



DRUGS OF BRONCHIAL ASTHMA

Bronchial asthma

- Impairment of airflow due to constriction of bronchial smooth muscle (bronchospasm)
- Swelling of bronchial mucus secretion.

Factors:

- Allergy, infection, psychological factors,
- Air way obstruction may be due to release of the mediators from sensitized mast cells in the lungs.



Bronchial asthma...

- Acute asthma
- Chronic asthma
- Status asthmaticus (acute severe asthma)

Drugs for bronchial asthma...

- Histamine
- 5-HT (serotonin)
- Prostaglandins
- Leukotriens (LTC_4 and LTCD_4)
- Protease
- Platelet activation factor (PAF)
- Bronchial asthma may be episodic or chronic.

Classification of antiasthmatic drugs

1. Bronchodilators

A. Sympathomimetics:

i) *Selective B₂-adrenergic agonists:*

salbutamol, terbutaline (short acting),
salmeterol, and formetrol (long acting).

ii) Non selective : adrenaline

B. Methylxanthine: theophylline, aminophylline,
etophylline

Classification of antiasthmatic drugs....

C. Anticholinergics: Ipratropium bromide, tiotropium bromide.

2. Leukotriene receptor antagonist: zafirlukast, montelukast.

3. Mast cell stabilizers: sodium chromoglycate, nedochromil sodium, ketotifen.

4. Glucocorticoids:

a) Inhaled glucocorticoids: beclomethasone, budesonide, fluticasone.

b) Systemic glucocorticoids: hydrocortisone, prednesolone, methylprednesolone.

5. Anti-Ig-E monoclonal antibody: omalizumab.

Bronchodilators

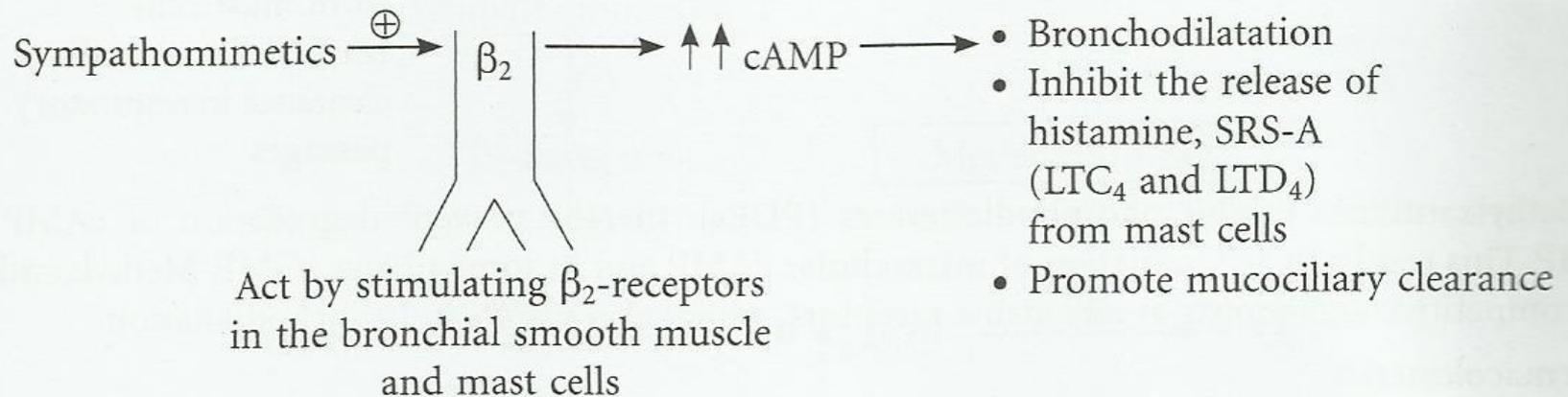
- **Adrenaline:** produce prompt and powerful bronchodilation by acting through β_2 adrenergic receptors.
- Useful in acute attack of asthma (0.2-0.5 ml of 1:1000 solution given s.c.)
- Its use decline due to serious cardiac side effects.

Mechanism of bronchodilation...

Bronchodilators

Sympathomimetics (see p. 84)

Mechanism of action



Bronchodilators...

- Selective β_2 - adrenergic agonists
- The first line drugs for bronchial asthma.
- Well tolerated when inhaled.
- At high doses may cause tremor, tachycardia, palpitation, hypokalaemia.

Bronchodilators...

Salbutamol and terbutaline	Salmeterol	Formoterol
<p><i>Selective β_2-agonists:</i> On inhalation, they have a rapid onset (within 1–5 minutes) and short duration of action. They are preferred for acute attack of asthma</p> <p><i>Route and dose:</i> Inhalation, salbutamol 100–200 mcg every 6 hours, or as and when required through metered dose inhaler (MDI) to terminate an acute attack. Other routes of administration are oral, i.m. and i.v.</p>	<p><i>Long-acting selective β_2-agonist:</i> It is preferred for maintenance therapy of asthma. It is not suitable for acute attack as it has a slow onset of action</p> <p><i>Route and dose:</i> Inhalation, 50 mcg twice daily</p>	<p><i>Long-acting selective β_2-agonist:</i> It has a rapid onset of action. It is preferred for prophylaxis due to long duration of action</p> <p><i>Route and dose:</i> Inhalation, 12–24 mcg twice daily</p>

Bronchodilators...

Methylxanthines:

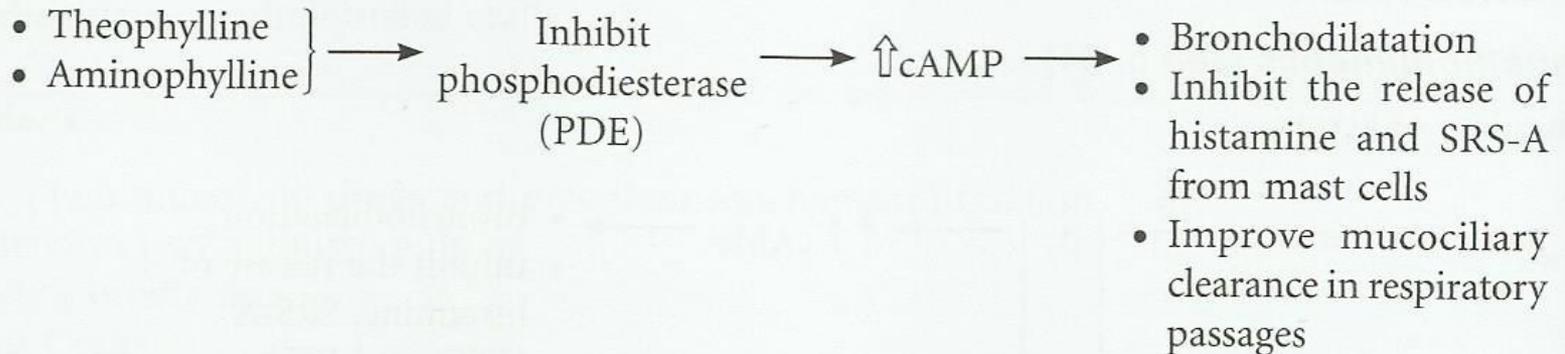
- Their uses are markedly reduced due to their narrow therapeutic index and available of better antiasthmatic drugs.
- Methylxanthine are third or fourth line drugs in the treatment of asthma.
- Methylxanthines are well absorbed after oral and parenteral administration.
- Food delays the rate of absorption of theophylline, well distributed, cross placenta & BBB, metabolised in liver and excreted in urine.

Methylxanthine Bronchodilators...

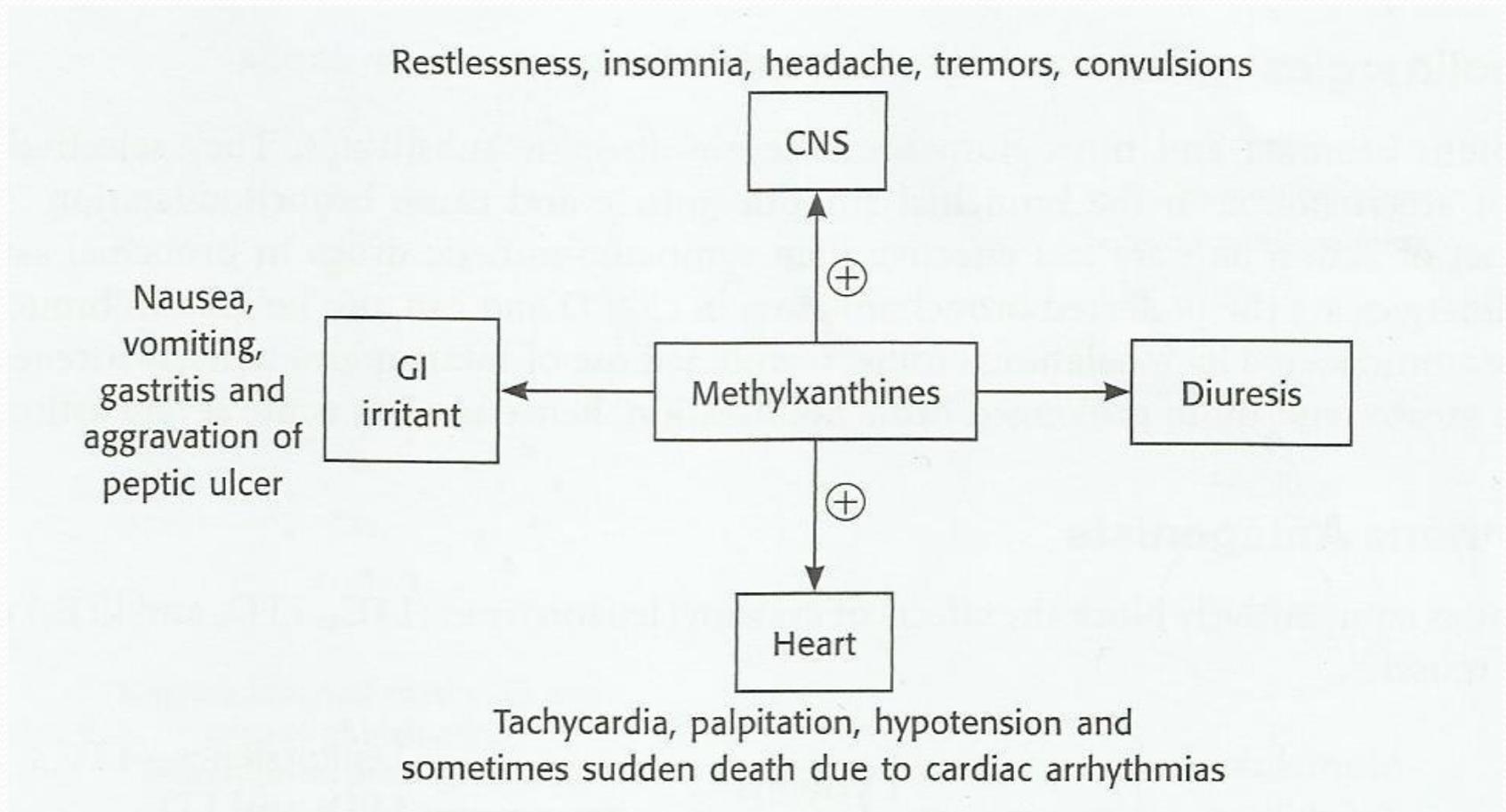
- **Theophylline:** poorly water soluble, hence not suitable for injection, available for oral administration.
- **Aminophylline:** water soluble but highly irritant. Administered orally or slow i.v.
- **Etophylline:** given by oral, i.m., i.v. routes.
- ***Adverse effects:*** have narrow margin of safety, tachycardia, palpitation, hypotension, death due to cardiac arrhythmias.

Mechanism of action of methylxanthine

Mechanism of action of methylxanthines



Adverse effects of methylxanthine



Drug interactions with methylxanthines

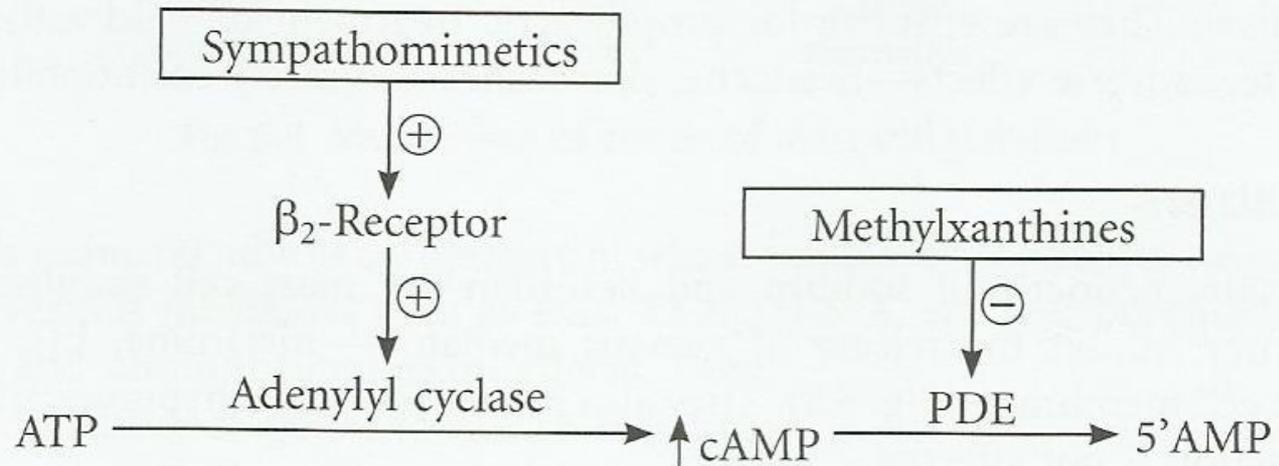
Drug interactions

- Phenytoin/ rifampicin/phenobarbitone x theophylline
- Cimetidine/ciprofloxacin/erythromycin x theophylline.
- **Uses:**
- Bronchial asthma and COPD
- Premature apnoea in infants.

Drug interactions

Drug interactions

1. Sympathomimetics × Methylxanthines



Anticholinergics

- Ipratropium bromide and tiotropium bromide are atropine substitutes.
- Selectively blocks the effects of Ach in bronchial smooth muscle and cause bronchodilation.
- Slow onset of action and are less effective.
- These drugs are preferred in COPD.
- Administered by inhalation route.
- Combination with B₂- adrenergic agonist have better effects.

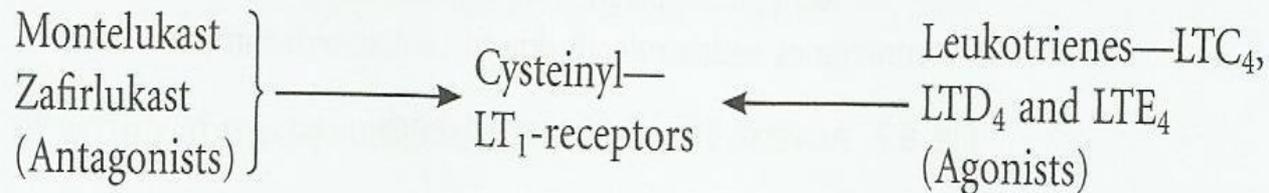
Leukotriene antagonists

- These drugs competitively blocks the effects of cysteinyl leukotrienes (LTC₄, LTD₄, LTE₄) on bronchial smooth muscle.
- Produce bronchodilation.
- Suppress bronchial inflammation
- Decrease hyper-reactivity
- Well absorbed after oral administration.
- Highly bound to plasma protein.
- Effective in prophylactic treatment of mild asthma.
- Well tolerated and has less side effects.

Mechanism

Leukotriene Antagonists

These drugs competitively block the effects of cysteinyl leukotrienes (LTC_4 , LTD_4 and LTE_4) on bronchial smooth muscle.



Mast cell stabilizers

- Sodium chromogluccate, nedocromil sodium, kitotefen.
- They are not bronchodilators.
- Inhibits release of various mediators-histamine, LTs, PGs PAF etc.
- Stabilizes the mast cell membrane.

Sodium chromoglycate: is not effective orally as it poorly absorbed from gut, given by inhalation route.

Mast cell stabilizers....

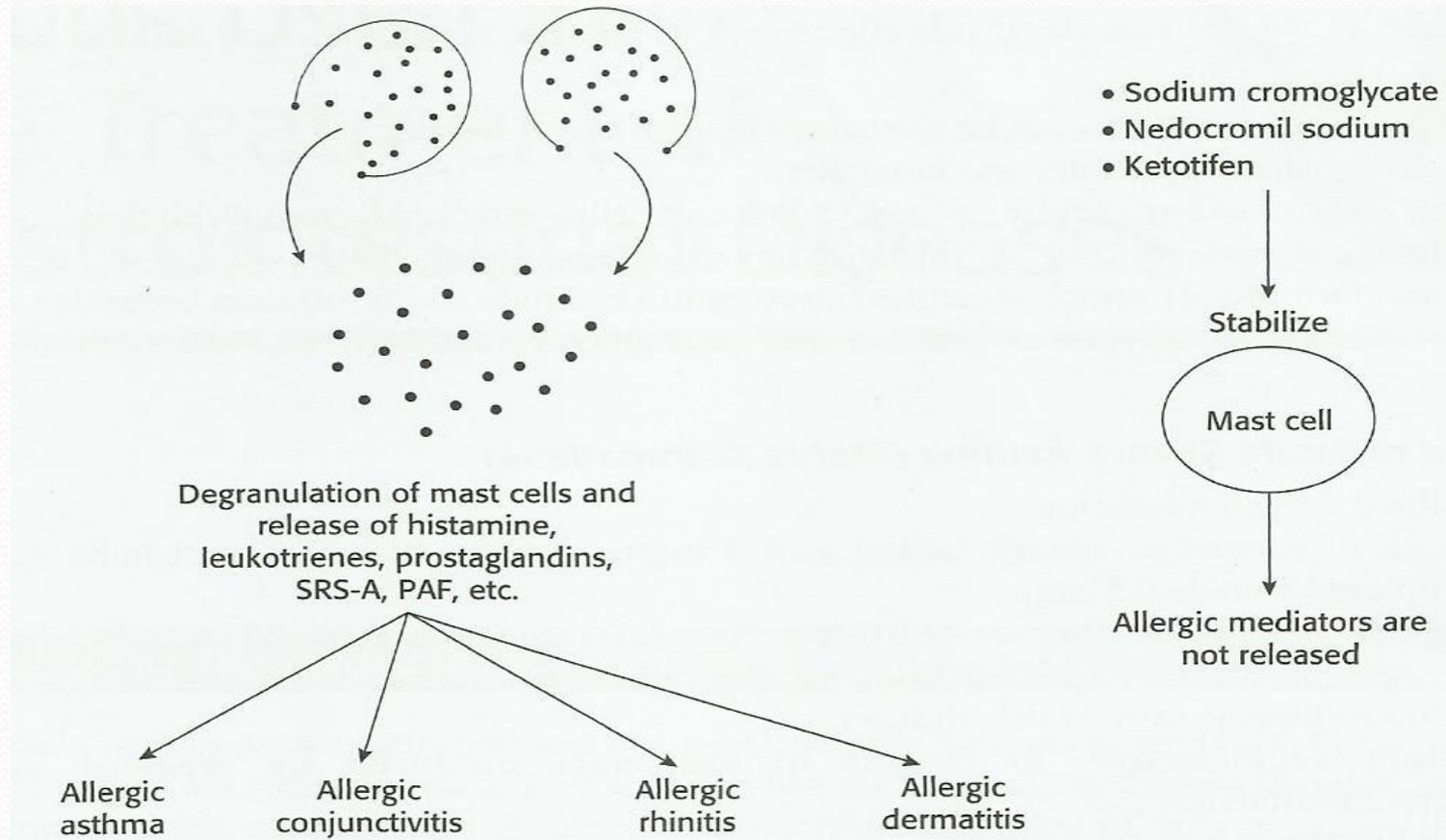
Uses of sodium chromoglycate

1. As prophylactic agent to prevent bronchospasm induced by allergens and irritants.
2. Can be used in allergic conjunctivitis, allergic rhinitis, allergic dermatitis, etc.
3. Used by topical route as prophylactic agent.

Mast cell stabilizers...

- ***Nedocromil sodium***: mechanism of action pharmacological effects are similar to sodium chromoglycate.
- Approved for use in patients above 12 years of age in bronchial asthma.
- ***Ketotefen***: mechanism is similar to sodium chromoglycate, has H₁-blocking effect. It is orally effective but has a slow onset of action.

Mechanism



Glucocorticoids

Systemic: hydrocortisone, prednisolone, methylprednisolone, and others

Inhalational: beclomethasone, budesonide and fluticasone.

- Glucocorticoids secrete lipocortin which inhibits phospholipase A₂ and thereby prevent formation of various mediators such as PGs, TXA₂ etc.
- Have antiallergic, antiinflammatory and immunosuppressant effects.

Glucocorticoids...

1. Suppress inflammatory response to Ag: Ab reaction.
2. Decrease mucosal oedema.
3. Reduced bronchial hyperreactivity.
4. Do not have direct bronchodilating effect but potentiates the effects of B-adrenergic agonists
5. They are well tolerated.

Glucocorticoids...

- Combination of long acting β -agonists (LABA) with steroid is available, e.g. fluticasone + salmeterol; budesonide + formetrol.
- They have synergistic action used in COPD and bronchial asthma.
- **Adverse effects:** gastric irritation, Na^+ and water retention, hypertension, muscle weakness, osteoporosis, HPA-axis suppression etc.

Anti-Ig-E antibody

Omalizumab: prevents binding of IgE to mast cell, thus prevent mast cell de-granulation.

- It has no effects on IgE already bound to mast cells.
- Administered parenterally.
- Used in moderate to severe asthma and allergic disorders such as nasal allergy, food allergy, etc. approved for use in patient above 12 years of age.

Inhalational devices

- **Metered dose inhaler (MDI)**- used with spacer device.
- **Dry powder inhalers**- spinhaler and rotahaler
- **Nebulizers**- useful in acute severe asthma, COPD, and children.

Treatment of acute severe asthma

- Humidified oxygen
- Nebulized β_2 -adrenergic agonist (salbutamol 5 mg/terbutaline 10 mg) + anticholinergic agents (ipratropium bromide 0.5 mg).
- Systemic glucocorticoids: i.v. hydrocortisone 200 mg stat followed by 30-60 mg prednisolone/day.
- I.V. fluid to correct dehydration.
- K^+ and sodium bicarbonates supplements.
- Antibiotics.

Dugs to be avoided in asthma

- NSAIDs
- β -adrenergic blockers.
- Cholinergic agents.