Asthma

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Asthma is one of the most common chronic diseases affects approximately 300 million people worldwide with approximately 10–12% of adults and 15% of children affected by asthma .

Asthma is a chronic inflammatory disorder of the airways manifests with episodic cough, chest tightness, shortness of breath, and wheezing particularly at night and 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.
In asthma there are increase air way hyper responsiveness to different trigger .

Relationship between asthma and allergen exposure is well establish include house dust mites, pets such as cats and dogs, pests such as cockroaches, and fungi (particularly .Aspergillus: (allergic bronchopulmonary aspergillosis).
Allergic mechanisms are also implicated in some cases of occupational asthma.

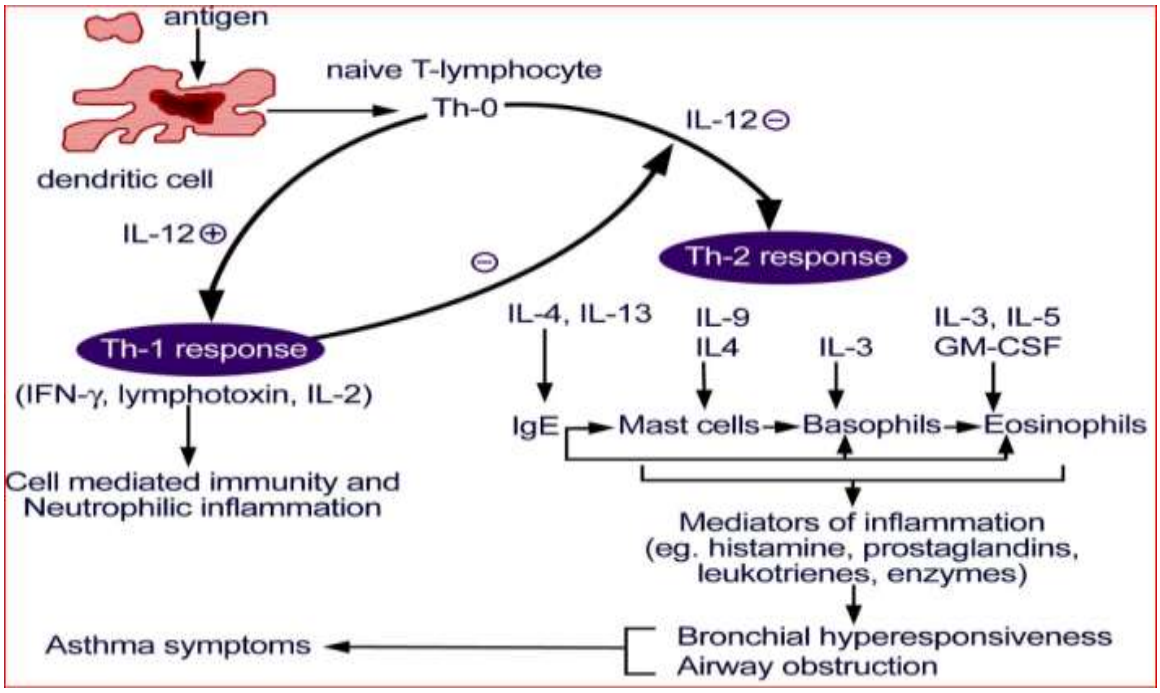
Although asthma can be managed very effectively in most cases, a minority of patients have severe disease that can result in frequent exacerbations and may lead to death.

Pathogenesis:

Airway inflammation in asthma is marked by infiltration with eosinophils, mast cells, lymphocytes, and neutrophils, subepithelial fibrosis, mucus gland hyperplasia and increased airway smooth muscle mass .
A large number of cytokines and mediators (histamines, tryptase, and leukotrienes) are released from inflammatory cells, such as mast cells, upon activation by inhaled allergens.
Ongoing airway inflammation or repeated asthma exacerbations may contribute to persistent airway injury with development of structural changes, known collectively as airway remodeling. These features include increased subepithelial fibrosis, increased smooth muscle mass, and mucus gland hyperplasia.
The relationship between atopy (the propensity to produce IgE) and asthma is well established, and in many individuals there is a clear relationship between sensitisation and allergen exposure, as demonstrated by skin prick reactivity or elevated serum specific IgE.

Asthma has three characteristics:

- Airflow limitation which is usually reversible spontaneously or with treatment
- Airway hyper responsiveness to a wide range of stimuli
- Inflammation of the bronchi with eosinophils, T lymphocytes and mast cells with associated plasma exudation, edema, marked smooth muscle hypertrophy, mucus plugging and epithelial damage.



Triggers Factors:

The potential role of indoor and outdoor allergens, microbial exposure, diet, tobacco smoke, air pollution have been consider as a risk factors for asthma

Classical precipitants include :

-Exercise, particularly in cold weather.
-Exposure to airborne allergens or pollutants.
-viral upper respiratory tract infections.
-stress.
-Beta-blockers, even when administered topically as eye drops, may induce bronchospasm.
-Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs).

Atopy and Allergy:

The term 'atopy' was used to describe a group of disorders, including asthma and hay fever, that appeared:

-To run in families
-To have characteristic wealing skin reactions to common allergens in the environment e.g.Dust mite, grass pollen, domestic pets e.c.t

Classification:

Asthma can be divided into:

Extrinsic - implying a definite external cause occurs most frequently in atopic individuals who show positive skin-prick reactions to common inhalant allergens. Positive skin-prick tests to inhalant allergens are shown in 90% of children and 50% of adults with persistent asthma. Childhood asthma is often accompanied by eczema.

Intrinsic or cryptogenic - when no causative agent can be identified. often starts in middle age ('late onset Asthma ').commonly have concomitant nasal polyps, and may be aspirin sensitive. They usually have more severe, persistent asthma.

Clinical Features :

Patients with asthma typically present with Episodic of

- cough can be dry but is often productive of thick, clear sputum
- dyspnea
- wheezing
- chest tightness.

Asthma is generally worse at night. Most patients report increased asthma symptoms at night or in the early morning due to decreased secretion of steroid in mid night till morning in the body symptoms such as cough and wheeze disturb sleep and have led to the term 'nocturnal asthma'.
. Symptomatic patients typically have tachypnea, polyphonic wheezing, and signs of nasal allergies .
Cough is a frequent symptom that sometimes predominates and is often misdiagnosed as bronchitis. Nocturnal cough can be a presenting feature.

There is different variation in the frequency and duration of the attacks. Some patients have only one or two attacks a year that last for a few hours, whilst others have attacks lasting for weeks. Some patients have chronic symptoms. Attacks may be precipitated by a wide range of triggers.
Asthma is a major cause of impaired quality of life with impact on work,school ,as well as physical activities and emotions.
Between attacks, patients with asthma can have a normal examination.

Investigations:

There is no single satisfactory diagnostic test for all asthmatic patients
Pulmonary function tests
Bronchial challenge test
Trial of corticosteroids
Blood and sputum tests
Chest X-ray
Skin tests
The diagnosis of asthma is predominantly clinical and based on a characteristic history.
Supportive evidence is provided by the demonstration of variable airflow obstruction, preferably by using spirometry to measure FEV1 and VC as below
Compatible clinical history plus either/or :

Pulmonary function tests:

- **FEV1 ≥ 15% (and 200 mL)** increase following administration of a bronchodilator/trial of corticosteroids
- **> 20% diurnal variation** on ≥ 3 days in a week for 2 weeks on **PEF** diary
- **FEV1 ≥ 15% decrease** after 6 mins of exercise

Bronchial challenge test:

Patients who have normal spirometer should undergo a bronchial challenge test to assess for airway hyper-responsiveness.

(The patient breathes in nebulized methacholine or histamine).The vast majority of patients with asthma have a positive test.Therefore, a negative bronchial challenge test makes an alternative diagnosis more likely.

Skin prick tests: presence of atopy may be demonstrated by skin prick tests. Skin-prick tests should be performed in all cases of asthma to help identify allergic causes.

Blood and sputum tests: Patients with asthma may have an increase in the number of eosinophils in peripheral blood (> 0.4 x 10^9 /L). The presence of large numbers of eosinophils in the sputum is a more useful diagnostic tool. Measurement of total and allergen-specific IgE.

Chest x –ray:

Appearances are often normal or show hyperinflation of lung fields. Lobar collapse may be seen if mucus occludes a large bronchus and, if accompanied by the presence of flitting infiltrates, may suggest that asthma has been complicated by allergic bronchopulmonary aspergillosis.

Management of Asthma:

The importance of the rapid identification of extrinsic causes of asthma and their removal wherever possible(e.g. house-dust mite, occupational agents, family pets, moulds and certain foods tuffs, particularly in childhood.)
Active and passive smoking should be avoided,
Avoid beta-blockers in either tablet or even eye drop form.
Aspirin and NSAIDs should be avoid

Medications for Asthma can be divided into :

Relievers*:* (used to treat acute symptoms) : medications include short-acting Bronchodilators(**Salbutamol**,**Terbutaline**), **systemic corticosteroids**, and **ipratropium** (Atrovent). are used intermittently as needed.

Controllers*:* (used to maintain long-term control and prevent exacerbations): are used on a regular basis and work via anti-inflammatory (inhaled corticosteroids, leukotriene-modifying drugs, and anti-IgE therapy) or bronchodilator (inhaled long-acting β2-agonists-(LABA) and sustained-release theophylline).

β2-Agonists: Short-acting β2-agonists (SABA) -Salbutamol and Terbutaline should be provided to all patients with asthma. These are the most effective bronchodilator medications available and have a rapid onset of action .delivered as aerosols or powders directly into the lungs (INHELAR OR NEBULIZER). The advantages of this method of administration are that drugs are delivered direct to the lung and the first-pass metabolism in the liver is avoided; thus lower doses are necessary and systemic unwanted effects are minimized.
Increased use of bronchodilator treatment to relieve increasing symptoms is an indication of deteriorating disease.
salbutamol (100 microgram) or terbutaline(250 microgram) should be prescribed as 'two puffs as required'.

Antimuscarinic bronchodilators: Non-selective muscarinic antagonists ipratropium bromide ((136 mcg inhaler) three or four times daily) inhalation may be additive to (β2-agonists)especially during asthma exacerbations.

Inhaled corticosteroid:

Mainstay controller therapy for asthma. They have a potent anti-inflammatory function, reducing the numbers and activity of inflammatory cells (eosinophils, mast cells, and lymphocytes). they also enhance the effectiveness of β2-agonists .

Regular use of inhaled corticosteroids reduces asthma exacerbations, hospitalizations, and asthma-related mortality.

Local side effects include hoarseness, cough, and oral thrush. These side effects can be reduced or eliminated by washing the mouth after each use, and lowering the corticosteroid dose.

All patients who have regular persisting symptoms need regular treatment with inhaled corticosteroids delivered.

Beclometasone dipropionateis the most widely used inhaled steroid and is available in doses of 50, 100, 200 and 250 ng per puff.Other inhaled steroids include budesonide, fluticasone، mometasone ,ciclesonide and triamcinolone.

Systemic corticosteroids: (oral or parenteral)are most effective in achieving prompt control of asthma during exacerbations or when initiating long-term asthma therapy in patients with severe symptoms. In patients with refractory, poorly controlled asthma, systemic corticosteroids may be required for the long-term suppression of symptoms. Repeated efforts should be made to reduce the dose to the minimum needed to control symptoms. Alternate-day treatment is preferred to daily treatment. Concurrent treatment with calcium supplements and vitamin D should be initiated to prevent corticosteroid-induced bone mineral loss in long-term administration.

Long-acting β2-agonists(LABAS):

Such as salmeterol and formoterol, are frequently added to an inhaled corticosteroid controller medication if symptoms are not adequately controlled.

Formoterol has a rapid onset and 12-hour duration of action, whereas salmeterol has a slower onset and equal duration of effect.

The addition of a long-acting β2-agonist generally results in better asthma control compared with increasing the dose of inhaled controller corticosteroids.

Because long-acting β2-agonists control asthma symptoms with no anti-inflammatory effects, treatment with long-acting β2-agonists as single-agent therapy in asthma is not appropriate; it can mask worsening of airway inflammation and lead to increased risk of asthma-related complications.

Sodium Cromoglicate:

Sodium cromoglicate and nedocromil sodium prevent activation of many inflammatory cells, particularly mast cells, eosinophils and epithelial cells, Recent asthma guidelines advise that inhaled corticosteroids are more efficacious than the cromones,but the latter are free of side-effects and, therefore, may offer some advantages in children

Leukotriene-Modifying Drugs:

Leukotrienes contribute to asthma by promoting mucus secretion, vasodilation, and inflammation. Leukotriene-modifying agents have been developed to block their receptors (Montelukast and Zafirlukast) or inhibiting 5-lipoxygenase (Zileuton).

Leukotriene receptor antagonists and zileuton have a modest anti-inflammatory and bronchodilator effect and have been shown to reduce asthma symptoms, improve quality of life, prevent exercise-induced asthma, and reduce the need for Salbutamol.

They are used primarily as add-on or alternative therapy to corticosteroid or β2-agonist therapy and are most appropriate in patients with mild persistent asthma who are intolerant of inhaled corticosteroids or in those with aspirin sensitivity..

Theophylline:

Theophylline is one of the oldest drugs for asthma. Its advantages include ease of use and low cost.

However, its disadvantages are weak bronchodilator effect and narrow therapeutic margin.. Therefore, dose adjustment and drug level monitoring should be done when patients are started on such medications or if they exhibit symptoms of potential toxicity (tremor, headache, nausea, palpitations).

More serious, life-threatening side effects include cardiac arrhythmias and seizure, which are seen at concentrations greater than 20 micrograms/mL

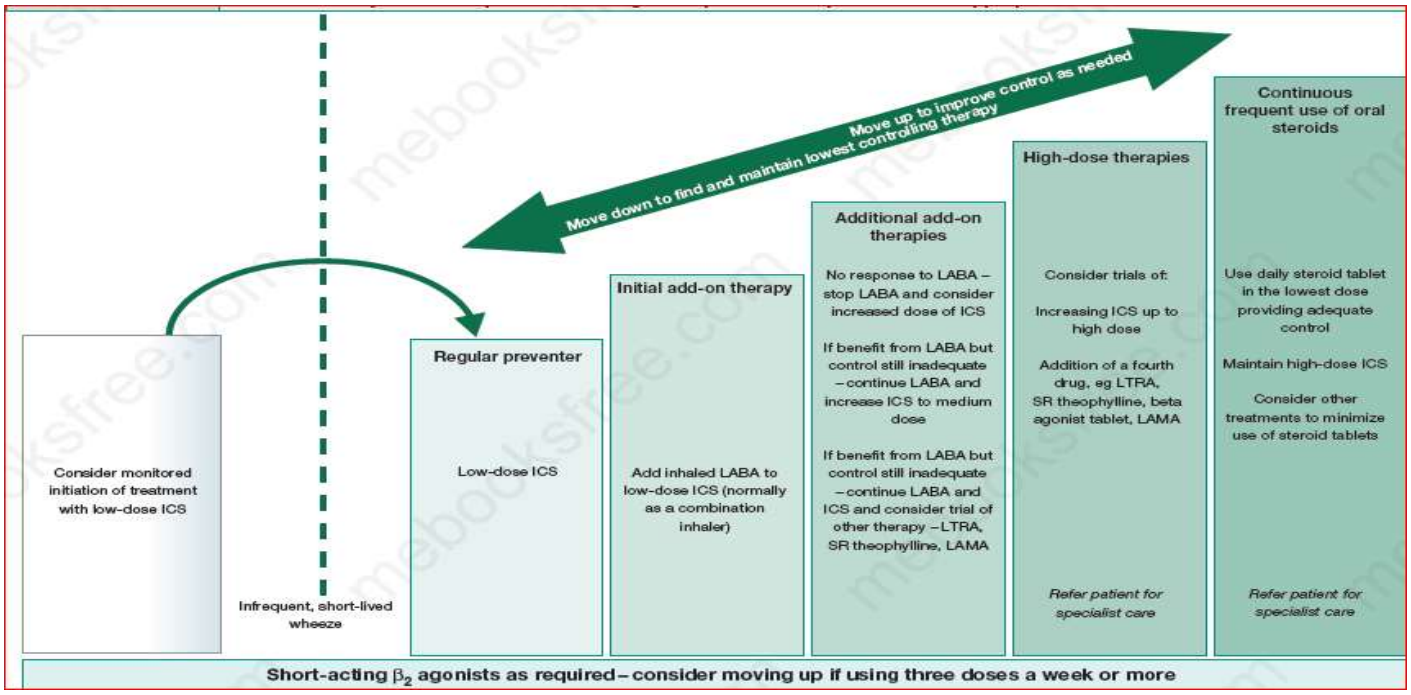
Theophylline is not recommended for use in acute asthma exacerbations and is considered a second-line alternative to inhaled corticosteroids for chronic asthma management.

Anti-IgE Antibody:

The cross-linking of IgE antibody on the surface of mast cells and basophils with antigen results in release of active mediators including histamine and leukotrienes, initiating the allergic inflammatory response.

Omalizumab: blocks IgE with a recombinant antibody against its FC (fragment crystallizable) portion and is effective in improving asthma control.

The stepwise management of asthma



Step-down therapy

Once asthma control is established, the dose of inhaled (or oral) glucocorticoid should be titrated to the lowest dose at which effective control of asthma is maintained. Decreasing the dose of glucocorticoid by around 25–50% every 3 months is a reasonable strategy for most patients.

Exacerbations of Asthma:

The course of asthma may be punctuated by exacerbations with increased symptoms, deterioration in lung function, and an increase in airway inflammation. Exacerbations are most commonly precipitated by viral infections, but moulds , pollens (particularly following thunderstorms) and air pollution are also implicated.Most attacks are characterized by a gradual deterioration over several hours to days but some appear to occur with little or no warning: so-called ***brittle asthma***.

An important minority of patients appear to have a blunted perception of airway narrowing and fail to appreciate the early signs of deterioration

Indications for 'rescue' courses include:

• Symptoms and PEF progressively worsening day by day, with a fall of PEF below 60% of the patient's personal best recording.
• Onset or worsening of sleep disturbance by asthma
• Persistence of morning symptoms until midday.
• progressively diminishing response to an inhaled bronchodilator.
• symptoms sufficiently severe to require treatment with nebulized or injected bronchodilators.

Management of mild to moderate exacerbations:

Doubling the dose of ICS does not prevent an impending exacerbation.

Short courses of 'rescue' oral Corticosteroids (prednisolone 30–60 mg daily) therefore are often required to regain control.

Tapering of the dose to withdraw treatment is not necessary, unless given for more than 3 weeks.

Acute Severe Asthma Criteria :

1- PEF 33–50% predicted (< 200 L/min)
2- Respiratory rate ≥ 25 breaths/min
3- Heart rate ≥ 110 beats/min
4- Inability to complete sentences in 1 breath

Management of Acute Severe Asthma:

Arterial blood gas, IV access, CXR, plasma theophylline level, plasma K+

1- High doses of inhaled bronchodilators: Nebulised salbutamol 5 mg or terbutaline 2.5 mg 6–12 times daily or as required

Short-acting β2-agonists are the agent of choice. In hospital, they are most conveniently given via a nebulizer driven by oxygen.

Ipratropium bromide provides further bronchodilator therapy and should be added to salbutamol in acute severe or life-threatening attacks

2-Oxygen.

High concentrations flow60% (humidified if possible) should be administered to maintain the oxygen saturation above 92% in adults.

The presence of a high $PaCO_2$ should not be taken as an indication to reduce oxygen concentration, but as a warning sign of a severe or life-threatening attack.
Failure to achieve appropriate oxygenation is an indication for assisted ventilation.

3-Systemic corticosteroids: Prednisolone 40 mg orally (or hydrocortisone 200 mg IV)
These reduce the inflammatory response and hasten the resolution of an exacerbation. They should be administered to all patients with an acute severe attack. They can usually be administered orally as prednisolone, but intravenous hydrocortisone may be used in patients who are vomiting or unable to swallow.

4-Intravenous magnesium may provide additional bronchodilatation in patients whose presenting PEF is below 30% predicted, magnesium sulphate 1.2–2.0 g over 20 mins, or aminophylline 5 mg/kg loading dose over 20 mins followed by a continuous infusion at 1 mg/kg/hr

5-intravenous aminophylline: Some patients take benefit its use, but cardiac monitoring is recommended

6-Intravenous fluids
many patients are dehydrated due to high insensible water loss and will probably benefit from Intravenous fluids

7-Potassium supplements may be necessary, as repeated doses of salbutamol can lower serum potassium.

PEF should be recorded every 15–30 minutes and then every 4–6 hours.
Pulse oximetry should ensure that SaO_2 remains above 92%.

Repeat arterial blood gases are necessary if the initial $PaCO_2$ measurements were normal or raised, the PaO_2 was below 8 kPa (60 mmHg), or the patient deteriorates.

Life-threatening features:

1- PEF < 33% predicted
(< 100 L/min)
2- SpO_2 < 92% or PaO_2
< 8 kPa (60 mmHg)
(especially if being treated
with oxygen)
3- Normal or raised $PaCO_2$
4- Silent chest
5-Cyanosis
6- Weak-respiratory effort
7- Bradycardia or arrhythmias
8- Hypotension
9- Exhaustion
10- Confusion
11- Coma

Indications for Assisted Ventilation in Acute Severe Asthma

1 - Exhaustion, confusion, drowsiness and Coma
2- Respiratory arrest
3- Deterioration of arterial blood gas tensions despite optimal therapy
***Pa*O2 < 8 kPa (60 mmHg) and falling**
***Pa*CO2 > 6 kPa (45 mmHg) and rising**
4- Low PH

Occupational Asthma:

Exposure to irritants, allergens, and sensitizing chemicals can be an important contributor to the development or worsening of asthma. Therefore, any patient with asthma should be asked about work-related exposures,

Patients with occupational asthma report feeling better when away from the offending environment, such as on weekends or vacations In addition to the history, measurement of spirometry or peak flow rate before and after work exposure over a period of a few weeks (which ideally would include at least 1 week away from work) may help establish a relationship between changes in lung function and workplace exposure.

It should be A negative test can occur when patients are away from occupational exposure. Avoidance of exposure to the offending agent (by changing jobs, changing the work environment, or using protective equipment) is recommended..

Reactive airways dysfunction syndrome (RADS) is a distinct type of occupational asthma that results from a single accidental exposure to high levels of irritant vapors, gases, or fumes such as chlorine gas, bleach, or ammonia. This exposure leads to significant airway injury with persistent airway inflammation, dysfunction, and hyperresponsiveness. Patients with RADS typically do not have a history of asthma and do not have “allergic sensitization” to the offending irritant prior to the accidental exposure. Their symptoms start within minutes to hours after the exposure and include cough, dyspnea, and chest tightness. Symptoms can persist for years afterward. Patients with RADS have a positive bronchial challenge test and may or may not have airway obstruction on spirometry. Similar to occupational asthma, patients with RADS can show improvement over time.

Cough-Variant Asthma:

Cough-variant asthma is present in patients who have cough as their main symptom. The cough is typically dry and is sometimes the only symptom of asthma. The diagnosis is confirmed with spirometry that demonstrates airway obstruction with improvement following inhaled bronchodilator administration or with bronchial challenge testing that demonstrates airway hyperresponsiveness. The syndrome should be distinguished from other causes of chronic cough, such as rhinitis, sinusitis, or GERD. Patients with chronic cough can have more than one cause for their cough; therefore, a comprehensive evaluation and management approach is essential.

Exercise-Induced Bronchospasm:

The majority of patients with asthma have exercise-induced bronchoconstriction (EIB) that manifests a few minutes after intense exercise**.**

EIB is enhanced when breathing cold, dry air. Bronchial obstruction in EIB peaks 5 to 10 minutes after cessation of exercise and resolves within 30 minutes;
symptoms are at their worst not during exercise but immediately following cessation of exercise..
Patients with typical EIB usually demonstrate a 15% or greater reduction in FEV1 within 5 to 10 minutes following exercise challenge.
Treatment with short-acting β2-agonists given 15 minutes before exercise prevents EIB in most patients.
The protection lasts up to 3 hours, allowing most patients to engage fully in desired physical activity.
Leukotriene-modifying drugs can also be used to prevent EIB; however, they are not as effective as inhaled β2-agonists.
Nonpharmacologic approaches to prevent EIB include gradual warmup before intense exercise, using a mask over the nose and mouth during cold weather, and avoidance of high-intensity intermittent exercise

Aspirin-induced asthma:

The triad of asthma, aspirin sensitivity, nasal polyps and rhinosinusitis affects 5-10% of patients with asthma. Most patients experience symptoms are females, during the third to fourth decade. A single dose can provoke an acute asthma exacerbation, accompanied by rhinorrhea, conjunctival irritation, and flushing of the head and neck. It can also occur with other nonsteroidal anti-inflammatory drugs and is caused by an increase in eosinophils and cysteinyl leukotrienes after exposure.

Asthma and Pregnancy:

Asthma (particularly poorly controlled asthma) is one of the most common medical problems that complicates pregnancy. Dyspnea of pregnancy should be distinguished from that related to asthma. When asthma is suspected, it should be confirmed with spirometry to demonstrate obstruction and reversibility with inhaled bronchodilators. Other diagnostic techniques are not recommended (such as skin testing) or are contraindicated (such as bronchial challenge testing) during pregnancy. Asthma can lead to low birth weight, preeclampsia, premature labor, and increased infant mortality. Therefore, better asthma control is likely to reduce the risk to both mother and fetus. During pregnancy, one third of patients have improvement in asthma control, another third have worsening asthma, and another third have no change.