DRUGS ACTING ON THE RESPIRATORY SYSTEM

The respiratory system includes the upper airway passages, the nasal cavities, the pharynx and the trachea as well as the bronchi and bronchioles.

Bronchial asthma: characterized by increased responsiveness of the trachea and bronchi to various stimuli and by widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy

Impairment of airflow in bronchial asthma is caused by three bronchial abnormalities.

I. Contraction of airway smooth muscles.
II. Thickening of bronchial mucosa from oedema and cellular infiltration.
III. Reduction in the airway lumen due to thick, viscid plugs of excessive mucus.

Drugs used in the treatment of bronchial asthma can be grouped into three main categories:

1. **Bronchodilators**

a. β-- Adrenergic agonists which include:

Non-selective β--agonists e.g. **adrenaline**

Selective β_2--agonists e.g. **salbutamol** metaproterenol, salmeterol, formaterol

b. **Methylxanthines**; theophylline derivatives

c. Muscarinic receptor **(parasympathetic)** antagonists e.g. **Ipratropium bromide** trade name **Atrovent**

2. **Mast cell stabilizers**, e.g. cromolyn sodium, nedocromil, **ketotifen**

3. **Antiinflammatory agents**: corticosteroids

β-- ADRENERGIC AGONISTS (SYMPATHOMIMETIC AGENTS)

Mechanism of Action, β –Agonists:

a. cause the Relaxation of smooth muscles
b. inhibit the release of an inflammatory mediator or broncho-constricting substances from mast cells.

Mechanism of Action Non-selective beta-agonists:

a. Cause more cardiac stimulation, they should be reserved for special situations.
b. Epinephrine: very effective, rapidly acting bronchodilator especially preferable for the relief of acute attacks of bronchial asthma.
c. Administered by inhalation or subcutaneously.

Side effects include arrhythmia and worsening of angina pectoris, increase blood pressure, tremors etc

Contraindications: - hypertension, arrhythmia,

Ephedrine: compared to epinephrine, it has a longer duration of action but a more pronounced central effect and lower potency. It can be given orally. The drug is currently infrequently used because of side effects.

Selective β_2- selective agonists: Largely replaced non–selective. β_2-agonists, are:

- effective after inhaled or oral administration.
- have got a longer duration of action.
- They are the most widely used sympathomimetics.
- Commonly used drugs both by oral and inhalation are **Salbutamol,** terbutaline, metaproterenol, pirbuterol and bitolterol.
- Salmeterol and formoterol are the new generations, long-acting β_2- selective agonists (with a duration of action of 12 hrs or more).
- These drugs appear to interact with inhaled corticosteroids to improve asthma control.
- Delivery of adrenoreceptor agonists through inhalation results in the greatest local effect on airway smooth muscle with the least systemic toxicity.

Side effects: Tremors, anxiety, insomnia, tachycardia, headache,

hypertension.

Contraindications: Sympathomimetics are contraindicated in patients with known hypersensitivity to the drugs

Precautions: They should be used cautiously in patients with hypertension, cardiac dysfunction, hyperthyroidism, glaucoma, diabetes, and pregnancy.

2. **METHYLXANTHINES**

The three important methylxanthines are **theophylline, theobromine, and caffeine**. natural xanthines, agents theophylline is most selective in its smooth muscle effect, while caffeine has the most marked central effect.

3. MUSCARINIC RECEPTOR ANTAGONISTS

Mechanism of Action: Muscarinic antagonists competitively **inhibit the effect of acetylcholine at muscarinic receptors** – hence blocking the contraction of airway smooth muscle and the increase in the secretion of mucus that occurs in response to vagal activity e.g atropine sulfate

4. **ANTI-INFLAMMATORY AGENTS: CORTICOSTEROIDS**

Used both for treatment and prophylactic purposes

Mechanism of action: They are presumed to act by their broad anti-inflammatory efficacy mediated in part by inhibition of the production of inflammatory mediators.

Effects on airway

- decreases bronchial reactivity.
- increases airway calibre.
- decreases the frequency of asthma exacerbation and severity of symptoms.

The corticosteroids commonly used are hydrocortisone, prednisolone, beclomethasone, triamcinolone, etc.

The drugs can be taken by inhalation as aerosol, oral, or an IV administration

Because of severe adverse effects when given chronically, oral and parenteral corticosteroids are reserved for patient who needs urgent treatment and those who have not improved with

Bronchodilator:

- Aerosol treatment is the most effective way to decrease the systemic adverse effect of corticosteroid therapy.
- Abrupt discontinuation should be discouraged because of the fear of adrenal insufficiency.
- Doses should be decreased after improvement.
- Regular or controlled therapy is better maintained with aerosol corticosteroids.

Clinical uses in bronchial asthma:

Urgent treatment of severe asthma not improved with bronchodilator:

use **IV, inhalation** or oral.

Nocturnal asthma prevention: oral or inhalation

Chronic asthma: Regular aerosol corticosteroids

Side effects:

- Suppression of the hypothalamic-pituitary-adrenal axis
- Osteoporosis
- Sodium retention and hypertension
- Cataract
- Impairment of growth in children
- Susceptibility to infection like oral candidiasis, tuberculosis

5. **MAST CELL STABILIZERS** e.g **cromolyn sodium**

Mechanism of action: Stabilize the mast cells so that release of histamine and other mediators is inhibited. It has no role once the mediator is released and is used for casual **prophylaxis**.

Clinical uses

- Exercise and antigen-induced asthma
- Occupational asthma

TREATMENT OF STATUS ASTHMATICS

Status asthmatics Very severe and sustained attack of asthma which fails to respond to treatment with usual measures

Management includes:

- Administration of oxygen.

- Frequent or continuous administration of aerosolized ß2 agonists like salbutamol.
- Systemic corticosteroids like methylprednisolone or hydrocortisone IV.
- Aminophylline IV infusion.
- Iv fluid to avoid dehydration.
- Antibiotics in the presence of evidence of infection.

ANTI-TUSSIVES: Cough is a protective reflex, which serves the purpose of expelling sputum and other irritant materials from the respiratory airway.

Types of cough:

a- Useful productive cough: Effectively expels secretions and exudates.

b- Useless cough: Non-productive chronic cough &cough Due to smoking.

Two Types of Antitussives:

1. **Central anti-tussive:** Suppress the medullary cough centre and may be divided into two groups:
   - Opoid antitussive e.g. codeine, hydrocodeine, etc
   - Non-opoid antitussives e.g. dextromethorphan
2. Peripheral antitussives: Decrease the input of stimuli from the cough receptor in the respiratory passage. e.g: Demulcents,

liquorice lozenges, honey

Local anaesthetics e.g. lidocaine aerosol

Demulcents coat the irritated pharyngeal mucosa and exert a mild analgesic effect locally.

Codeine is a narcotic relatively less addicting drug and central antitussive agent and its main side effects are dryness of mouth, constipation and dependence.

Dextromethorphan: is an opioid synthetic antitussive, essentially free of analgesic and addictive properties and the main side effects are respiratory depression.

Expectorant is a drug that aids in removing thick tenacious mucus from respiratory passages, e.g. Ipecac alkaloid, sodium citrate, saline expectorant, potassium salts **Mucolytics** are agents that liquefy mucus and facilitate expectoration, e.g.**acetylcysteine**.

Decongestants: are drugs that reduce congestion of nasal passages, which in turn open clogged nasal passages and enhance drainages of the sinuses. e.g phenylephrine, oxymetazoline etc.

Mechanism of Action: Mucus membrane decongestants are **α1** agonists, which produce localized vasoconstriction on the small blood vessels of the nasal membrane. Reduce congestion in nasal passages.

Clinical uses: Used in congestion associated with rhinitis, hay fever, allergic rhinitis and the common cold.

Drugs can be administered nasally or orally for a longer duration of action.

Classification:

1. Short-acting decongestants administered topically – phenylephrine, phenylpropanolamine
2. Long-acting decongestants administered orally - ephedrine, pseudoephedrine, naphazoline
3. Long-acting topical decongestants: Xylometazoline, oxymetazoline