Team Medicine

Bronchial Asthma

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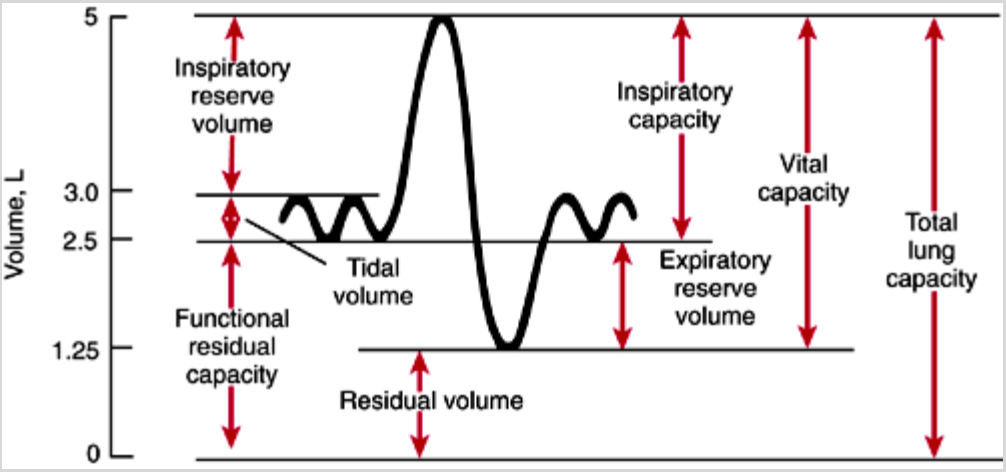
431 Teams

■ Important notes ■ doctor notes

Normal Physiology of the Respiratory System: (Extra)

Lung Volumes :

1. **Tidal volume (TV)**:
   Is the volume of air inspired or expired with each normal breath. (about 500ml)
2. **Inspiratory reserve volume (IRV):**
   Is the extra volume of air that can be inspired over and above the normal tidal volume. (about 3000ml) (used in exercising)
3. **Expiratory reserve volume (ERV):**
   Is the extra amount of air that can be expired by forceful expiration after the end of a normal tidal expiration. (about 1100 ml)
4. **Residual volume (RV):**
   Is the volume of air remaining in the lungs after the most forceful expiration. (about 1200 ml) (It cannot be measured by spirometer)



5. Dead space:

a. Anatomic dead space:

-The air in the conducting airways that does not engage in gas exchange.
-Approximately 150mL normally.

b. Alveolar dead space:

-The air in the gas exchange portions of the lung that cannot engage in gas exchange in gas exchange; it is zero in normal individuals.

c. Physiological dead space:

- Functional measurement .
-The sum of the anatomic dead space and the alveolar dead space i.e, the total dead space air.(approximately it's equal to anatomic dead space in normal lungs)
-In lung diseases associated with ventilation/perfusion (V/Q) defects , the physiologic dead space might increase.

Ventilation Rate:

Minute ventilation = TV x (RR) Respiratory Rate (L/min).
Alveolar ventilation = (TV - VD) x Breaths/min

V_D: Physiologic dead space
V_T: Tidal volume

Lung Capacities:

1. **Inspiratory capacity** = TV + IRV
2. **Functional residual capacity (FRC)** = ERV + RV

Is the volume remaining in the lungs after a tidal volume is expired >Includes the RV, so it cannot be measured by spirometer.

3.Vital capacity (VC), or forced vital capacity (FVC) = TV + IRV + ERV
Is the volume of air that can be forcibly expired after a maximal inspiration.

4.Total lung capacity (TLC) = all 4 lung volumes summed up (TV+IRV+ERV+RV)
Is the volume in the lungs after maximal inspiration
It includes the RV, so it cannot be measured by spirometer.

Forced Expiratory Volume (FEV1):

FEV1 is the volume of the forced maximal expiration at the first second
FEV1 normally is 80% of the forced vital capacity.
It is expressed as: FEV1/FVC=0.8

In obstructive lung diseases, e.g. asthma,
FEV1 is reduced more than FVC, so FEV1/FVC is decreased

In restrictive lung diseases, e.g. firbosis,
both FEV1 & FVC are reduced, and FEV1/FVC is either normal or increased.

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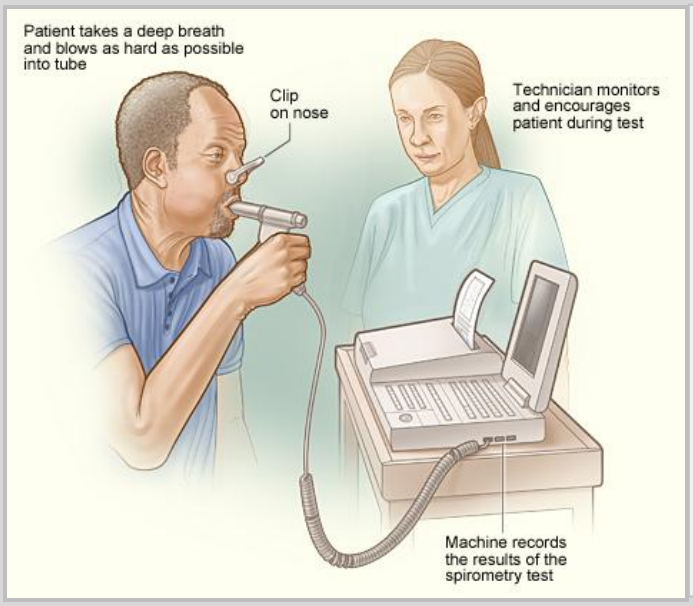


Spirometry Test:

- Most Common pulmonary function test.

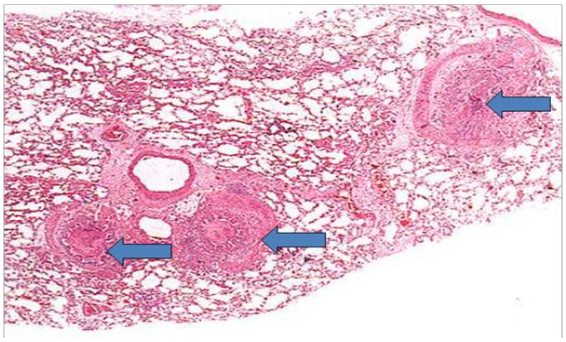
- It Measures the volume and flow of the inspired and expired air.

- Helpful In assessing conditions such as asthma, pulmonary fibrosis, cystic fibrosis and COPD.

- It Is performed by the Spirometer.

What is Asthma ?

- A chronic inflammatory disorder of the airway.
- Infiltration of mast cells, eosinophils and lymphocytes in response to allergens.
- Airway hyper-responsiveness.
- Recurrent episodes of wheezing, chest tightness, coughing, and shortness of breath.
- Variable and often reversible airflow limitation (airway obstruction).



Obstructed Inflammed Bronchi

Clinical Features:

- Intermittent symptoms: SOB, wheezing, Chest tightness and cough **(Not Specific)**
- Symptoms are variable in severity and may not be present simultaneously.
- Usually occur within 30 minutes of exposure to triggers
- **Wheezing is the most common finding in physical examination.**
- **Remember : Absence of symptoms at the time of examination does not exclude the diagnosis of asthma.**
- Asthma is diagnosed clinically by history and physical examination.

Exacerbations of asthma:
characterized by:
- Increased symptoms
- Deterioration in lung function (gradually over several hours or days)
- Increase in airway inflammation.

Exacerbations are mostly precipitated by **viral infections.**

Fatigue Patients with mild intermittent asthma are usually Asymptomatic between exacerbations. An inspection for nasal polyps and eczema should be performed on examination. Asthma characteristically displays as a diurnal pattern, with symptoms and lung function being worse in the morning. Particularly when poorly controlled, symptoms such as cough and wheeze disturb sleep, so when the disease is uncontrolled, symptoms are worst during the night.

Epidemiology:

The prevalence of asthma increased steadily over the past couple of years, studies suggest that 300 million people world-wide have bronchial asthma. The rapid rise in the prevalence of asthma implies that environmental factors are critically important in terms of its expression.
In Saudi Arabia 20% of school students have asthma. Around 1 out 5 have asthma . Civilization is one cause of increased Asthma prevalence.
It is one of the most common chronic diseases in Saudi Arabia, affecting more than 2 million Saudis. (SINA Booklet)

Triggers of Asthma:

1. Allergens
2. Irritants: Infections, Chemicals
Diet/Medications , Emotional stress
Exercise , Cold temperature
Exposure to smoke

Examples:
- Allergens: cat fur, cockroach allergens, house dust mite allergens, dog dander, fungi/molds
- Infections: Rhinitis, Sinusitis, and Viral infections
- Diet/Medications: Aspirin sensitivity, Sulfite sensitivity, Beta Blockers
- Irritants: Animal dander, Exposure to indoor chemicals. Dust, Outdoor pollutants (like ozone), Mold, fungi, Pollen

Pathophysiology:

When exposed to an asthma trigger...
- Bronchioles constrict to limit exposure to the trigger.
- Mucous membrane becomes irritated and swells.
- Mucous is produced to trap the irritant.
- Coughing initiated to pop open bronchioles and expel the mucous build-up.
- Air retention volume in alveolar sacs increases - can't get air out or in
- CO_2 build-up in alveolar sacs and in system tissues, which can lead to acidosis.
- The body attempts to blow off the excess CO_2 - rapid shallow breathing. (Hyperventilation)

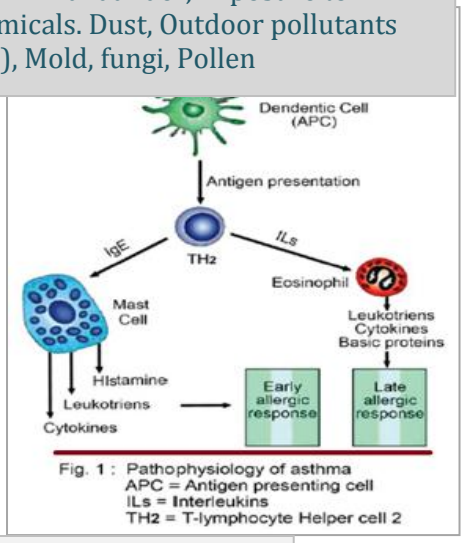
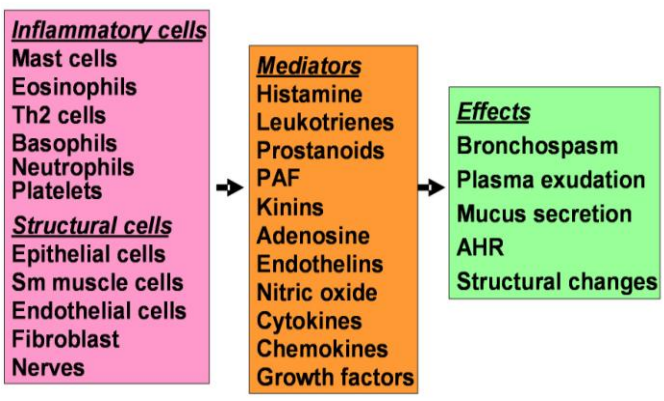


Fig. 1 : Pathophysiology of asthma
APC = Antigen presenting cell
ILs = Interleukins
TH2 = T-lymphocyte Helper cell 2

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, patients with asthma who are in the early stages of an acute episode have hypoxemia in the absence of carbon dioxide retention. Hyperventilation triggered by the hypoxic drive also causes a decrease in $PaCO_2$. An increase in alveolar ventilation in the early stages of an acute exacerbation prevents hypercarbia. 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.(medscape)

- Hungry for O_2 and trying to get rid of CO_2 at the same time.
- Fatigued muscles in this effort.
- If this continues, the person with asthma can die.

A person with asthma undergoes what is called "airway remodeling" - where there is permanent damage to the airways and decreased overall capacity and airway hyperactivity. A hyperactive airway is more susceptible to triggers.



More on the Pathophysiology:

It starts with an allergen entering the hyper-reactive airways (airways that have the tendency to contract easily to triggers that have little or no effect on normal airways) causing inflammation of the airways (Chronic eosinphilic bronchitis) which will lead to airway hyper-responsiveness and both the inflammation and airway hyper-responsiveness will lead to the symptoms of the bronchial asthma.

Type 2 T-helper cells (Th2) have a major role in the activation of the immune cascade that leads to the release of many mediators such as interleukins (IL)-3, IL-4, IL-5, IL-13 (SINA Booklet), **The inflammatory component is driven by Th2-type T lymphocytes which facilitate IgE synthesis through production of IL-4 and eosinophilic inflammation through IL-5.**
Infiltration of mast cells and lymphocytes will appear.

The hyper-responsiveness is presented through infiltration of blood vessels by immune cells, inflammation and swelling of the bronchus, contraction and hypertrophy of the smooth muscles and excess mucus production through profusion of mucus glands, which will, along with the contraction, cause narrowing of the lumen (decreasing lumen diameter) and **wheezing sounds**.

Remodeling:

A characteristic feature of chronic asthma is an alteration of structure and functions of the formed elements of the airways. Together, these structural changes interact with the inflammatory cells and mediators to cause the characteristic features of the disease. The remodeling is seen through changes in the epithelium, epithelial basement membrane, smooth muscles and nerves.

1. **Epithelium:**
    - Stressed and damaged epithelium with loss of ciliated columnar cells .
    - Increase in the number and activity of mucus-secreting goblet cells.
    - Increased in production of nitric oxide (NO) « It is useful as a non-invasive test of continuing inflammation.

Damage of the epithelium make it more vulnerable to infection by common respiratory viruses (e.g. rhinovirus, coronavirus) and the effects of air pollutants.

2. **Epithelial Basement Membrane:**
    - Deposition of repair collagens (types I, III and V) and proteoglycans in the lamina reticularis beneath the basement membrane.
    - Deposition of matrix proteins (e.g. Laminin, tenascin and fibronectin)

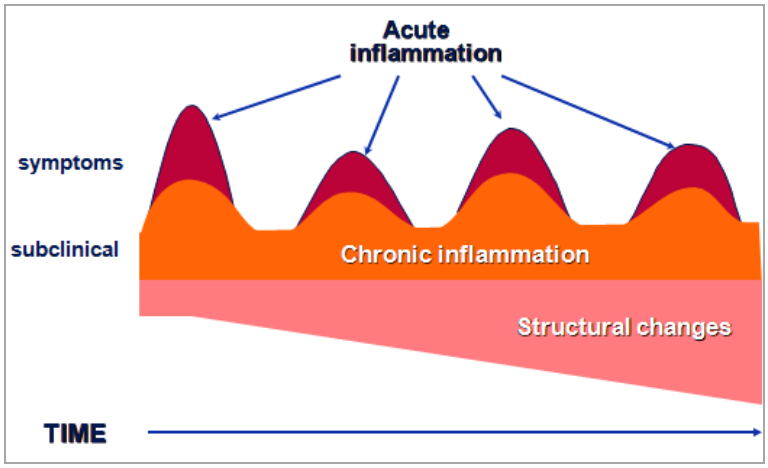
These depositions together cause the appearance of a thickened basement membrane. Aberrant signaling between the epithelium and underlying myoflbroblasts is thought to be the principal cause of airway wall remodeling.

3. **Smooth Muscles:**
    - Hyperplasia of the helical bands of airway smooth muscles (prominent feature of asthma)

- Alteration in the function of the smooth muscles which make them easily contracted and stay contracted because of a change in actin-myosin cross-link cycling (The contraction happens too much and too easily at the least provocation)
- Asthmatic smooth muscles also secret a wide range of cytokines, chemokines and growth factors that help sustain the chronic inflammatory response.

4. Nerves:

Neural reflexes, both central and peripheral contribute to the irritability of asthmatic airways.



The course of Asthma:

The Red waves: Patients present with Asthma symptoms

The Orange wave: Subclinical phase, no symptoms are present but there is chronic inflammation of the airways

The Pink wave: It represents the remodeling happening with time because of the chronic inflammation

Diagnosis:

- **History and patterns of symptoms**

PATIENT HISTORY : (SINA Booklet)

- Does the patient or his/her family have a history of asthma or other atopic conditions, such as eczema or allergic rhinitis?
- Does the patient have recurrent attacks of wheezing?
- Does the patient have a troublesome cough at night?
- Does the patient wheeze or cough after exercise?
- Does the patient experience wheezing, chest tightness, or cough after exposure to pollens, dust, feathered or furry animals, exercise, viral infection, or environmental smoke (cigarettes, burning incense "Bukhoor", or wood?
- Does the patient experience worsening of symptoms after taking aspirin/ nonsteroidal inflammatory medication or use of B-blockers?
- Does the patient's cold "go to the chest" or take more than 10 days to clear up?
- Are symptoms improved by appropriate asthma treatment?
- Any allergies or Family history of Allergies? (Allergies and asthma often coexist)
- **If the patient answers "YES" to any of the above questions, suspect asthma**

Some patients, particularly children, have a cough as the main or the only symptom without wheezing or shortness of breath, which is called cough variant asthma. In this situation, the diagnosis may be confirmed by a positive response to asthma medication. Others may have their asthma induced by exercise only, a condition called exercise-induced asthma (EIA). Symptoms of asthma could be worsened by coexistent gastro-esophageal reflux disease (GERD), rhinosinusitis, or the use of some medications such as beta blockers and nonsteroidal anti-inflammatory agents (NSAID), and Aspirin (ASA). Asthma and rhino-sinusitis commonly occurs concomitantly. (SINA)

- **Physical examination**
  - **Wheeze : Usually heard with or without a stethoscope.**

  Bronchial Asthma wheezing is :
    - **Multi-tonus and Bilateral (Because all airways inflamed and narrowed) (Mono-tone and unilateral wheezing is more likely to be obstruction)**
    - **Expiratory (But in severe cases could be inspiratory and expiratory)**

  - Rhonchi : heard with a stethoscope.
  - Dyspnea : Use of accessory muscles.
  - **Crackles(also called, crepitations, or rales) are not feature of Asthma)**

Physical examination usually **reveals bilateral expiratory** wheezing, which may be absent between attacks. Examination of the upper airways is important to look for evidence of allergic rhinitis, such as mucosal swelling, nasal polyps, and postnasal dripping. Other allergic manifestations, such as atopic dermatitis/eczema may also support the diagnosis of allergic asthma. (SINA)

- **Measurements of lung function.**
- **Asthma is diagnosed clinically by history**
- **and Physical examination.**
- **In case of doubt :**
  - **PFT** (Pulmonary Function Tests)
  - **Methacholine challenge test**

PFT:
- ↓in expiratory flow rate.
- ↓FEV1.
- ↓FEV1/FVC

A bronchial challenge test (also be called **a methacholine challenge** test or histamine challenge) is a medical test used to assist in the diagnosis of asthma. The patient breathes in nebulized methacholine or histamine. Both drugs provoke bronchoconstriction, or narrowing of the airways. The degree of narrowing can then be quantified **by spirometry**. People with pre-existing airway hyperreactivity, such as asthmatics, will react to lower doses of drug.

Sometimes, to assess the reversibility of a particular condition **(if Reversible , It is Asthma)** , a bronchodilator is administered to counteract the effects of the bronchoconstrictor before repeating the spirometry tests. This is commonly referred to as a **reversibility test**, or a post bronchodilator test (post BD), and may help in distinguishing asthma from chronic obstructive pulmonary disease.

To confirm diagnosis:

1. Lung function tests:

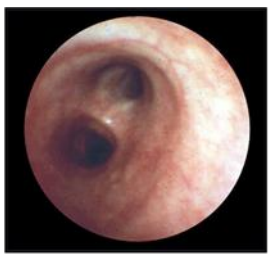
Demonstrates the variable airflow obstruction, preferably done by using Spirometry. The measurement of FEV1 and VC identify the obstructive nature of the ventilatory defect define its severity, and provide the basis of bronchodilator reversibility.

Peak Flow Meter

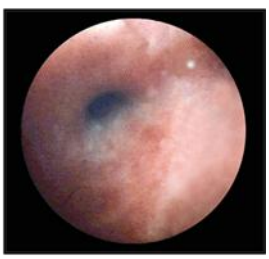
If spirometry is not available, a peak flow meter is used. The diurnal variation in Peak Expiratory Flow Rate (PEER) is a good measure of asthma activity; it is also helpful in the long-term assessment of the patient's disease and its response to treatment.

Normally FEV1 = 600 mL in males & 500 mL in females (80% of predicted based on height, weight and race).
Patients with asthma cannot reach the normal FEV1 because of the bronchial narrowing .
FEV1 normally is 80% of the forced vital capacity.
It is expressed as: FEV1/FVC=0.8
In asthma, FEV1 is reduced more than FVC, so FEV1/FVC is decreased

2. Exercise tests (used widely in children)
3. Histamine or Methacholine bronchial provocation test: Indicates the presence of airway hyper-responsiveness. It is useful in investigating patients whose main symptom is cough. *This test should not be performed on individuals with poor lung .
4. Trial of corticosteroids: (A substantial improvement in FEV1 (>15%) after the corticosteroids administration, confirms the presence of a reversible element and indicates that the administration of inhaled steroids will prove beneficial to the patient)
5. Blood and sputum tests (Increase in **eosinophils** in blood and sputum, sputum is a more useful diagnostic tool).
6. Chest X-ray (normal in mild cases, hyperinflated in severe cases. May be helpful in excluding pneumothorax, but no diagnostic features of Asthma appear on the X-ray)
7. Skin-prick tests (Helpful in identifying the allergic causes)
8. Allergen provocation tests (required in suspected occupational asthma only).



Before



10 Minutes After Allergen Challenge

Management: (The doctor focused mainly on diagnosis, not in the treatment)

The goal of management should be to obtain and sustain complete control.
Management options:

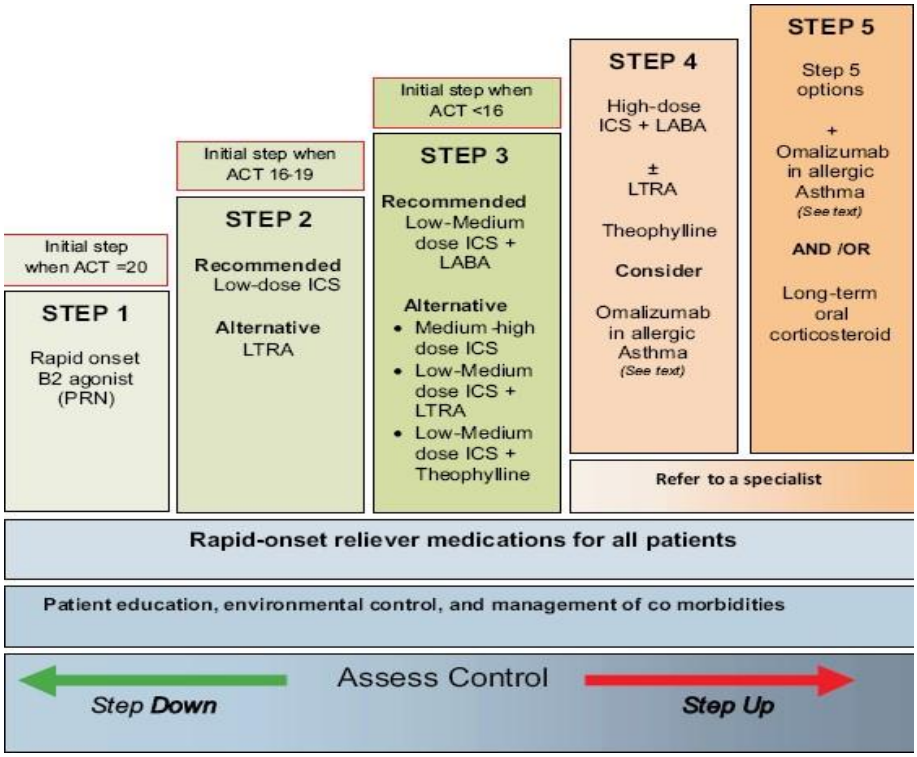
1. Avoid aggravating factors.
2. Short-acting relievers
   - Inhaled B2 agonists
   [Short-acting B2 Agonists; SABA] (e.g. **Salbutamol ,** terbutaline)

3. Long-acting relief/disease controllers
- Inhaled long-acting B2 agonists
(Rapid acting: **Formoterol**, Non-rapid acting: **Salmeterol**)
- Inhaled corticosteroids [ICS] (e.g. **beclometasone, budesonide, fluticasone, cicleosenide, mometasone**)
- Compound inhaled salmeterol and fluticasone [Seretide]
- Compound Budesonide and Formoterol [Symbicort]
- Sodium cromoglicate
- Leukotriene modifiers (e g. montelukast, zafirlukast, zileuton)

4. Other agents with bronchodilator activity
- Inhaled antimuscarinic agents (e.g. ipratropium, oxitropium)
- Theophylline preparations
- Oral cotncosteriods (e.g. prednisolone 40 mg daily)

5. Steroid-sparing agents - Methotrexate - Ciclosporin - Intravenous immunoglobulin - Anti-IgE monoclonal antibody - omalizumab - Etanercept
6. Combinations:
- Symbicort: budesonide + formoterol
- Seretide: fluticasone + salmeterol

Drugs and its marketing name:
budesonide = Pulmicort
fluticasone = Flixotide
Ciclosenide = Alvesco (Ciclosenide is an inhaled corticosteroid that is activated inside the lungs. It is useful in children with Asthma)



Asthma Control Test (ACT) :

ACT is a test recommended for all asthmatic patient of the age 12 years and above. The Test is a 5-Questions assessment tool. The total ACT score is based on range of 5 to 25.

Poor Asthma Control .... Why?

Before increasing medications, check :
Inhaler technique.
Adherence to prescribed regimen.
Environmental changes.
Also consider alternative diagnoses.

Another Classification:

Reliever/ Rescue	• Bronchodilator (beta$_2$ agonist) • Quickly relieves symptoms (within 2-3 minutes) • **Not for regular use**
Preventer/ Controller	• Anti-inflammatory • Takes time to act (1-3 hours) • Long-term effect (12-24 hours) • **Only for regular use** (whether well or not well)
Preventer/ Controller	• Inhaled glucocorticosteroids • Leukotriene modifiers • Systemic glucocorticosteroids • Anti-IgE

Rule of Two:

Use of a quick-relief inhaler more than: **2 times** per week.
Awaken at night due to asthma symptoms more than: **2 times** per month.
Refill of a quick-relief inhaler prescription more than: **2 times** per year.
If happen patient will Need controller medication

Patients should learn to :

Avoid risk factors.
Take medications correctly.
Understand the difference between "controller" and "reliever" medications.
Monitor their status using symptoms and, if available, PEF. (ACT)
Recognize signs that asthma is worsening and take action.
Seek medical help as appropriate.

Why inhalation therapy?

Oral	Inhaled
Slow onset of action	Rapid onset of action
Large dosage used	Less amount of drug used
Greater side effects	Better tolerated
Not useful in acute	Very effective

Summary :

- Asthma can be controlled but not cured.
- It can present in anybody at any age.
- It produces recurrent attacks of symptoms of SOB , cough with or without wheeze.
- Between attacks people with asthma live normal lives as anyone else.
- In most cases there is some history of allergy in the family.
- Understanding the disease, learning the technique and compliance with medications is the key for good control of asthma.

References:
Guyton & Hall, 11th edition
SINA Booklt
Medicine team 430
Medecine team 429
Bronchial Asthma Slides

Questions:

What is the characteristic feature of chronic asthma ?

- Airway remodeling

1- Characteristics of Bronchial Asthma wheezing:

A. Mono-Tonus , unilateral , Expiratory with crackles.
B. Multi-Tonus, Unilateral , Inspiratory.
C. Multi-tonus , Bilatral, Expiratory.

2- In Asmathatic Patient FEV1 is :

A. Increased.
B. Normal.
C. Reduced.

Answers: C, C