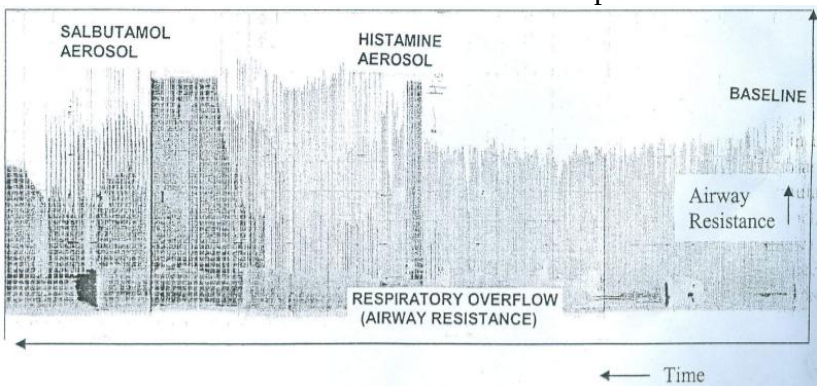
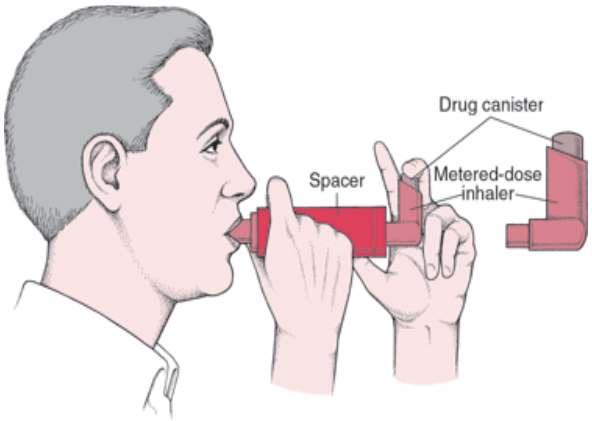
Unit II – Problem 3 – Pharmacology Demonstration: Effects of Bronchodilators

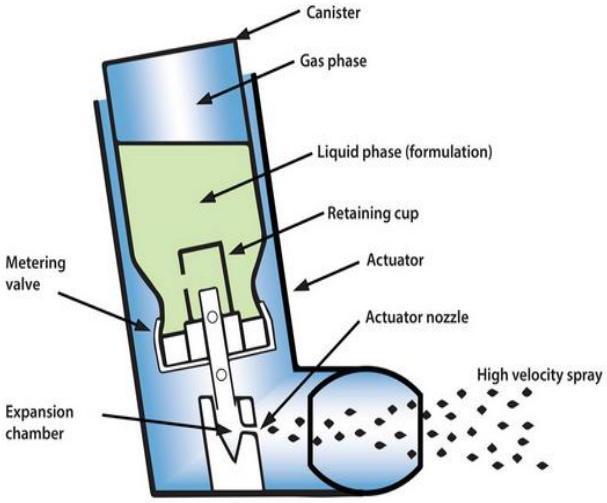
- **Demonstration of the effect of bronchodilators in an experimental model of bronchial asthma:**
  - **Introduction**: asthma is a syndrome characterized by airflow obstruction that varies markedly, both spontaneously and with treatment. Asthmatics harbor a type of inflammation in the airways that makes them more responsive than non-asthmatics to a wide range of triggers, leading to excessive narrowing with consequent reduced airflow and symptomatic wheezing, dyspnea and cough. Narrowing of the airways is usually reversible, but in some patients with chronic asthma there may be an element of irreversible airflow obstruction.
  - **Drugs for asthma can be broadly divided into two main classes:**
    - ✓ Bronchodilators.
    - ✓ Anti-inflammatory.
  - **Objective**: to demonstrate the effect of salbutamol on histamine-induced bronchoconstriction in an experimental animal.
  - **Parameter measured**: respiratory overflow – ROF (indirect measure of airway resistance).
  - **Animal used**: anesthetized Guinea pig.
  - **Drugs and chemicals used:**
    - ✓ Salbutamol 100 mcg aerosol.
    - ✓ Histamine 1% aerosol.
    - ✓ Urethane 25% (anesthetic drug).
  - **Procedure**: a guinea pig is anesthetized with urethane 25% administered intraperitoneally in a dose of 1.5 g/kg body weight. Once anesthetized, the trachea of the animal is exposed through an incision in the neck region. Through a cut in the trachea, a tracheal cannula is inserted. This cannula is connected by tubes to a respiratory pump and a bronchospasm measuring unit (airflow sensor0. The respiratory pump ventilates the animal (tidal volume and respiratory rate being adjustable). Histamine is administered as an aerosol to produce bronchoconstriction, increasing airway resistance and respiratory overflow (ROF). This is followed by administration of salbutamol and its effect is observed.
  - **Results**: salbutamol reverses histamine-induced bronchospasm.



- **Inhalation of drug by metered-dose inhalers in asthma:**
  - **Advantages:**
    - ✓ Delivers the drug directly to the site of action.
    - ✓ Allows rapid relief of bronchoconstriction with short-acting β_2-agonists (bronchodilators).
    - ✓ Causes less systemic adverse effects as a result of using small dosage of drugs.
  - **Disadvantages:**
    - ✓ It is difficult to use for children even with supervision (this problem can be overcome by using a spacer device).

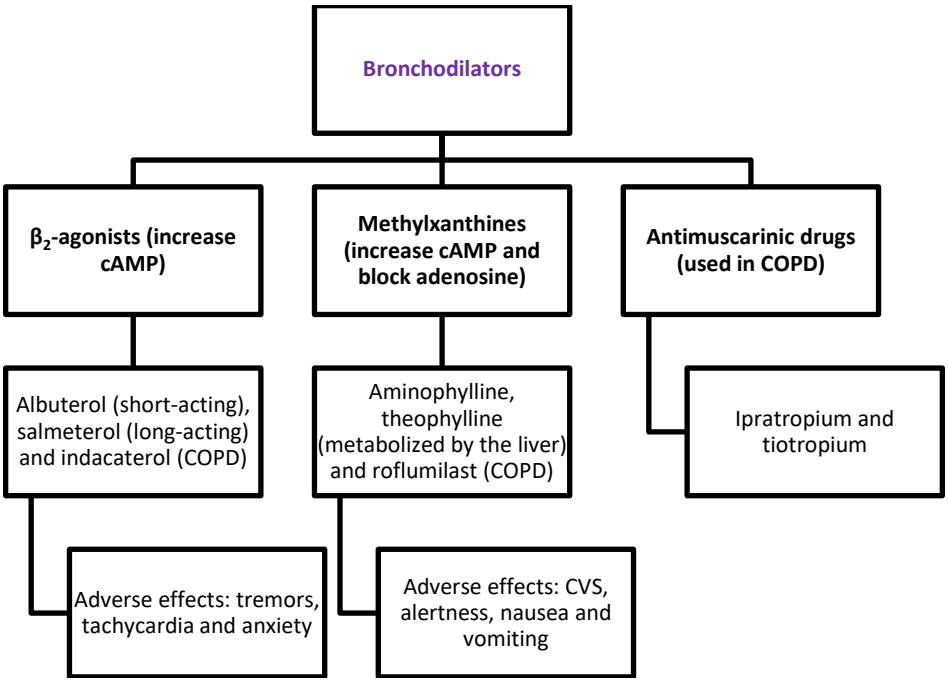
- ✓ Inhaled corticosteroids may sometimes cause oral thrush (candidiasis) which can be prevented by washing the mouth after inhaling the drug.
- ✓ Voice problems (hoarsness).

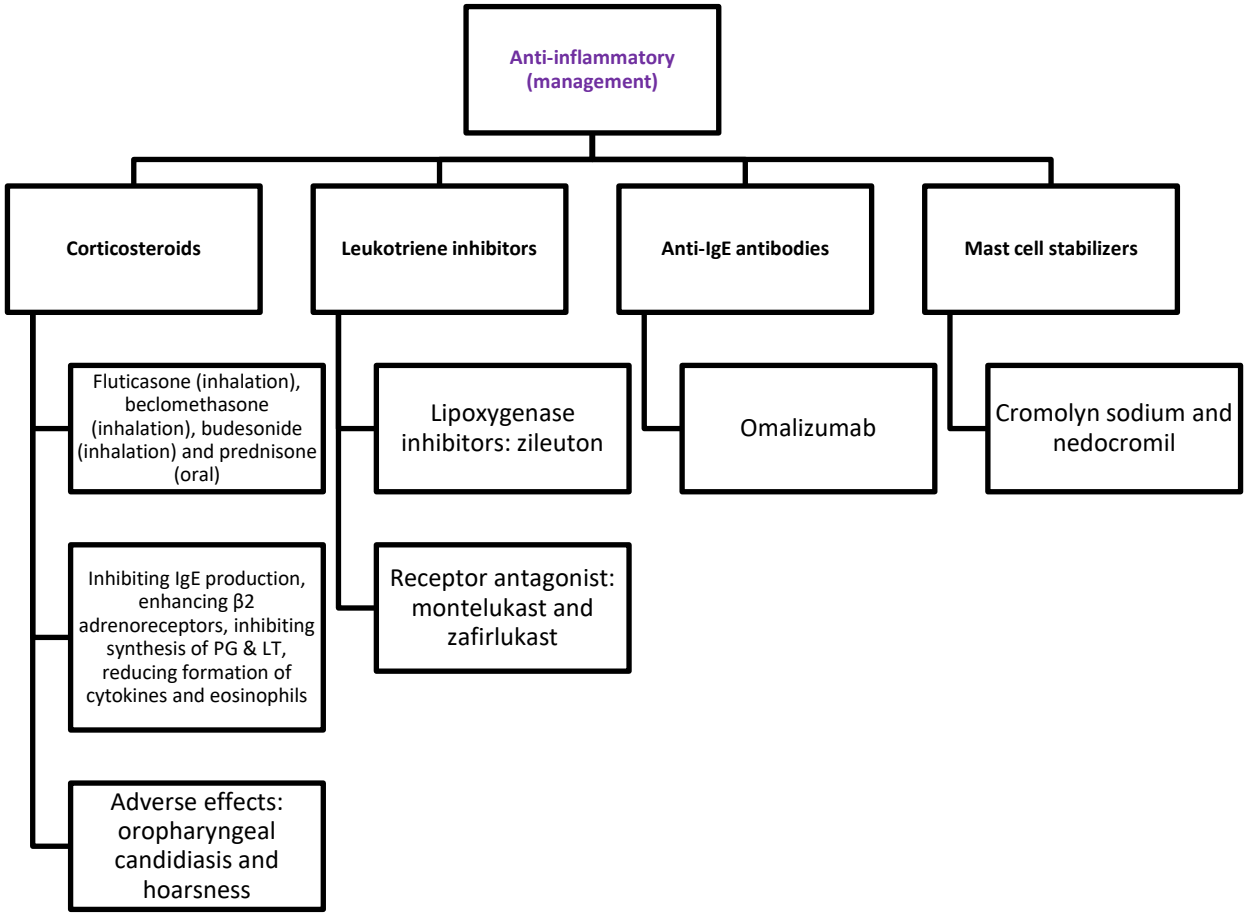




- **Recommendations for management of asthma:**

Severity	Symptoms	Recommended treatment (acute)	Recommended treatment (long-term)
Mild intermittent	Symptoms < 2 a week; nighttime symptoms < 2 a month	Short-acting β_2-agonist	No daily medication required
Mild persistent	Symptoms > 2 a week; nighttime symptoms > 2 a month	Short-acting β_2-agonist	Daily inhaled corticosteroid, cromolyn or nedocromil
Moderate persistent	Symptoms daily; nighttime symptoms > 1 a week	Short-acting β_2-agonist	Inhaled corticosteroid (medium dose) and long-acting β_2-agonist
Severe persistent	Continual symptoms; frequent	Short-acting β_2-agonist	Inhaled corticosteroid (high dose), long-acting β_2-agonist and oral corticosteroids




Anti-inflammatory (management)
Corticosteroids
Leukotriene inhibitors
Anti-IgE antibodies
Mast cell stabilizers
Fluticasone (inhalation), beclomethasone (inhalation), budesonide (inhalation) and prednisone (oral)
Inhibiting IgE production, enhancing β2 adrenoreceptors, inhibiting synthesis of PG & LT, reducing formation of cytokines and eosinophils
Adverse effects: oropharyngeal candidiasis and hoarsness
Lipoxygenase inhibitors: zileuton
Receptor antagonist: montelukast and zafirlukast
Omalizumab
Cromolyn sodium and nedocromil