> <p>*Glucocorticosteroid = GCST</p>		

**Criteria for Control of Asthma**

- Absence of hospitalization
- Absence of unscheduled medical care
- Absence of interference with sleep or activities (including competitive athletics)
- Infrequent intervention with short courses of high dose daily oral corticosteroids (< 4 times yearly ideally, but some young children may have viral respiratory induced exacerbations more frequently for an occasional year for which, there is no good alternative to an oral corticosteroid)
- Normal or best attainable post-bronchodilator pulmonary function by office spirometry
- Absence of adverse medication effects
- Absence of effects of asthma or its treatment on quality of life

**Bad prognostic factors**

- Age older than 40 years
- Smoking more than 20-pack years
- Blood eosinophilia,
- Forced expiratory volume in one second (FEV<sub>1</sub>) of 40-69% predicted
- Greater reversibility.

#### Nedocromil or sodium cromoglycate

can be used as an adjunct to inhaled steroids or as an alternative in those patients who cannot tolerate or do not wish to take inhaled steroids.

They should be considered as second line treatment to inhaled steroids.

No evidence to prefer nedocromil over sodium cromoglycate or vice versa

#### Monoclonal Antibody Therapy

Omalizumab is a humanized murine IgG antibody against the Fc component of the IgE antibody (the part that attaches to mast cell surfaces). Use of this antibody prevents IgE from binding directly to the mast cell receptor, thereby preventing cell degranulation without causing degranulation itself.

It was approved by the FDA in 2003 for adults and adolescents ( $\geq 12$  y) with moderate-to-severe persistent asthma who have a positive skin test result or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Patients should have IgE levels between 30-700 IU/ml, and should not weigh more than 150 kg.

#### **Nocturnal asthma**

Patients with asthma may experience nocturnal symptoms once or twice a month. Some patients only experience symptoms at night and have normal pulmonary function in the daytime. This is due, in part, to the exaggerated response to the normal circadian variation in airflow. Children with nocturnal asthma tend to cough after midnight and during the early hours of morning. Bronchoconstriction is highest between the hours of 4:00 am and 6:00 am (the highest morbidity and mortality from asthma is observed during this time). These patients may have a more significant decrease in cortisol levels or increased vagal tone at night

#### **Exercise asthma**

There is no indication for regularly scheduled medications in persons with isolated exercise induced bronchospasm without underlying asthma, prophylaxis in the form of inhaled medications administered 15- 30 min prior to exercise is usually required, the most common used medications are: short acting  $\beta$ - agonist such as Albuterol, Sodium Cromolyn & Nedocromolyn used 30 minutes prior to exercise  
Long acting  $\beta$  agonists such Salmeterol given 90 minutes before repetitive exercise

#### **Surgery & asthma**

Airway hyperresponsiveness, airflow limitation, and mucus hypersecretion predispose patients with asthma to intraoperative and postoperative respiratory complications, particularly with thoracic and upper abdominal surgeries.

*Asthma-related complications associated with surgery include:*

acute bronchoconstriction resulting from intubation, impaired cough, hypoxemia, hypercapnia, atelectasis, respiratory tract infection.

The likelihood of these complications occurring depends on the severity of the underlying asthma, the type of surgery (thoracic and upper abdominal), and the type of anesthesia.

Patients with asthma should have an evaluation before surgery that includes a review of asthma symptoms, medication use (particularly oral systemic corticosteroids for longer than 2 weeks in the past 6 months), and measurement of pulmonary function.

If evidence of airflow obstruction ( $< 80\%$  of baseline values) is present, a brief course of corticosteroids is recommended. Patients who have received oral corticosteroids for an asthma exacerbation in the past 6 months should receive systemic corticosteroids 100 mg hydrocortisone i.v q 8 h in the perioperative period.

## **Pregnancy & asthma**

It is safer to be treated with asthma medications than to have asthma symptoms and exacerbations as uncontrolled asthma represents the greatest danger to the fetus:

maternal complications (hyperemesis, hypertension, pre-eclampsia, vaginal haemorrhage, complicated labour)

fetal complications (intrauterine growth restriction and low birth weight, preterm birth, increased perinatal mortality, neonatal hypoxia)

The ultimate goal of asthma therapy is to maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother.

With the exception of alpha-adrenergic compounds other than pseudoephedrine, most drugs used to treat asthma and allergic rhinitis have not been shown to increase any risk to the mother or fetus. Drugs like albuterol, cromolyn, beclomethasone, budesonide, prednisone and theophylline, when clinically indicated, are considered appropriate for the treatment of asthma in pregnancy, even oral leukotriene receptor antagonists showed no evidence of harm to the fetus and they should not be stopped in women who have previously demonstrated significant improvement in asthma control prior to pregnancy.

It should be noticed that Prostaglandin F<sub>2α</sub>: may induce bronchospasm and should be used with extreme caution.

During labour, women on maintenance prednisolone > 7.5 mg/day should receive hydrocortisone 100 mg 6-8-hourly.

Breastfeeding: use medications as normal.

## **.Further information**

\*Patients requiring short acting β<sub>2</sub> agonists more than two or three doses a day should be treated with inhaled steroids

\*Inhaled steroids are not used as first line treatment.

\*Inhaled steroids are effective on a twice daily basis.

\*The only prescribable long acting inhaled β<sub>2</sub> agonist was salmeterol, 50 µg twice daily.

\*Used twice daily it is more effective than short acting inhaled β<sub>2</sub> agonists used four times daily.

\*Inhaled steroids should be considered if overnight relief is required

\*If symptoms are not controlled on twice daily dosing and there is concern about the total daily dose, then increasing the dosage frequency to four times daily but at the same total daily dose should be tried

\*If symptoms are not controlled with standard doses (up to a daily equivalent of 800 µg beclomethasone) higher doses of inhaled steroids should be used up to a daily equivalent of 2000 µg beclomethasone

\*1 – 3 months period of stability should be shown before stepwise reduction in inhaled steroids is undertaken, decreasing the dose by 25-50% at each step

\* When systemic steroids are used in short courses of up to two weeks, tapering is not needed

\*Rescue courses of steroids indicated when :

- *persistence of morning symptoms till midday*
- *day by day worsening of symptoms*
- *sleep disturbance by asthma*
- *diminishing response to inhaled bronchodilators*
- *fall in peak expiratory flow to below 60% of patient's best*
- *emergency use of nebulised or injected bronchodilators*

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