* Asthma is a recurrent bronchoconstriction due to bronchial hypersensitivity and hyper-responsiveness lead to bronchial mucosal edema and smooth muscle constriction.
* First exposure to Ag lead to stimulation of IgE that bind on most cells of bronchial wall, re-exposure to the Ag lead to Ag-Ab complex reaction on most cells and cause release of mediators which are:
1. **Mediator of early reaction:**
2. Histamine, tryptase, protease.
3. Leukotrien.
4. **Mediator of late reaction:**
5. Interleukine, IL4, 5, 9, 13.
6. GM-CSF.
7. Adenosin
8. PAF

These causes severe bronchoconstriction.

* Receptor found on bronchial smooth muscle:
* {β1, cAMP, PG} are **dilators**.
* {α1, Ca, LT, M3'neurokinin(substance p,neurokinine A and B)} are **constrictors**.
* The most important mediator in asthma is LT.

**Treatment of asthma:**

I-**Bronchodilator**:

1. **Methylxanthine**: (Theophylline, Aminophyllin, Caffeine)

**Mechanism**:

* + Phosphodiestrase inhibitor so ↑ cAMP.
	+ Block bronchoconstrictor effect of adenosine.
	+ Anti-inflammatory action (only theophyllin).
	+ Stimulate respiratory center.

**Uses**:

1. Acute asthma.
2. Chronic obstructive airway disease.
3. Pulmonary edema and heart failure due to ↑ cAMP that activate myocardium.
4. **Sympathomimetic agents:**
* **Non-selective β agonist**: (epinephrine, ephedrine, isoproterenol).

These active β1 and β2. Lead to bronchodilation and severe adverse effects due to stimulation of β1 receptor.

* **Selective β2 agonist:**
1. **1st generation**: (Albuterol, terbutaline, bitoterol).
* Given orally and by aerosol.
* Rapid acting.
* Short duration.
1. **2nd generation**: (salmetrol, formoterol).
* More potent.
* Slow acting.
* Long duration.
* Not used for acute asthma, only for chronic asthma.

**Indications of β2 agonist:**

1. Asthma.
2. Hyperkalemia.
3. Premature labor.

**S.E.**

1. Tremor, nervousness.
2. Tachycardia.
3. hypokalemia
4. **Antimuscarnic agent**: (Tiotropium, Ipratropium, atropine)
	* Block acetylcholine effect on bronchial smooth muscle.
	* Block M3.
	* In very high dose block bronchial smooth muscle response to any stimuli.
	* Less potent that β2.
	* Used in patient less tolerant to β2 agonist.
5. **Corticosteroids:** (triamcinolone, beclomethason, mometasone)

**Act by:**

* ↓ Inflammatory cytokine.
* ↓ Bronchial activity.
* ↓ Asthma exacerbation.
* Potentiate effects of β2 agonist.
* ↓ Mucosal inflammation by ↓ lymphocytes and esinophils.
	+ To ↓ systemic S.E. corticosteroid given by inhalation.
	+ S.E. of inhaled corticosteroid
1. Oropharyngeal candidiasis.
2. Hoarseness of voice.
3. ↑ Risk of cataract and osteoporosis.

**Prevention of asthmatic attacks:**

1. **Cromolyn and Nedocromile:-**
* Given by inhalation only due to very low bioavailability.
* Stabilize the mast cell and ↓ release of mediators.
* Not affect smooth muscle tone, so ineffective for acute attack of bronchoconstriction.
* Inhibit the mast cell of lung only.
* Not affect the mediator release from esinophils

**Uses**:

1. Prevention of asthma.
2. Allergic rhinoconjuctivitis.

**S.E.:**

1. Bronchoconstriction.
2. Cough, gastroenteritis.
3. Eosinophilia and anaphylaxis.

Orally mast cell stabilizer called **ketotifen**.

1. **Leukotriene pathway inhibitors:**
2. ↓ LT formation by blocking 5-lipo-oxygenase, this called **Zileuton**.
3. Block LT receptor (Zafirlukast, Montelukast).

**Action**:

1. Block neutrophil chemoattractant.
2. ↓ Bronchial reactivity and mucosal edema.
3. Prevent bronchoconstriction.

S.E.: Churg – Straus – syndrome.

1. **Anti-IgE monoclonal antibody:**

Block Fc1, Fc2 receptor of IgE on mast cell; used for prevention of asthma, this Ab called (Omalizumab).

1. **Ca-channel blocker:** inhibit bronchoconstriction and mediater release from mast cell..
2. **K+-channel opener:** (Cromockalim) cause bronchial smooth muscle hyperpolarization and thenrelaxation.
3. **Other**:
	* Cytokine antagonist (IL4, IL5).
	* Immunomodulator.

Drugs for (COPD): **C**hronic **O**bstructive **P**ulmonary **D**isease

* Inhaled bronchodilator and antimuscarnic are mainly used.
* Inhaled corticosteroid is less effective.
* Salmetrol more acting by improving lung function.

**Steroid resistant asthma**: is a failed to respond to aggressive courses of both inhaled and oral corticosteroid therapy.

**The type 1**: glucocorticoid receptor **binding** defect and it's localized to the T cell. Demonstrate sever adverse effects of corticosteroid.

The **type 2** decreases in numbers of glucocorticoid receptors, and appears to be genetic. These patients fail to derive any benefit from glucocorticoids and demonstrate few adverse effects from corticosteroids, despite long histories of chronic oral corticosteroid use.

**Therapy**: Methotrexate, Cyclosporine, Intravenous immunoglobulin,leukotriene antagonists,Nedocromil sodium,Dapsone,antibiotics and troleandomycin,gold

Diagnoses other than asthma, such as gastro-oesophageal reflux, hyperventilation, vocal cord dysfunction and sleep apnoea, should be sought as these may be a cause of glucocorticosteroid treatment failure and this called **pseudo-SRA**.

**Drugs treat allergic rhinitis**

1. **H1-receptor block**: more effective.
2. **α-agonist:** locally like oxymetazoline, not used for long time due to rebound congestion.
3. **Corticosteroid.**
4. **Cromolyn**: intranasal used.

Drugs treat cough

1. **Dry** cough treated by drugs that inhibit the cough center, they are: **codien**, **hydrocodone**, **hydromorphone**, **Dextromethorphan**.
2. **Productive** cough treated by:
	* **Expectorant** → guaicialate: ↑ sputum fluidity and ease the expectoration.
	* **Mucolytic** → Bromhexin: break silfid bond of mucoid and make it smaller.