A BRIEF INTRODUCTION ON ASTHMA


P.S.G.V.P.M’s College of Pharmacy, Shahada-425409, Dist-Nandurbar, Maharashtra, India

ABSTRACT
Asthma is often associated with various comorbidities. The most frequently reported asthma comorbid conditions include rhinitis, sinusitis, gastroesophageal reflux disease, obstructive sleep apnea, hormonal disorders and psychopathologies. These conditions may, first: share a common pathophysiological mechanism with asthma; second: influence asthma control, its phenotype and response to treatment; and third: be more prevalent in asthmatic patients but without obvious influence on this disease. For many of these, how they interact with asthma remains to be further documented, particularly for severe asthma. If considered relevant, they should, however, be treated appropriately. Further research is needed on the relationships between these conditions and asthma.

KEYWORDS: Asthma, Rhinitis, Sinusitis, Treatment, Pathophysiology.

INTRODUCTION

Asthma (from the Greek \( \text{\textit{asthma}} \), "panting") is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction and bronchospasm. Common symptoms include wheezing, coughing, chest tightness, and shortness of breath.

Asthma is thought to be caused by a combination of genetic and environmental factors. Its diagnosis is usually based on the pattern of symptoms, response to therapy over time and spirometry. It is clinically classified according to the frequency of symptoms, forced expiratory volume in one second (FEV1), and peak expiratory flow rate. Asthma may also be classified as atopic (extrinsic) or non-atopic (intrinsic) where atopy refers to a predisposition toward developing type 1 hypersensitivity reactions.

Treatment of acute symptoms is usually with an inhaled short-acting beta-2 agonist (such as salbutamol) and oral corticosteroids. In very severe cases, intravenous corticosteroids, magnesium sulfate, and hospitalization may be required. Symptoms can be prevented by
avoiding triggers, such as allergens and irritants, and by the use of inhaled corticosteroids. Long-acting beta agonists (LABA) or leukotriene antagonists may be used in addition to inhaled corticosteroids if asthma symptoms remain uncontrolled. The occurrence of asthma has increased significantly since the 1970s. In 2011, 235–300 million people globally have been diagnosed with asthma, and it caused 250,000 deaths.

**Signs and symptoms:**
Asthma is characterized by recurrent episodes of wheezing, shortness of breath, chest tightness, and coughing. Sputum may be produced from the lung by coughing but is often hard to bring up. During recovery from an attack it may appear pus like due to high levels of white blood cells called eosinophils. Symptoms are usually worse at night and in the early morning or in response to exercise or cold air. Some people with asthma rarely experience symptoms, usually in response to triggers, whereas others may have marked and persistent symptoms.

**Associated conditions:**
A number of other health conditions occur more frequently in those with asthma, including gastro-esophageal reflux disease (GERD), rhinosinusitis, and obstructive sleep apnea. Psychological disorders are also more common, with anxiety disorders occurring in between 16–52% and mood disorders in 14–41%. However, it is not known if asthma causes psychological problems or if psychological problems lead to asthma.

**Causes:**
Asthma is caused by a combination of complex and incompletely understood environmental and genetic interactions. These factors influence both its severity and its responsiveness to treatment. It is believed that the recent increased rates of asthma are due to changing epigenetics (heritable factors other than those related to the DNA sequence) and a changing living environment. (fig.no.1)
**Environmental:**

Many environmental factors have been associated with asthma's development and exacerbation including allergens, air pollution, and other environmental chemicals. Smoking during pregnancy and after delivery is associated with a greater risk of asthma-like symptoms. Low air quality from factors such as traffic pollution or high ozone levels has been associated with both asthma development and increased asthma severity. Exposure to indoor volatile organic compounds may be a trigger for asthma; formaldehyde exposure, for example, has a positive association. Also, phthalates in PVC are associated with asthma in children and adults.

Asthma is associated with exposure to indoor allergens. Common indoor allergens include: dust mites, cockroaches, animal dander, and mold. Efforts to decrease dust mites have been found to be ineffective. Certain viral respiratory infections, such as respiratory syncytial virus and rhinovirus, may increase the risk of developing asthma when acquired as young children. Certain other infections, however, may decrease the risk.

**Hygiene hypothesis:**

The hygiene hypothesis attempts to explain the increased rates of asthma worldwide as a direct and unintended result of reduced exposure, during childhood, to non-pathogenic bacteria and viruses. It has been proposed that the reduced exposure to bacteria and viruses is due, in part, to increased cleanliness and decreased family size in modern societies. Exposure to bacterial endotoxin in early childhood may prevent the development of asthma, but exposure at an older age may provoke bronchoconstriction. Evidence supporting the hygiene hypothesis includes lower rates of asthma on farms and in households with pets.

Use of antibiotics in early life has been linked to the development of asthma. Also, delivery via caesarean section is associated with an increased risk (estimated at 20–80%) of asthma—this increased risk is attributed to the lack of healthy bacterial colonization that the newborn would have acquired from passage through the birth canal. There is a link between asthma and the degree of affluence.

**Genetic:**

CD14-endotoxin interaction based on CD14 SNP C-159T

<table>
<thead>
<tr>
<th>Endotoxin levels</th>
<th>CC genotype</th>
<th>TT genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>High exposure</td>
<td>Low risk</td>
<td>High risk</td>
</tr>
<tr>
<td>Low exposure</td>
<td>High risk</td>
<td>Low risk</td>
</tr>
</tbody>
</table>
Family history is a risk factor for asthma, with many different genes being implicated. If one identical twin is affected, the probability of the other having the disease is approximately 25%. By the end of 2005, 25 genes had been associated with asthma in six or more separate populations, including GSTM1, IL10, CTLA-4, SPINK5, LTC4S, IL4R and ADAM33, among others. Many of these genes are related to the immune system or modulating inflammation. Even among this list of genes supported by highly replicated studies, results have not been consistent among all populations tested. In 2006, over 100 genes were associated with asthma in one genetic association study alone; more continue to be found.

Some genetic variants may only cause asthma when they are combined with specific environmental exposures; an example is a specific single nucleotide polymorphism in the CD14 region and exposure to endotoxin (a bacterial product). Endotoxin exposure can come from several environmental sources including tobacco smoke, dogs, and farms. Risk for asthma, then, is determined by both a person's genetics and the level of endotoxin exposure.

**Medical conditions:**

A triad of atopic eczema, allergic rhinitis and asthma is called atopy. The strongest risk factor for developing asthma is a history of atopic disease; with asthma occurring at a much greater rate in those who have either eczema or hay fever. Asthma has been associated with Churg–Strauss syndrome, an autoimmune disease and vasculitis. Individuals with certain types of urticaria may also experience symptoms of asthma.

Beta blocker medications such as propranolol can trigger asthma in those who are susceptible. Cardioselective beta-blockers, however, appear safe in those with mild or moderate disease. Other medications that can cause problems are ASA, NSAIDs, and angiotensin-converting enzyme inhibitors.

**Exacerbation:**

Some individuals will have stable asthma for weeks or months and then suddenly develop an episode of acute asthma. Different individuals react differently to various factors. Most individuals can develop severe exacerbation from a number of triggering agents. Home factors that can lead to exacerbation of asthma include dust, animal dander (especially cat and dog hair), cockroach allergens and mold. Perfumes are a common cause of acute attacks in women and children. Both viral and bacterial infections of the upper respiratory tract can worsen the disease.

**Pathophysiology:**
Obstruction of the lumen of a bronchiole by mucoid exudate, goblet cell metaplasia, and epithelial basement membrane thickening in a person with asthma.

Asthma is the result of chronic inflammation of the airways which subsequently results in increased contractability of the surrounding smooth muscles. This among other factors leads to bouts of narrowing of the airway and the classic symptoms of wheezing. The narrowing is typically reversible with or without treatment. Occasionally the airways themselves change. Typical changes in the airways include an increase in eosinophils and thickening of the lamina reticularis. Chronically the airways' smooth muscle may increase in size along with an increase in the numbers of mucous glands. Other cell types involved include: T lymphocytes, macrophages, and neutrophils. There may also be involvement of other components of the immune system including: cytokines, chemokines, histamine, and leukotrienes among others.

**Diagnosis**

While asthma is a well recognized condition, there is not one universal agreed upon definition. It is defined by the Global Initiative for Asthma as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment".

There is currently no precise test with the diagnosis typically based on the pattern of symptoms and response to therapy over time. A diagnosis of asthma should be suspected if there is a history of: recurrent wheezing, coughing or difficulty breathing and these symptoms occur or worsen due to exercise, viral infections, allergens or air pollution. Spirometry is then used to confirm the diagnosis. In children under the age of six the diagnosis is more difficult as they are too young for spirometry.

**Spirometry**

Spirometry is recommended to aid in diagnosis and management. It is the single best test for asthma. If the FEV1 measured by this technique improves more than 12% following administration of a bronchodilator such as salbutamol, this is supportive of the diagnosis. It however may be normal in those with a history of mild asthma, not currently acting up. As caffeine is a bronchodilator in people with asthma, the use of caffeine before a lung function test may interfere with the results. Single-breath diffusing capacity can help differentiate asthma
from COPD. It is reasonable to perform spirometry every one or two years to follow how well a person's asthma is controlled.

**Others**

The methacholine challenge involves the inhalation of increasing concentrations of a substance that causes airway narrowing in those predisposed. If negative it means that a person does not have asthma; if positive, however, it is not specific for the disease. Other supportive evidence includes: a ≥20% difference in peak expiratory flow rate on at least three days in a week for at least two weeks, a ≥20% improvement of peak flow following treatment with either salbutamol, inhaled corticosteroids or prednisone, or a ≥20% decrease in peak flow following exposure to a trigger. Testing peak expiratory flow is more variable than spirometry, however, and thus not recommended for routine diagnosis. It may be useful for daily self-monitoring in those with moderate to severe disease and for checking the effectiveness of new medications. It may also be helpful in guiding treatment in those with acute exacerbations.

**Table no.1 (clinical classification ≥12 years old)**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Symptom frequency</th>
<th>Night time symptoms</th>
<th>%FEV₁ of predicted</th>
<th>FEV₁ Variability</th>
<th>SABA use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent</td>
<td>≤2/week</td>
<td>≤2/month</td>
<td>≥80%</td>
<td>&lt;20%</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>Mild persistent</td>
<td>&gt;2/week</td>
<td>3–4/month</td>
<td>≥80%</td>
<td>20–30%</td>
<td>&gt;2 days/week</td>
</tr>
<tr>
<td>Moderate persistent</td>
<td>Daily</td>
<td>&gt;1/week</td>
<td>60–80%</td>
<td>&gt;30%</td>
<td>daily</td>
</tr>
<tr>
<td>Severe persistent</td>
<td>Continuously</td>
<td>Frequent (7×/week)</td>
<td>&lt;60%</td>
<td>&gt;30%</td>
<td>≥twice/day</td>
</tr>
</tbody>
</table>

**Classification**

Asthma is clinically classified according to the frequency of symptoms, forced expiratory volume in one second (FEV₁), and peak expiratory flow rate. Asthma may also be classified as atopic (extrinsic) or non-atopic (intrinsic), based on whether symptoms are precipitated by allergens (atopic) or not (non-atopic). While asthma is classified based on severity, at the
moment there is no clear method for classifying different subgroups of asthma beyond this system. Finding ways to identify subgroups that respond well to different types of treatments is a current critical goal of asthma research.

**Asthma exacerbation**

An acute asthma exacerbation is commonly referred to as an asthma attack. The classic symptoms are shortness of breath, wheezing, and chest tightness. While these are the primary symptoms of asthma, some people present primarily with coughing, and in severe cases, air motion may be significantly impaired such that no wheezing is heard.

Signs which occur during an asthma attack include the use of accessory muscles of respiration (sternocleidomastoid and scalene muscles of the neck), there may be a paradoxical pulse (a pulse that is weaker during inhalation and stronger during exhalation), and over-inflation of the chest. A blue color of the skin and nails may occur from lack of oxygen.

In a mild exacerbation the peak expiratory flow rate (PEFR) is ≥200 L/min or ≥50% of the predicted best. Moderate is defined as between 80 and 200 L/min or 25% and 50% of the predicted best while severe is defined as ≤ 80 L/min or ≤25% of the predicted best.

Acute severe asthma, previously known as status asthmaticus, is an acute exacerbation of asthma that does not respond to standard treatments of bronchodilators and corticosteroids. Half of cases are due to infections with others caused by allergen, air pollution, or insufficient or inappropriate medication use.

Brittle asthma is a kind of asthma distinguishable by recurrent, severe attacks. Type 1 brittle asthma is a disease with wide peak flow variability, despite intense medication. Type 2 brittle asthma is background well-controlled asthma with sudden severe exacerbations.

**Table no.2 (severity of an acute exacerbation)**

<table>
<thead>
<tr>
<th>Severity of an acute exacerbation</th>
<th>Clinical signs</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Near-fatal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Life threatening (any one of)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Altered level of consciousness</td>
<td>Peak flow &lt; 33%</td>
<td></td>
</tr>
<tr>
<td>Exhaustion</td>
<td>Oxygen saturation &lt; 92%</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>PaO2 &lt; 8 kPa</td>
<td></td>
</tr>
<tr>
<td>Low blood pressure</td>
<td>&quot;Normal&quot; PaCO2</td>
<td></td>
</tr>
<tr>
<td>Cyanosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silent chest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Poor respiratory effort

| Acute severe (any one of) | Peak flow 33–50%
| | Respiratory rate ≥ 25 breaths per minute
| | Heart rate ≥ 110 beats per minute
| | Unable to complete sentences in one breath

| Moderate | Worsening symptoms
| | Peak flow 50–80% best or predicted
| | No features of acute severe asthma

**Exercise-induced**

Exercise can trigger bronchoconstriction in both people with and without asthma. It occurs in most people with asthma and up to 20% of people without asthma. In athletes is diagnosed more commonly in elite athletes, with rates varying from 3% for bobsled racers to 50% for cycling and 60% for cross-country skiing. While it may occur with any weather conditions it is more common when it is dry and cold. Inhaled beta2-agonists do not appear to improve athletic performance among those without asthma however oral doses may improve endurance and strength.

**Occupational**

Asthma as a result of (or worsened by) workplace exposures, is a commonly reported occupational disease. Many cases however are not reported or recognized as such. It is estimated that 5–25% of asthma cases in adults are work–related. A few hundred different agents have been implicated with the most common being: isocyanates, grain and wood dust, colophony, soldering flux, latex, animals, and aldehydes. The employment associated with the highest risk of problems include: those who spray paint, bakers and those who process food, nurses, chemical workers, those who work with animals, welders, hairdressers and timber workers.

**Differential diagnosis**

Many other conditions can cause symptoms similar to those of asthma. In children, other upper airway diseases such as allergic rhinitis and sinusitis should be considered as well as other causes of airway obstruction including: foreign body aspiration, tracheal stenosis or laryngotracheomalacia, vascular rings, enlarged lymph nodes or neck masses. In adults, COPD,
congestive heart failure, airway masses, as well as drug-induced coughing due to ACE inhibitors should be considered. In both populations vocal cord dysfunction may present similarly.

Chronic obstructive pulmonary disease can coexist with asthma and can occur as a complication of chronic asthma. After the age of 65 most people with obstructive airway disease will have asthma and COPD. In this setting, COPD can be differentiated by increased airway neutrophils, abnormally increased wall thickness, and increased smooth muscle in the bronchi. However, this level of investigation is not performed due to COPD and asthma sharing similar principles of management: corticosteroids, long acting beta agonists, and smoking cessation. It closely resembles asthma in symptoms, is correlated with more exposure to cigarette smoke, an older age, less symptom reversibility after bronchodilator administration, and decreased likelihood of family history of atopy.

**Prevention**

The evidence for the effectiveness of measures to prevent the development of asthma is weak. Some show promise including: limiting smoke exposure both in utero and after delivery, breastfeeding, and increased exposure to daycare or large families but none are well supported enough to be recommended for this indication. Early pet exposure may be useful. Results from exposure to pets at other times are inconclusive and it is only recommended that pets be removed from the home if a person has allergic symptoms to said pet. Dietary restrictions during pregnancy or when breast feeding have not been found to be effective and thus are not recommended. Reducing or eliminating compounds known to sensitive people from the work place may be effective. It is not clear if annual influenza vaccinations.

**Classification of the anti-asthma drugs—**

**Approach to Treatment—**

- Prevention of the exposure to antigen
- Reduction of bronchial inflammation and hyperactivity
- Dilatation of the narrowed bronchi

**Bronchodilators—**

Sympathomimetics (β₂ receptor agonist), Xanthine derivatives, Anti-cholinergics / muscarinics.
Sympathomimetic drugs—adrenalin is an agonist for the $\alpha_1$, $\alpha_2$, $\beta_1$, $\beta_2$ receptors. Binding with the $\beta_2$ receptor it causes bronchodilatation but binding on the $\beta_1$ receptors it causes ↑ HR, ↑ BP, ↑ $O_2$ demand.

- **Non-selective**—Epinephrine, Ephedrine, Isoproterenol {ephrine causes tachyphylaxis / acute tolerance}
- **$\beta$ receptor selective drugs**—Isopropanolol, Isoprenalin
- **$\beta_2$ receptor selective**—Salbutamol, Terbutaline, Femoterol

$\beta$ receptors are also present in the peripheral vasculature, so long term use may cause hypotension.

### Table no.3 (classification of anti-asthmatic drug)

<table>
<thead>
<tr>
<th>Anti-muscarinic drugs</th>
<th>Ipratropium bromide</th>
<th>Oxitropium</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_2$ receptor agonists</td>
<td>Salbutamol</td>
<td>Terbutalin</td>
</tr>
<tr>
<td>Xanthine derivatives</td>
<td>Theophylline</td>
<td>Aminophylline</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Beclomethasone</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Mast cell stabilizer</td>
<td>Sodium chromoglycate</td>
<td>Nedocromil sodium</td>
</tr>
<tr>
<td>Leukotrien pathway inhibitor</td>
<td>Zafirleukast</td>
<td>Zileuton</td>
</tr>
</tbody>
</table>

The selective $\beta_2$ agonists—

1. salbutamol

They can be given orally or inhalation

- They act selectively on $\beta_2$ receptors
They have long duration of action

Bronchodilatation is maximal in 30 min when given by inhalation and persists for 2-3 hours

They produce less cardio-vascular side effects

Orally they are given in doses of 4mg 3-4 times

Mechanism of Action—it acts in the following ways—

1. Salbutamol → Stimulates β₂ receptors of the bronchial smooth muscle → Stimulation of the Adenylate Cyclase enzyme → Increased intracellular cyclic AMP (also reduction of the intracellular calcium) → Smooth muscle relaxation → Bronchodilatation occurs.

2. Salbutamol → Acts on the β₂ receptor of the mast cell → ↑ c-AMP production → Stabilization of the mast cell membrane → No Histamine release → No bronchoconstriction.

3. Salbutamol increases the muco-ciliary action of the lung.

4. Decreases micro-vascular permeability of the lung.

Xanthine derivatives—

Chemically they are purine having similar chemical structure with adenine and uric acid. Wide spreads pharmacological action so, not used. These drugs have low therapeutic index. Increases intra-cellular cyclic-AMP concentration within the bronchial smooth muscle cell.

Theophylline is the prototype, it is water insoluble but it’s salts are water soluble.

{Aminophylline—Theophylline Ethylene di-Amine}. Aminophylline is given with dextrose aqua.

Mechanism of Action of Theophylline—

1. Combines with the adenosine receptor (PI) and acts as antagonist of adenosine thus prevents it to cause contraction of the bronchial smooth muscle.
2. Combines and inactivates phospho-diesterase enzyme and degradation of the cyclic-AMP stops. C-AMP accumulates in the bronchial smooth muscle and causes bronchodilatation. C-AMP has negative effect on the release of the calcium from the endoplasmic reticulum.

**Pharmacological effects—**

- Lung—bronchodilatation
- CVS—positive ionotropic and chronotropic effects. ↑ CO, ↑ HR, ↑ force of contraction. At large doses it causes cerebral vaso-constriction. In high level—toxicity—cardiac arrhythmia, tachycardia
- Kidney—diabetic action. ↑ renal blood supply and GFR. ↓ Na⁺ and other electrolyte absorption.
- Skeletal muscle—diaphragmatic contraction is stimulated. ↓ fatigue of the skeletal muscle. Causes tremor.
- GIT—↑ gastric acid secretion.

**Loading dose**—the dose which is given initially to attain a desired level in the plasma

**Maintenance dose**—to maintain the level

**Adverse effects of Theophylline**—

- Therapeutic index is very low
- Nausea, vomiting may appear in <2mg/100ml
- Nausea, vomiting may appear in <2mg/100ml
- Convulsion in >4mg/100ml
- Cardiac arrhythmia may occur

**Indications**

Bronchial asthma, COPD, apnea / preterm infant apnea.
### Table no.4 (Comparison between Salbutamol and Aminophylline as anti-asthma drug)

<table>
<thead>
<tr>
<th>Points</th>
<th>Salbutamol</th>
<th>Aminophylline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of Action</td>
<td>Selective stimulation of the $\beta_2$ adrenocptor of bronchial smooth muscle and causes bronchodilatation</td>
<td>Competitive inhibition of the bronchial adenosine receptors and causes bronchodilatation</td>
</tr>
<tr>
<td>Onset of action</td>
<td>Slower</td>
<td>Rapid</td>
</tr>
<tr>
<td>Duration of action</td>
<td>Longer</td>
<td>Shorter</td>
</tr>
<tr>
<td>Therapeutic index</td>
<td>Larger</td>
<td>Narrow</td>
</tr>
<tr>
<td>In acute asthma</td>
<td>Suitable in inhaler form</td>
<td>Suitable in IV form</td>
</tr>
<tr>
<td>Drug of choice</td>
<td>Mildest asthmatic with intermittent attack</td>
<td>Severe acute asthma and chronic asthma</td>
</tr>
<tr>
<td>Side effects</td>
<td>Tremor, headache, cardiac arrhythmia</td>
<td>Headache, vomiting</td>
</tr>
</tbody>
</table>

**Anticholinergic drugs**

Atropine is the prototype, cheap, causes bronchodilatation.

**Mechanism of Action**

Vagal nerve innervation $\rightarrow$ acetyl choline $\rightarrow$ muscarinic receptor $\rightarrow$ bronchoconstriction

Anticholinergics act here by inhibiting the muscarinic receptors $\uparrow$

**Adverse effects of Atropine**

- Can cross the BBB and go to the CNS.
- Mouth dryness.
- Destroy the cilia of the respiratory tract—prone to infection.

**Ipratropium Bromide (atropine methyl nitrate)**
anti-inflammatory drugs

**Glucocorticoids**
- Phospholipase A\(_2\) blocker
- Acts by inhibiting the PG secretion, no leukotriens secretion

Decrease permeability to capillaries—\(\downarrow\) exudation and transudation

**Corticosteroids**

anti-inflammatory drug (inhalation, tablet, IV) cannot suddenly stop these drugs, tapering of the dose to avoid withdrawal syndrome and to avoid precipitating acute problems.

**Mast cell stabilizer**

Na-chromoglycate, Nedocromil-Na
Table no.5(Uses)

<table>
<thead>
<tr>
<th>Uses</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Reduces the hyper-reactivity of the bronchial tree</td>
<td>- Prophylaxis in allergic bronchial asthma.</td>
</tr>
<tr>
<td>- Prevention of another attack</td>
<td>- Allergic rhinitis</td>
</tr>
<tr>
<td>- Prevents eosinophilic and neutrophilic chemotaxis</td>
<td>- Allergic conjunctivitis</td>
</tr>
<tr>
<td>- Stabilizes the mast cell of the bronchial airway</td>
<td>- Leukotriens pathway inhibitor</td>
</tr>
<tr>
<td>- They should be given only by inhalation</td>
<td>- Zafirleukast</td>
</tr>
<tr>
<td>- Also reduce the irritation of airway nerve endings</td>
<td>- Zileuton</td>
</tr>
</tbody>
</table>

**Indication**

- Prophylaxis in allergic bronchial asthma.
- Allergic rhinitis
- Allergic conjunctivitis

**Leukotriens pathway inhibitor**

Leukotriens are produced from the action of 5-lipoxegenase on arachidonic acid by variety of cells like basophiles, eosinophils, monocytes etc.
They are of 2 categories
- 5-lipoxegenase enzyme inhibitor (Zileuton)
- LTD$_4$ receptor antagonist (Zafirleukast, Monteleukast)

*** these drugs are effective when given orally and have important role in aspirin induced asthma.

⇒ Side-effects of inhalation
a. Oropharyngeal candediasis (steroid causes immuno-suppresion)—advised for frequent mouthwash
b. Patient may have harshness / coarse voice

Side-effects of tablet
Peptic ulcer, glaucoma, osteoporosis, hypertension, aggravation of diabetes mellitus

Treatment steps
1. Occasional use of short acting $\beta_2$ agonists
2. Low dose inhaled steroids (or other anti-inflammatory drugs)
3. High dose of inhaled steroid or low dose inhaled steroid plus long acting inhaled $\beta_2$ agonist
4. High dose inhaled steroids and regular bronchodilators
5. Addition of regular oral steroid therapy

Management of Acute Severe Asthma
The aim of management is to prevent death, to restore pulmonary function, to maintain optimum pulmonary function and to prevent early relapse.

Status Asthmaticus
Acute emergency condition.

Immediate treatment in “Status Asthmaticus”
1. Oxygen—given at highest concentration possible
2. High dose of inhaled $\beta_2$ agonist—Salbutamol 2.5-5 mg as nebulizer and repeated every 30min
3. Systemic corticosteroids—IV hydrocortisone or oral prednisolone (if patient can swallow)
4. If severity persists then additional measurements used
5. Monitoring of the patient

While there is no cure for asthma, symptoms can typically be improved. A specific, customized plan for proactively monitoring and managing symptoms should be created. This plan should include the reduction of exposure to allergens, testing to assess the severity of symptoms, and the usage of medications. The treatment plan should be written down and advise adjustments to treatment according to changes in symptoms.

The most effective treatment for asthma is identifying triggers, such as cigarette smoke, pets, or aspirin, and eliminating exposure to them. If trigger avoidance is insufficient, the use of medication is recommended. Pharmaceutical drugs are selected based on, among other things, the severity of illness and the frequency of symptoms. Specific medications for asthma are broadly classified into fast-acting and long-acting categories. Bronchodilators are recommended for short-term relief of symptoms. In those with occasional attacks, no other medication is needed. If mild persistent disease is present (more than two attacks a week), low-dose inhaled corticosteroids or alternatively, an oral leukotriene antagonist or a mast cell stabilizer is recommended. For those who have daily attacks, a higher dose of inhaled corticosteroids is used. In a moderate or severe exacerbation, oral corticosteroids are added to these treatments.

**Medications**

Medications used to treat asthma are divided into two general classes: quick-relief medications used to treat acute symptoms; and long-term control medications used to prevent further exacerbation.

**Fig no.2(Fast-acting)**

![Fig no. 2(fast acting)]
Salbutamol metered dose inhaler commonly used to treat asthma attacks.

- Short-acting beta$_2$-adrenoceptor agonists (SABA), such as salbutamol (albuterol USAN) are the first line treatment for asthma symptoms. They are recommended before exercise in those with exercise induced symptoms.

- Anticholinergic medications, such as ipratropium bromide, provide additional benefit when used in combination with SABA in those with moderate or severe symptoms. Anticholinergic bronchodilators can also be used if a person cannot tolerate a SABA.

- Older, less selective adrenergic agonists, such as inhaled epinephrine, have similar efficacy to SABAs. They are however not recommended due to concerns regarding excessive cardiac stimulation.

![Salbutamol metered dose inhaler](image)

**Fig no. 3 (long term control)**

Fluticasone propionate metered dose inhaler commonly used for long-term control.

- Corticosteroids are generally considered the most effective treatment available for long-term control. Inhaled forms such as beclomethasone are usually used except in the case of severe persistent disease, in which oral corticosteroids may be needed. It is usually recommended that inhaled formulations be used once or twice daily, depending on the severity of symptoms.

- Long-acting beta-adrenoceptor agonists (LABA) such as salmeterol and formoterol can improve asthma control, at least in adults, when given in combination with inhaled corticosteroids. In children this benefit is uncertain. When used without steroids they increase the risk of severe side-effects and even with corticosteroids they may slightly increase the risk.
• Leukotriene antagonists (such as montelukast and zafirlukast) may be used in addition to inhaled corticosteroids, typically also in conjunction with LABA. Evidence is insufficient to support use in acute exacerbations. In children they appear to be of little benefit when added to inhaled steroids. In those under five years of age, they were the preferred add-on therapy after inhaled corticosteroids by the British Thoracic Society in 2009.

• Mast cell stabilizers (such as cromolyn sodium) are another non-preferred alternative to corticosteroids.

CONCLUSION

It is likely that after reading this Guide and practicing your skills on the Practice Examples, you will still have many questions about your asthma. There will be specific items that you are not yet clear about. You will have heard different information about some points, including from reliable sources, and will want to clarify the conflicting opinions. And, we hope, you will want to learn more about many subjects not specifically discussed in this booklet, such as the role of allergy shots in asthma, managing asthma during pregnancy, and the long-term effects of asthma on your lungs.

Like all introductory guides, this Asthma Guide is only a first step. Your learning about asthma will be lifelong. Many helpful sources of information are available to you. You begin, of course, with your own observations and experiences. You learn in this way about what works and what doesn't work for you.

Your asthma care is a cooperative undertaking between you and your doctor; your shared understanding about asthma will help to strengthen that collaboration.

Be an asthma learner — and keep breathing freely.

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For Correspondence
Varsha B. Patil
Email: missvarsha0202@gmail.com