

# COUGH:

- Coughing is a common reflex action that clears throat of mucus or foreign irritants.
- A cough that lasts for less than three weeks is an acute cough. Most episodes of coughing will clear up or at least significantly improve within two weeks.
- The most common cause of a cough is a [respiratory tract infection](#), such as a [cold](#) or [flu](#).

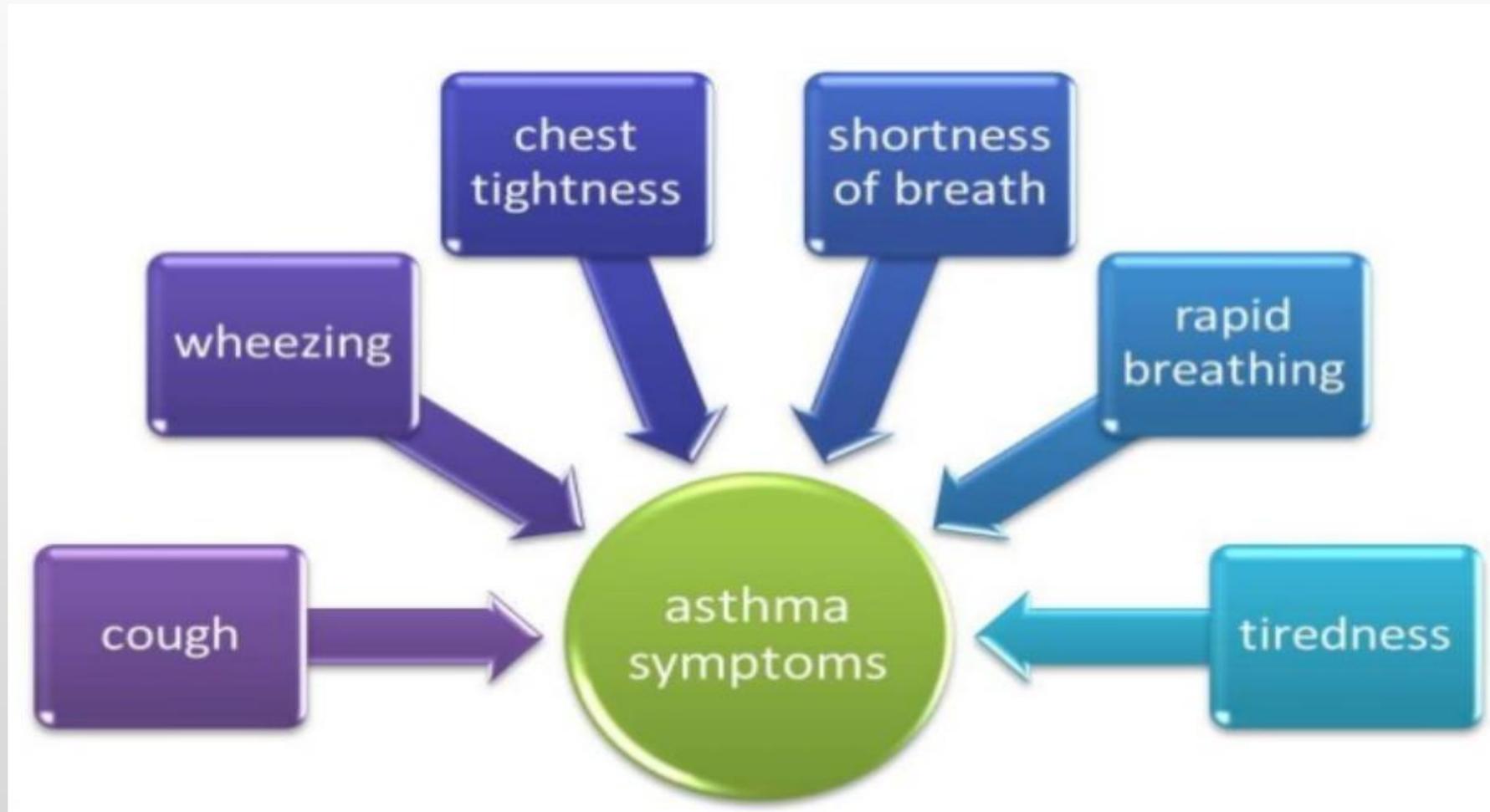
# BRONCHIAL ASTHMA:Hyper-responsiveness of trachio-bronchial smooth muscle.

Bronchial asthma is a noncommunicable lung disease characterized by:

- airways inflammation
- Airways obstruction
- Narrowing of airways
- Wheezing
- Coughing
- dyspnea
- mucus plugging.



# SYMPTOMS OF ASTHMA:



# Type of Asthma

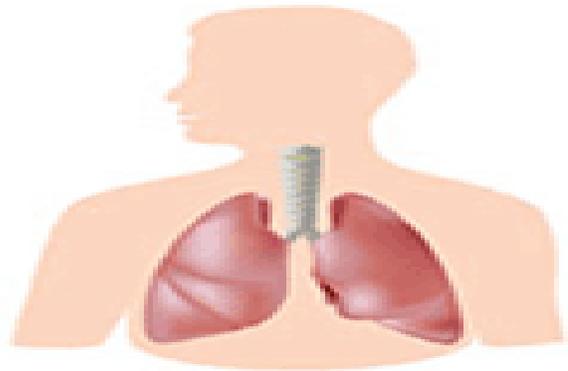
A variety of trigger factors (infection, irritants, pollution, exercise, exposure to cold air, psychogenic) may be involved:

**EXTRINSIC ASTHMA  
MOSTLY EPISODIC  
LESS PRONE TO  
STATUS  
ASTHMATICUS**

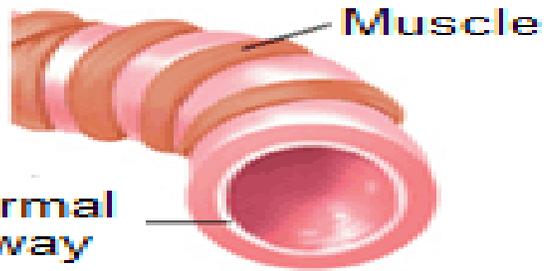
**INTRINSIC ASTHMA  
TENDS TO BE  
PERENNIAL,  
STATUS  
ASTHMATICUS MORE  
COMMON**

# BRONCHIAL ASTHMA

## Asthma

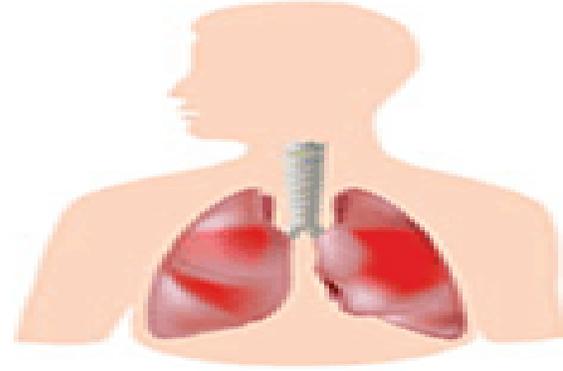


**Normal airway**



Normal airway lining

Muscle

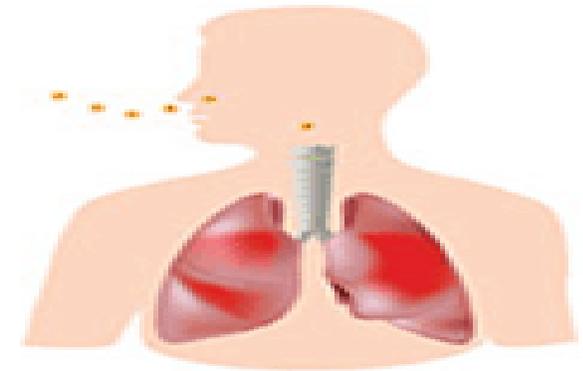


**Asthma**

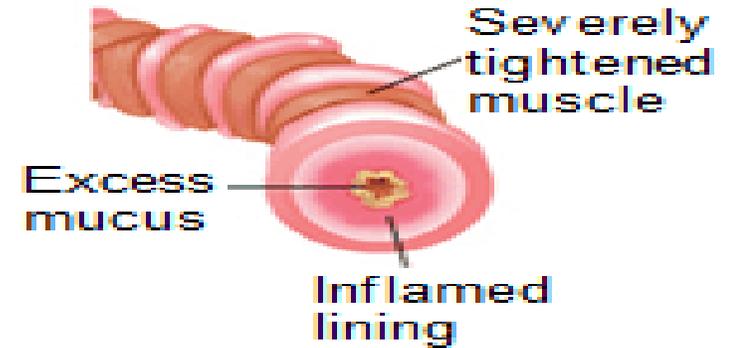


Tightened muscle

Inflamed lining



**Sever Asthma**



Severely tightened muscle

Excess mucus

Inflamed lining

**ENVIRONMENTAL FACTORS**

**GENETIC FACTORS**

**BRONCHIAL INFLAMMATION**

**BRONCHIAL HYPERACTIVITY+TRIGGER FACTORS**

**OEDEMA, BRONCHOCONSTRICTION, INCREASE  
MUCOUS PRODUCTION**

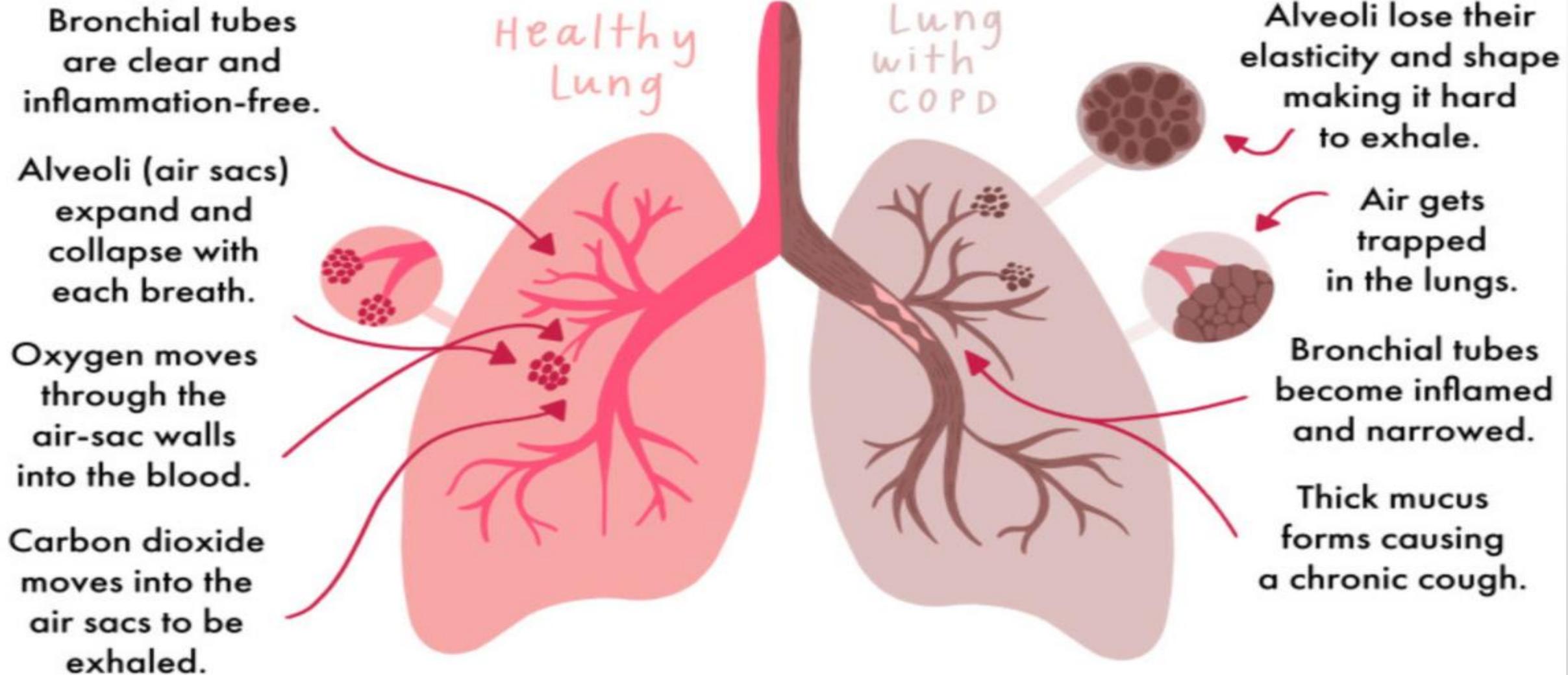
**AIRWAYS  
NARROWING**

**SYMPTOMS: COUGH, WHEEZING, BREATHLESSNESS, CHEST TIGHTNESS**

# COPD- Chronic obstructive Pulmonary Disorder:

- COPD is an inflammatory disorder of the lungs characterized by progressive alveolar destruction & bronchiolar fibrosis in variable proportions
- Loss of bronchial elasticity leads to closure of smaller air tubes during expiration.
- Air obstruction accentuated during exercise causing shortness of breath

Learn what damage from COPD looks like and why it becomes so hard to breathe.



# APPROACHES TO TREATMENT

1. Prevention of AG:AB reaction— **avoidance of antigen, hyposensitization— possible in extrinsic asthma and if antigen can be identified.**
2. Neutralization of IgE (reaginic antibody)— **Omalizumab.**
3. Suppression of inflammation and bronchial hyperreactivity— **corticosteroids.**
4. Prevention of release of mediators— mast **cell stabilizers.**
5. Antagonism of released mediators— **leukotriene antagonists, antihistamines, PAF antagonists**

# APPROACHES TO TREATMENT:

6. Blockade of constrictor neurotransmitter—**anticholinergics.**

7. Mimicking dilator neurotransmitter—**sympathomimetics.**

8. Directly acting bronchodilators— **methylxanthines.**

# DRUG CLASSIFICATION:

I.

## BRONCHODILATOR

**β<sub>2</sub> Sympathomimetics:**  
Salbutamol, Terbutaline,  
Bambuterol, Salmeterol,  
Formoterol, Ephedrine.

**Methylxanthines:**  
Theophylline (anhydrous),  
Aminophylline, Choline  
theophyllinate, Hydroxyethyl  
theophylline, Theophylline  
ethanolate of piperazine,  
Doxophylline.

**Anticholinergics**  
Ipratropium  
bromide,  
Tiotropium  
bromide.

# DRUG CLASSIFICATION

II. Leukotriene antagonists **Montelukast, Zafirlukast.**

III. Mast cell stabilizers **Sodium cromoglycate, Ketotifen.**

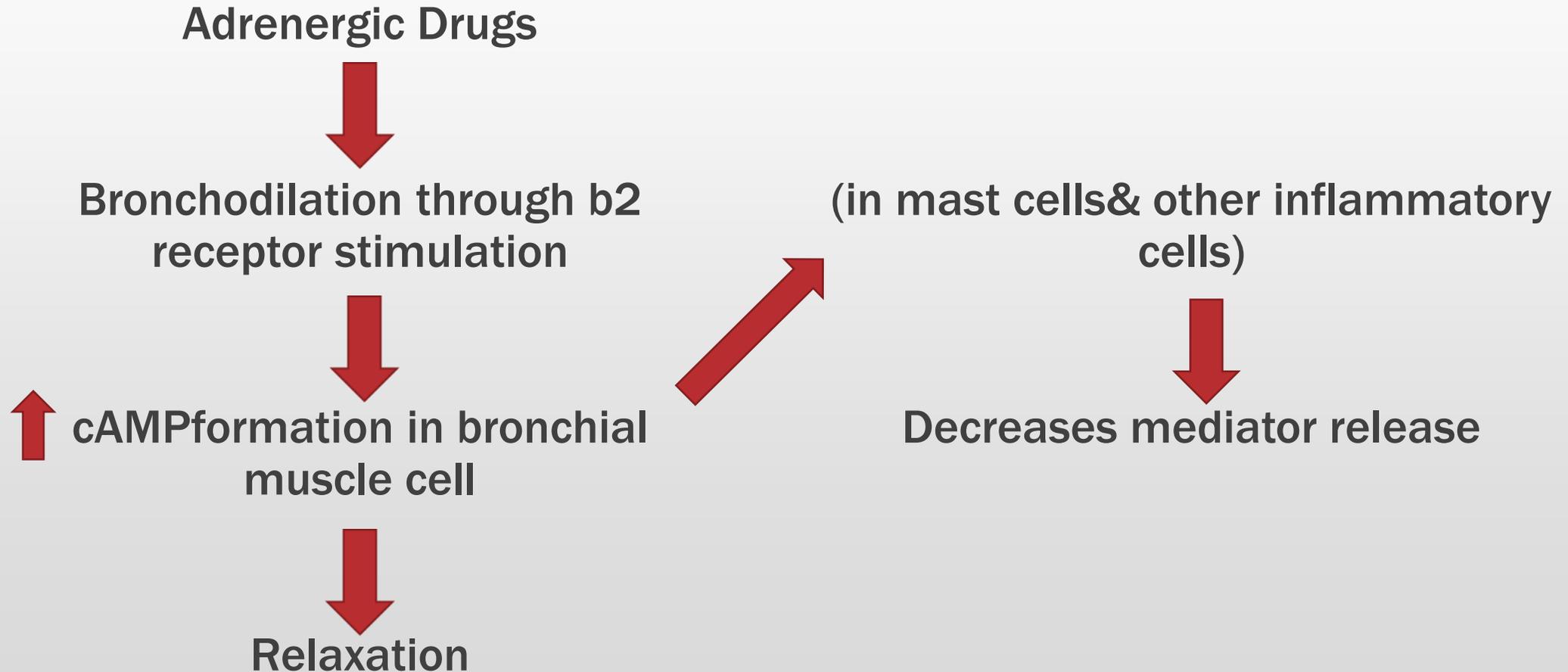
IV. Corticosteroids

A. Systemic: **Hydrocortisone, Prednisolone and others.**

B. Inhalational: **Beclomethasone dipropionate, Budesonide, Fluticasone propionate, Flunisolide, Ciclesonide.**

V. Anti-IgE antibody **Omalizumab**

# SYMPATHOMIMETICS :



# SYMPATHOMIMETICS:

- *$\beta$ 2 Receptor* on inflammatory cells desensitize quickly,
- The contribution of this action to the beneficial effect of  $\beta$ 2 agonists in asthma where airway inflammation is chronic is uncertain.
- Adrenergic drugs are the mainstay of treatment of reversible airway obstruction but should be used cautiously in hypertensive, ischemic heart disease patients.

# SALBUTAMOL:

- A highly selective  $\beta_2$  agonist
- cardiac side effects are less prominent
- Inhaled salbutamol delivered mostly from pressurized metered dose inhaler

(produces bronchodilatation within 5 min and the action lasts for 2–4 hours)

- used to abort and terminate attacks of asthma
- not suitable for round-the-clock prophylaxis

## PHARMACOKINETICS:

oral bioavailability is 50%.

Oral salbutamol acts for 4–6 hours

## SIDE EFFECTS:

- Palpitation,
- Nervousness,
- irritation,
- ankle edema
- Restlessness

# METHYL XANTHINE:

- Theophylline and its compounds have been extensively used in asthma, but are not considered first line drugs.
- Theophylline is one of the three naturally occurring methylated xanthine alkaloids caffeine, theophylline and theobromine.
- They are used more often in COPD .

# PHARMACOLOGICAL ACTIONS:

**CNS:**

**Caffeine & theophylline are CNS stimulants ,Primarily affect the centers.**

**caffeine > Theophylline**

**Produces effect like: beats boredom, alterness, fatigue,**

**Higher dose causes nervousness, restlessness, panic, insomnia and excitement**

**(higher doses may produce tremor, convulsions)**

**Theophylline is more toxic than  
caffeine**

# PHARMACOLOGICAL ACTION:

## CVS:

- Directly stimulate heart & increase force of contraction
- Tends to increase heart rate by cardiac actions, but decrease by causing vagal stimulation
- Tachycardia is more common with theophylline but caffeine lowers heart rate ↓
- Cardiac output and cardiac work are ↑
- Higher doses may produce arrhythmia
- Theophylline dilate systemic blood vessels including coronary by direct action peripheral resistance ↓

# Pharmacological action:

## Smooth muscle:

Relaxed(exerted on bronchi(in case of asthma especially))

Theophylline more potent than caffeine

Biliary spasm is relived , but effect on intestine and urinary tract is negligible.

## Kidney :

- Mild diuretics acts by inhibiting tubular Reabsorption of  $\text{Na}^+$  & water as well as increased renal blood flow and GFR.
- Theophylline is more potent.

# Pharmacological action:

## **Stomach:**

Enhances secretion of acid & pepsin in stomach

Also gastric caffeine

## **Metabolism:**

Increases BMR plasma free fatty acid levels raised

Release of endogeneous CAs appears to be partly responsible for these effects

## **Mast cell & Inflammatory cells:**

- ✓ Theophylline decrease release of histamine and other mediators from mast cells and activate inflammatory cells.
- ✓ Leads to therapeutic effects in ASTHMA

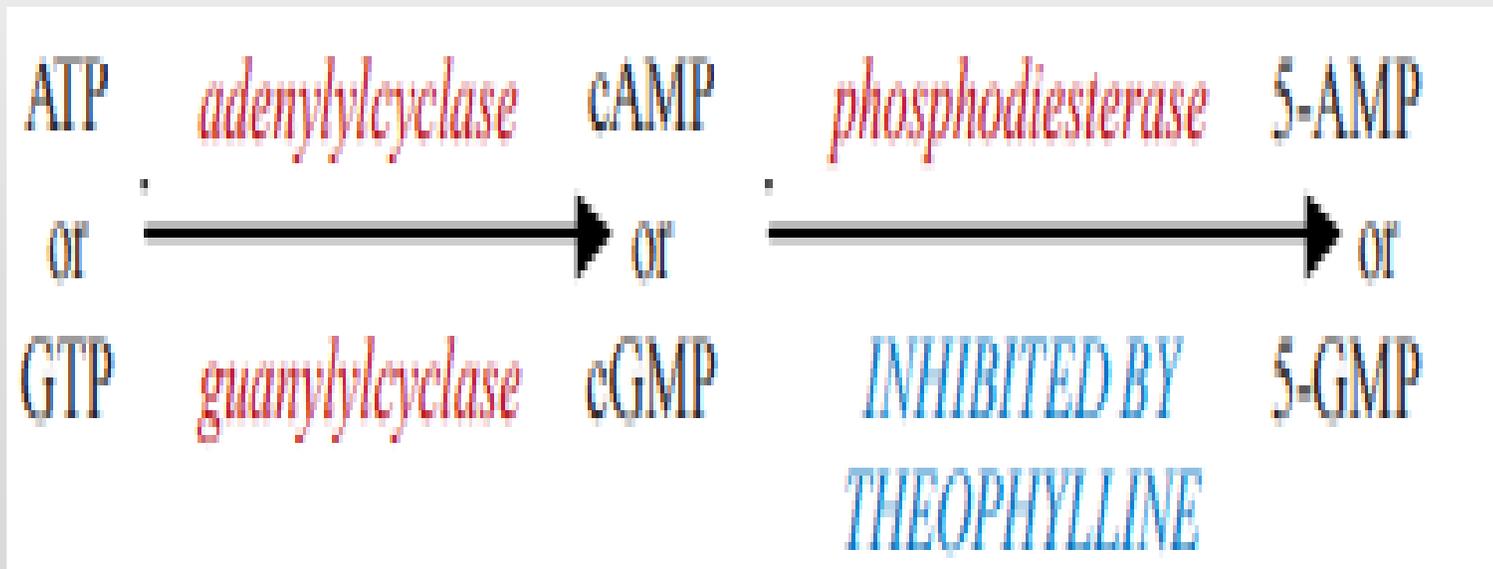
# PHARMACOLOGICAL ACTION

## **SKELETAL MUSCLE:**

- Caffeine enhances contractile power of skeletal muscle
- At higher concentration increases release of  $\text{Ca}^{2+}$  forms by direct action.
- caffeine facilitates neuromuscular transmission by increasing ACh release.

# Mechanism of Action: Three distinct cellular actions of methylxanthines have been defined—

- (a) Release of  $\text{Ca}^{2+}$  from sarcoplasmic reticulum, especially in skeletal and cardiac muscle
- (b) Inhibition of phosphodiesterase (PDE) which degrades cyclic nucleotides intracellularly



# Mechanism of action:

(c) Blockade of adenosine receptors:

Adenosine acts as a local mediator in CNS, CVS and other organs—

- contracts smooth muscle (Especially bronchial)
- dilates cerebral blood vessels
- depresses cardiac pacemaker
- Inhibits gastric secretion

**(Methylxanthines produce opposite effects)**

# Pharmacokinetics: Theophylline

- well absorbed orally
  - rectal absorption from suppositories is erratic
  - distributed in all tissues
  - **Crosses placenta & secreted in milk**
  - 50% plasma protein bound
  - Extensively metabolised in liver by demethylation & oxidation
- Elimination rate varies with age
    - $t_{1/2}$  in adults is 7–12 hours
    - $t_{1/2}$  in children 3–5 hrs
    - In case of elderly it is slow
    - In case of premature infant it prolongs 24 hrs

# Interaction:

- Agents which enhance theophylline metabolism: Smoking, phenytoin, rifampicin, phenobarbitone, charcoal broiled, meat meal.
- Drugs which inhibit theophylline metabolism and increase its plasma level are—erythromycin, ciprofloxacin, cimetidine, oral contraceptives.
- Theophylline enhances the effects of—furosemide, sympathomimetics, digitalis, oral anticoagulants, hypoglycaemics.
- Theophylline decreases the effects of—phenytoin, lithium.

# Uses

- In case of bronchial asthma & COPD:

Theophylline benefits by causing bronchodilatation as well as by decreasing release of inflammatory mediators

Sustained release theophylline can be used in mild-to moderately severe asthma, as a 3rd line or alternative/adjuvant drug

- Use in case of Apnoea in premature infant:

Theophylline reduces the frequency and duration of episodes of apnoea that occur in some preterm infants in the first few weeks of life.

# Anticholinergic drugs:

## Mechanism of action:

- Acetylcholine (Ach) causes bronchial constriction and narrowing of the airways.
- Anticholinergics bind to the Ach receptors, preventing Ach from binding.
- Results: Bronchoconstriction is prevented, airways dilate.

## Side effects:

### ABCD

- Agitation
- Blurred vision
- Constipation
- Dry mouth

# Leukotrienes Antagonist: Montelukast, Zafirlukast

## Mechanism of Action:

Leukotrienes are substances released when a trigger, such as cat hair or dust, starts a series of chemical reactions in the body



Leukotrienes cause inflammation, bronchoconstriction, and mucus production



results

Coughing, wheezing, shortness of breath

# Leukotrienes Antagonist: Montelukast, Zafirlukast

- Leukotriene antagonist prevent leukotrienes from attaching to receptors on cells in the lungs and in circulation
- Inflammation in the lung is blocked and asthma symptoms are relieved.

## Side Effects:

Headache, Dyspepsia(bloating), Nausea, Insomnia, liver dysfunction, diarrhea

# Mast cell stabilizer: Sodium cromoglycate, Ketotifen

- Decreased degranulation of mast cell & other inflammatory cells triggered direct stimuli
- Decreased mediators of asthma: H<sub>2</sub> , LT
- Used in long term treatment- reduced inflammatory cellular response
- Bronchospasm(induced by allergens, cold air ) is reduced
- For asthma: induced as an aerosol through inhaler only a small fraction is absorbed systemically
- Rapidly eliminated unchanged by urine & bile.
- Uses: asthma, allergic rhinitis, allergic conjunctivitis

# Corticosteriod:

## Mechanism of action:

- ✓ Stabilize membranes of cells that release harmful bronchoconstricting substances.
- ✓ These cells are leukocytes or white blood cells.
- ✓ Also increase responsiveness of bronchial smooth muscle to beta-adrenergic stimulation.

## Inhaled corticosteroids:

Beclomethasone dipropionate, triamcinolone acetonide, dexamethasone sodium phosphate, flunisolide.

## Side effects:

- ✓ Pharyngeal irritation
- ✓ Dry mouth
- ✓ Oral fungal infections

