



- You must know that asthma is reversible obstructive pulmonary disease in which bronchoconstriction can be reversed or prevented by the use of the following medical agents:

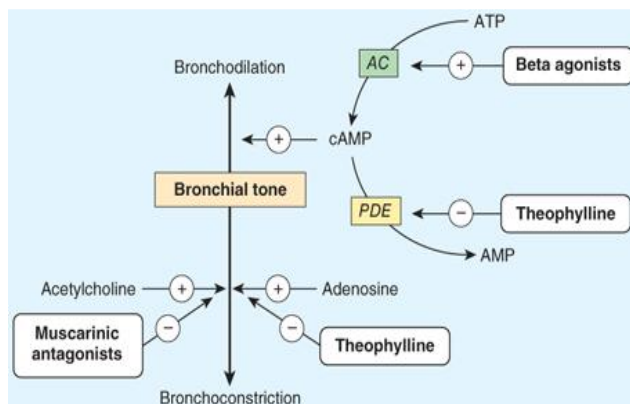
- **Drugs which relax bronchial smooth muscles (causing in bronchodilation):**
 - ✓ β_2 -agonists:
 - ❖ *Short-acting:* albuterol.
 - ❖ *Long-acting:* salmeterol.
 - ✓ Theophylline.
- **Drugs which inhibit bronchoconstriction that is induced by acetylcholine:** muscarinic antagonists.
- **Leukotriene modifiers:** zileuton and zafirlukast
- **Drugs which prevent mast cell degranulation:** cromolyn sodium.
- **Drugs which reduce the amount of IgE (which in the process of asthma binds to mast cells and induce the release of different mediators which result in the disease):** anti-IgE monoclonal antibodies.
- **Corticosteroids:** beclomethasone and fluticasone.

Notice that the following medications are used for long-term control and prevention of bronchial hyperactivity: corticosteroids, mast cell stabilizers and leukotriene modifiers.

- Bronchodilation is promoted by cAMP. Intracellular levels of cAMP can be increased by:

- **β_2 -agonists:** which increase the rate of cAMP synthesis by adenylyl cyclase (AC).
- **Phosphodiesterase (PDE) inhibitors (such as theophylline):** which slow the rate of cAMP degradation.

Notice that bronchoconstriction can be inhibited by muscarinic antagonists and possibly by adenosine antagonists.



- How to apply these medications clinically in treatment of different patients?

- **Management of acute exacerbation of asthma in emergency (status asthmaticus):**
 - ✓ Oxygen supply.
 - ✓ Short-acting β_2 -agonist (albuterol)
 - ✓ Systemic steroids (orally for 10-14 days).
- **β_2 -agonists:**
 - ✓ Short-acting β_2 -agonists:
 - ❖ *Examples:* albuterol and salbutamol.
 - ❖ *Mechanism of action:* increase cAMP after stimulating the enzyme adenylyl cyclase.
 - ❖ *Use:* acute symptomatic relief.



- ❖ *Adverse effects:* tremor (most common). Others include: tachycardia and hypokalemia.
- ✓ Long-acting β_2 -agonist:
 - ❖ *Example:* salmeterol (effect lasts for 12 hours).
 - ❖ *Mechanism of action:* increase cAMP after stimulating the enzyme adenylyl cyclase.
 - ❖ *Use:* it is effective in patients having:
 - Nocturnal cough variant of asthma.
 - Exercise-induced asthma.
 - ❖ *Adverse effects:* tremor (most common). Others include: tachycardia and hypokalemia.
 - ❖ *Note:* it is not effective during an acute attack of asthma.
- **Aminophylline/theophylline:**
 - ✓ They are available in the form of: tablets of injections.
 - ✓ Mechanism of action: PDE inhibitors (thus increasing cAMP).
 - ✓ Use: chronic management of asthma especially in patients with nocturnal cough.
 - ✓ Adverse effects: tachycardia/palpitations, epigastric pain, nervousness and seizures.
- **Anticholinergic drugs:**
 - ✓ Example: ipratropium bromide.
 - ✓ Mechanism of action: Blockage of muscarinic receptor (M3).
 - ✓ Use: used in patients with heart disease in whom it is dangerous to give a β_2 -agonist or theophylline and in COPD patients.
 - ✓ Notice: they take 90 minutes to achieve bronchodilation.
- **Corticosteroids:**
 - ✓ Inhaled corticosteroids (e.g. beclomethasone) are the cornerstone of chronic asthma therapy in adults. They work by reducing airway inflammation:
 - ❖ They inhibit phospholipase A₂ (arachidonic acid will not be broken down) thus COX enzyme does not work.
 - ❖ They also inhibit IgE production and reduce cytokines.
 - ✓ ADR: oral thrush with INHALED corticosteroids (thus advise your patient to wash his mouth after using it). Other adverse effects include: cataract, glaucoma, diabetes and osteoporosis.
 - ✓ If inhaled corticosteroids do not work in managing chronic asthma, try leukotriene inhibitors as your last option before starting the patient on systemic corticosteroids (e.g. prednisone).
- **Leukotriene inhibitors:**
 - ✓ Lipoxygenase inhibitors:
 - ❖ Example: zileuton (tablet).
 - ❖ Mechanism of action: selective 5-lipoxygenase inhibition.
 - ❖ Use: long-term prevention of asthma in CHILDREN.
 - ❖ Adverse effects: hepatotoxicity and flu-like syndrome.
 - ✓ Leukotriene receptor blockers:
 - ❖ Example: zafirlukast (tablet).
 - ❖ Mechanism of action: blocks LTD₄ receptors.
 - ❖ Use: long-term prevention of asthma in CHILDREN.
- **Mast cell stabilizers:**
 - ✓ Example: cromolyn sodium.
 - ✓ Mechanism of action: prevents the release of mast cell granules (thus there will be no production of histamine, leukotriene or other mediators).
 - ✓ Use: long-term prevention of asthma in children.
 - ✓ Adverse effects: cough and irritation of airways.



- **Anti-IgE antibodies:**
 - ✓ Example: omalizumab (subcutaneous).
 - ✓ Mechanism of action: blocks binding of IgE to IgE receptors and reduce the circulating IgE antibodies.
 - ✓ Use: long-term control and prevention of asthma (but notice that it is considered as your last option).
 - ✓ Adverse effects: arthralgia and anaphylaxis (rare).
- **Treatment of asthma according to its classification:**
 - **Mild intermittent asthma:**
 - ✓ Symptoms: ≤ 2 times/week; nighttime symptoms: ≤ 2 times/month
 - ✓ Treatment: short-acting $\beta 2$ agonist (e.g. salbutamol).
 - **Mild persistent asthma:**
 - ✓ Symptoms: > 2 times/week; nighttime symptoms: > 2 times/month.
 - ✓ Treatment: short-acting $\beta 2$ agonist + low-dose inhaled corticosteroid.
 - **Moderate persistent asthma:**
 - ✓ Symptoms: daily; nighttime symptoms: ≥ 5 times/month.
 - ✓ Treatment: short-acting $\beta 2$ agonist + long-acting $\beta 2$ agonist (for nighttime symptoms) + moderate-dose inhaled corticosteroids.
 - **Severe persistent asthma:**
 - ✓ Continuous symptoms (day and night).
 - ✓ Treatment: short-acting $\beta 2$ agonist + long-acting $\beta 2$ agonist (for nighttime symptoms) + high-dose inhaled corticosteroids + systemic corticosteroids (at lowest dose possible).