ASTHMA PHARMACOLOGY COLLEGE OF NURSING

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Definition

- Asthma is characterized: clinically by recurrent bouts of shortness of breath, chest tightness, and wheezing, often associated with coughing
- Physiologically by widespread, reversible narrowing of the bronchial airways and a marked increase in bronchial responsiveness to inhaled stimuli.
- Pathologically by lymphocytic, eosinophilic inflammation of the bronchial mucosa.

Many cells and cellular elements play a role in asthma, in particular:

- *Mast cells*
- *Eosinophils*
- *Neutrophils*
- *T lymphocytes*
- *Macrophages*
- *Epithelial cells*

Symptoms

- *Coughing (particularly at night or early in the morning)*
- *Wheezing*
- *Breathlessness*
- *Chest tightness*
- *Reversible airflow obstruction*

Goals of Therapy

- To ***Reduce Impairment.***
- To ***Reduce Risk***

Asthmatic bronchospasm results from a combination of release of mediators and an exaggeration of responsiveness to their effects predicts that asthma may be effectively treated by drugs with different modes of action.

- Drugs that reduce the amount of IgE bound to mast cells (anti-IgE antibody)
- Drugs prevent mast cell degranulation (cromolyn or nedocromil, sympathomimetic agents, calcium channel blockers)
- Drugs block the action of the products released (antihistamines and leukotriene receptor antagonists)
- Drugs inhibit the effect of acetylcholine released from vagal motor nerves (muscarinic antagonists)
- Drugs directly relax airway smooth muscle (sympathomimetic agents, theophylline).

SYMPATHOMIMETIC AGENTS

- They relax airway smooth muscle.
- They inhibit release of bronchoconstricting mediators from mast cells.
- They may also inhibit microvascular leakage and increase mucociliary transport by increasing ciliary activity.

- As in other tissues, the β agonists stimulate adenylyl cyclase and increase the formation of intracellular cAMP.
- They causes tachycardia and skeletal muscle tremor as side effects.
- Adrenoceptor agonists are best delivered by inhalation because this results in the greatest local effect on airway smooth muscle with the least systemic toxicity

- **Non-selective β agonists:**
- Epinephrine
- Ephedrine
- Isoproterenol

- **Epinephrine:** is an effective, rapidly acting bronchodilator when injected subcutaneously or inhaled. Maximal bronchodilation is achieved 15 minutes after inhalation and lasts 60–90 minutes.
- its use in asthma has been displaced by other, more β_2-selective agents.

- **Selective β 2 agonists:**
- Salbutamol
- Terbutaline
- Metaproterenol
- Salmoterol
- Formoterol

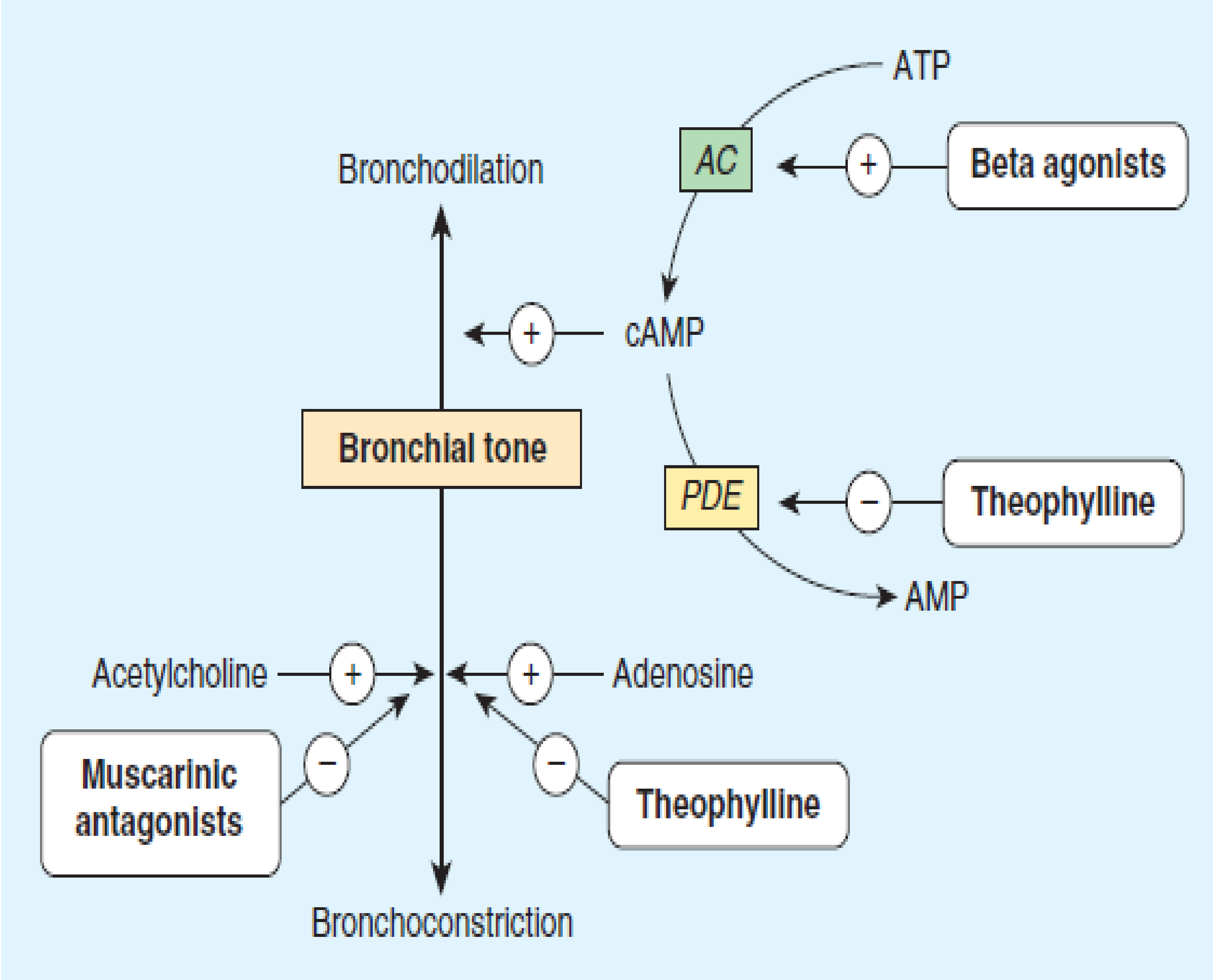
- They are effective after inhaled or oral administration and have a long duration of action.
- Bronchodilation is maximal within 15–30 minutes and persists for 3–4 hours.
- All can be diluted in saline for administration from a hand-held nebulizer.
- Oral dosage forms are associated with systemic side effects like tremors and nervousness.

METHYLXANTHINE DRUGS

- The three important methylxanthines are **theophylline, theobromine,** and **caffeine.**
- Their major source is beverages (tea, cocoa, and coffee, respectively).
- A theophylline preparation commonly used for therapeutic purposes is **aminophylline**

Mechanism of Action

- Several mechanisms have been proposed for the actions of methylxanthines, but none has been firmly established.
- At high concentrations, they can be shown in vitro to inhibit several members of the phosphodiesterase (PDE) enzyme family.


ATP
AC
+
Beta agonists
Bronchodilation
+
cAMP
Bronchial tone
PDE
−
Theophylline
AMP
Acetylcholine
+
+
Adenosine
Muscarinic antagonists
−
−
Theophylline
Bronchoconstriction

Clinical Uses

- Theophylline is the most effective bronchodilator, and it has been shown repeatedly both to relieve airflow obstruction in acute asthma and to reduce the severity of symptoms and time lost from work or school in patients with chronic asthma.
- Theophylline should be used only where methods to measure theophylline blood levels are available because it has a narrow therapeutic window.
- Its' therapeutic and toxic effects are related to its blood level.

- Theophylline improves long-term control of asthma when taken as the sole maintenance treatment or when added to inhaled corticosteroids.
- Its use requires occasional measurement of plasma levels; it often causes unpleasant minor side effects (especially insomnia); and accidental or intentional overdose can result in severe toxicity or death.

ANTIMUSCARINIC AGENTS

- Observation of the use of leaves from *Datura stramonium for* asthma treatment in India led to the discovery of atropine, a potent competitive inhibitor of acetylcholine at postganglionic muscarinic receptors, as a bronchodilator.

Mechanism of Action

- Muscarinic antagonists competitively inhibit the effect of acetylcholine at muscarinic receptors. So, they block smooth muscle contraction induced through muscrinic receptors, in addition, they reduce mucus secretion.

Clinical Uses

- **Atropine:** it causes bronchodilation in a small dose. But, its' systemic absorption limited its' use (systemic side effects).
- **Ipratropium bromide:** when inhaled, it is poorly absorbed into the circulation and does not readily enter the central nervous system.

- Antimuscarinic agents are valuable for patients intolerant of inhaled β-agonist agents.
- The addition of ipratropium enhances the bronchodilation produced by nebulized salbutamol in acute severe asthma.

CORTICOSTEROIDS

- Corticosteroids have been used to treat asthma since 1950 and are presumed to act by their broad anti-inflammatory efficacy, mediated in part by inhibition of production of inflammatory cytokines.
- They do not relax airway smooth muscle directly but reduce bronchial reactivity and reduce the frequency of asthma exacerbations if taken regularly.

- The most important action is inhibition of the infiltration of asthmatic airways by lymphocytes, eosinophils, and mast cell.

Clinical Uses

- Clinical studies of corticosteroids consistently show them to be effective in improving all indices of asthma control—severity of symptoms, bronchial reactivity, frequency of exacerbations, and quality of life.

- Because of severe adverse effects when given chronically, oral and parenteral corticosteroids are reserved for patients who require urgent treatment, ie, those who have not improved adequately with bronchodilators or who experience worsening symptoms despite maintenance therapy.

- A special problem caused by inhaled topical corticosteroids is the occurrence of oropharyngeal candidiasis.
- Hoarseness can also result from a direct local effect of inhaled corticosteroids on the vocal cords.
- They may increase the risks of osteoporosis and cataracts over the long term.
- In children, inhaled corticosteroid therapy has been shown to slow the rate of growth by about 1 cm over the first year of treatment.

- Chronic use of inhaled corticosteroids effectively reduces symptoms and improves pulmonary function in patients with mild asthma. Moreover, it reduces the need for oral corticosteroid for more severe form of asthma.
- Inhaled corticosteroids are indicated for patients who need short acting beta agonist more than occasionally.