

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](#).

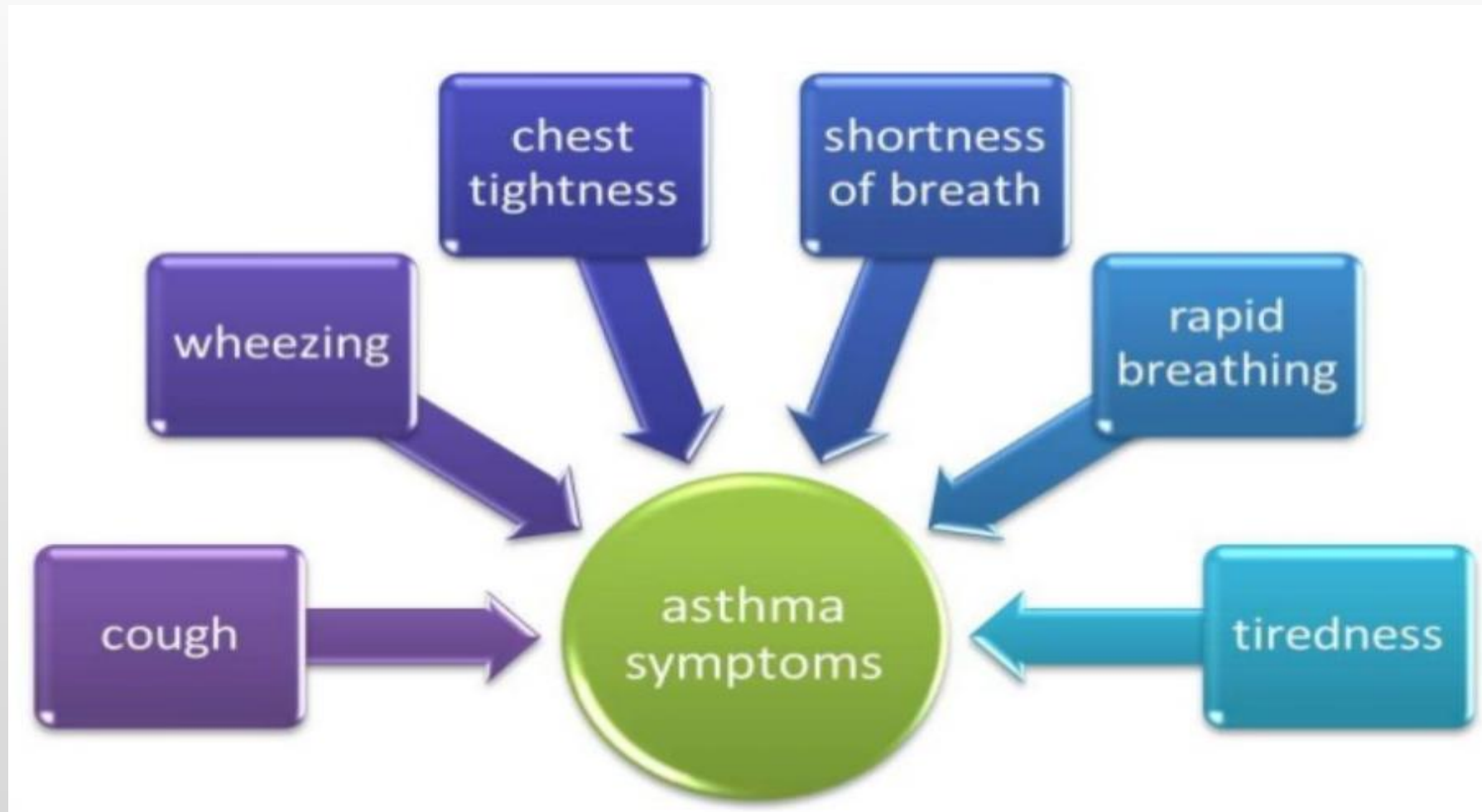
BRONCHIAL ASTHMA:Hyper-responsiveness of trachio-bronchial smooth muscle.

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

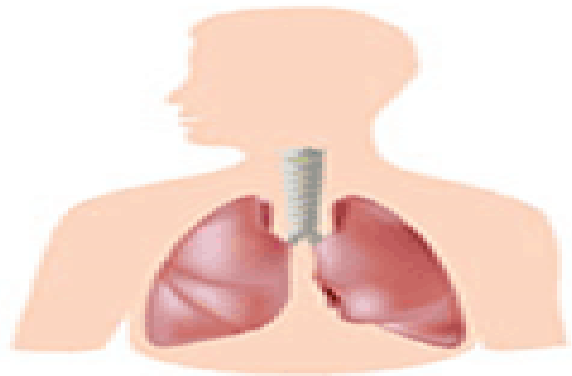
A variety of trigger factors (infection, irritants, pollution, exercise, exposure to cold air, psychogenic) may be involved:

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

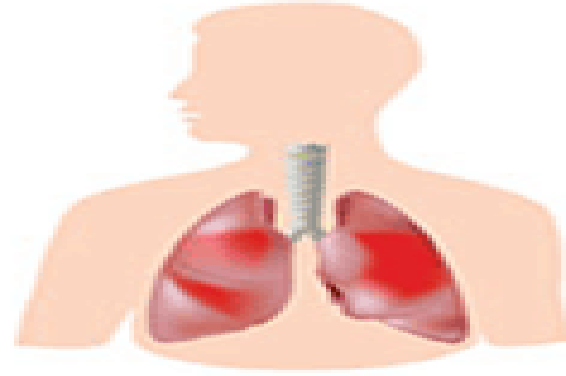
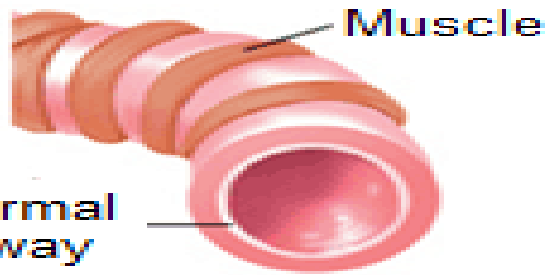
**INTRINSIC ASTHMA
TENDS TO BE
PERENNIAL,
STATUS
ASTHMATICUS MORE
COMMON**

BRONCHIAL ASTHMA

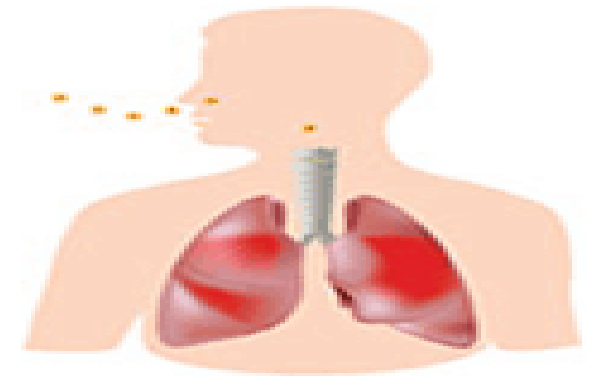
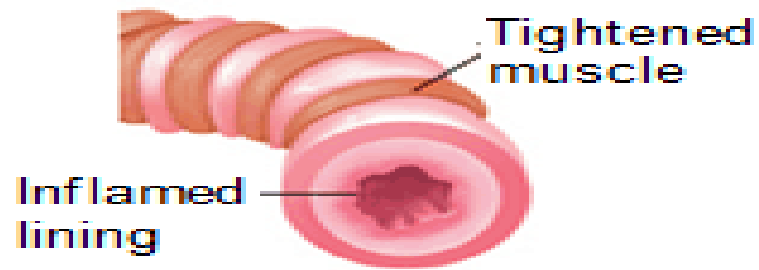
Asthma



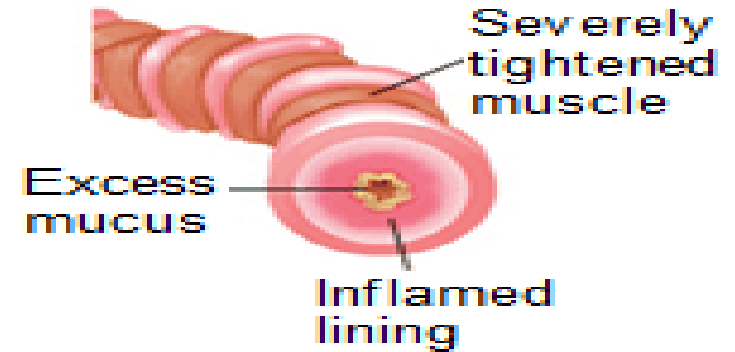
Normal airway



Asthma



Sever Asthma



ENVIRONMENTAL FACTORS

GENETIC FACTORS

BRONCHIAL INFLAMMATION

BRONCHIAL HYPERACTIVITY+TRIGGER FACTORS

**OEDEMA, BRONCHOCONSTRICTION, INCREASE
MUCOUS PRODUCTION**

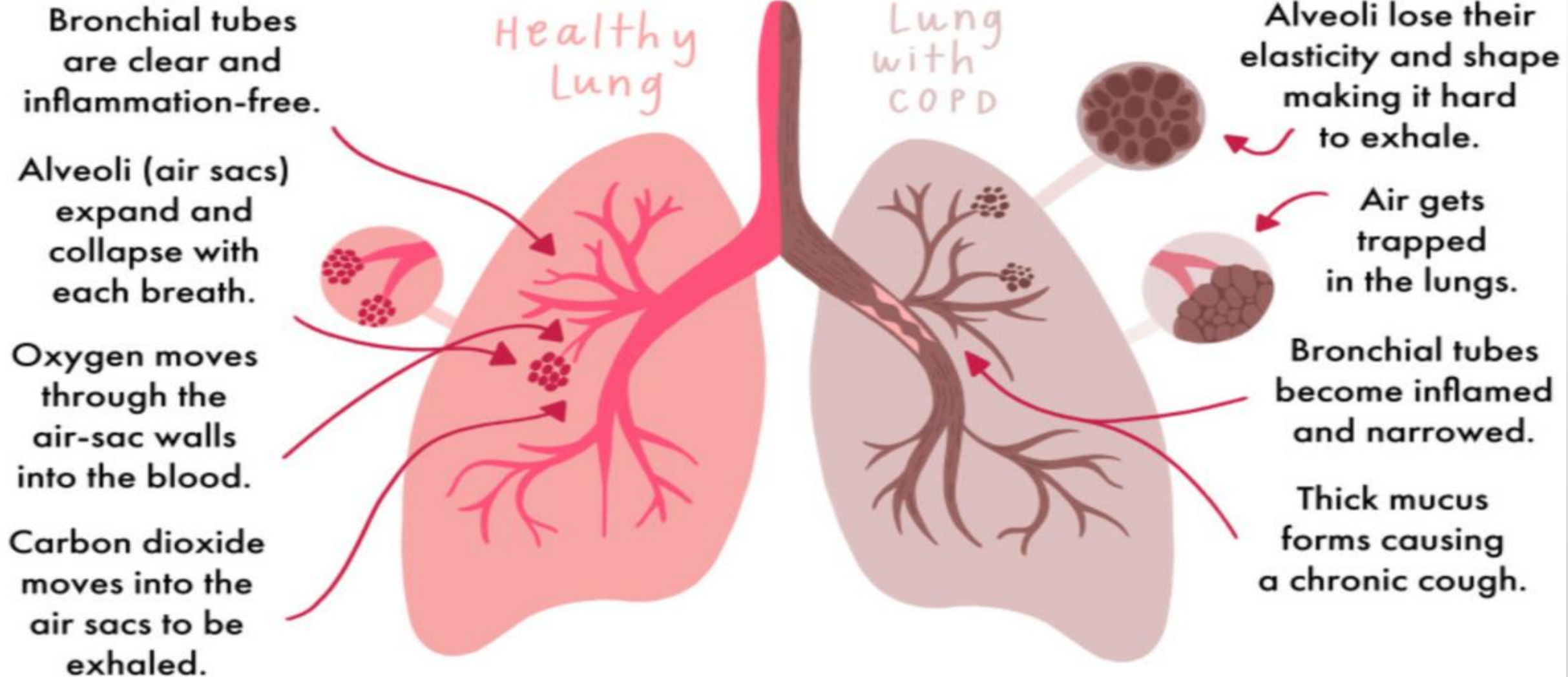
**AIRWAYS
NARROWING**

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

β₂ 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.**

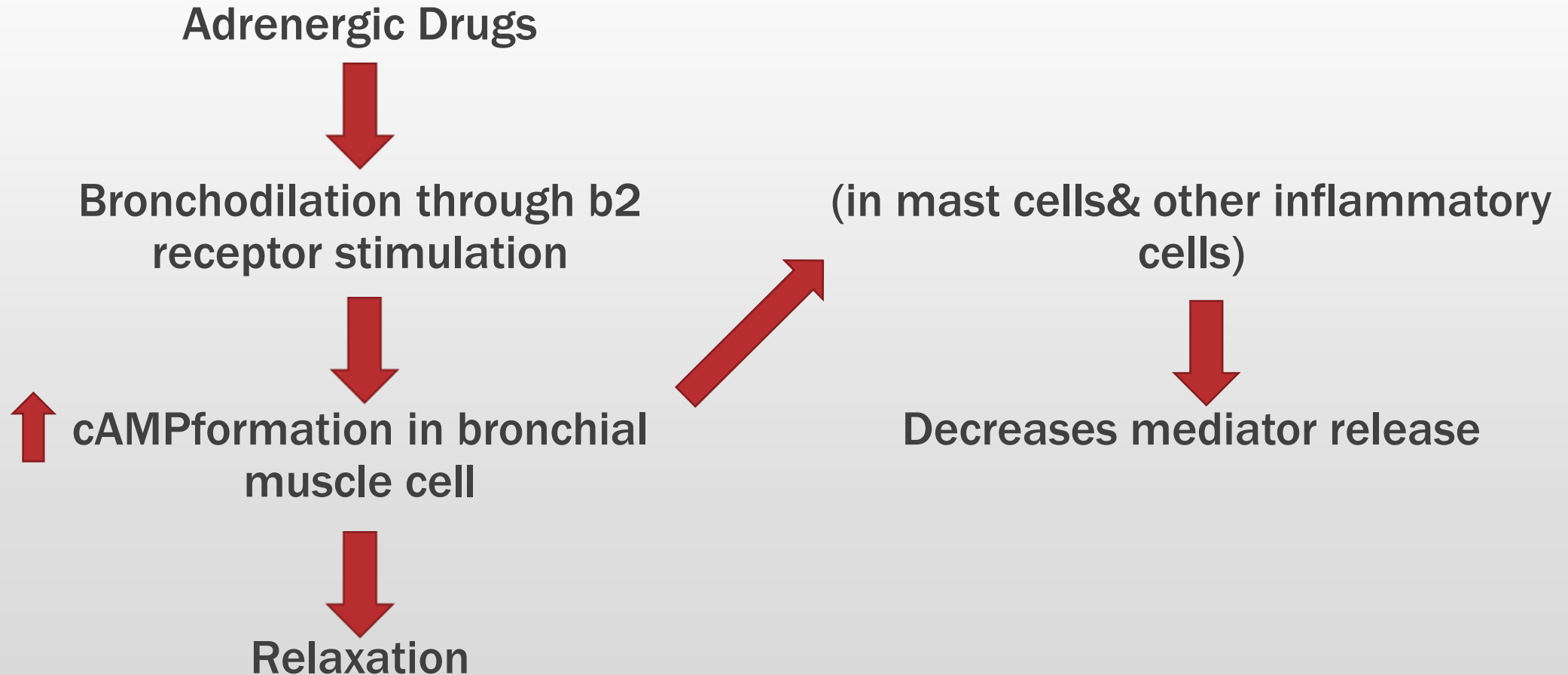
IV. Corticosteroids

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

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

V. Anti-IgE antibody **Omalizumab**

SYMPATHOMIMETICS :



SYMPATHOMIMETICS:

- *β 2 Receptor* on inflammatory cells desensitize quickly,
- The contribution of this action to the beneficial effect of β 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 β_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 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

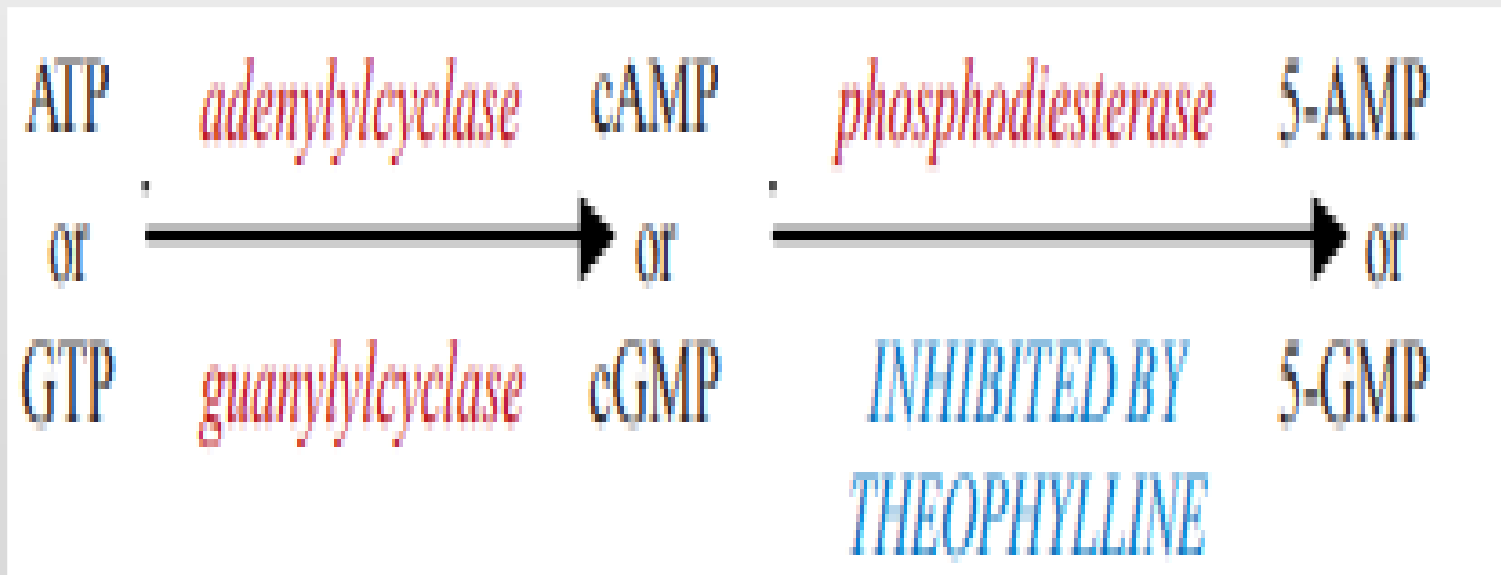
PHARMACOLOGICAL ACTION

SKELETAL MUSCLE:

- Caffeine enhances contractile power of skeletal muscle
- At higher concentration increases release of 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 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: H₂ , 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

