UNIT-1

Anti-Asthmatic Drugs

Asthma is the reversible obstruction of large and small airways. Bronchial asthma is characterized by hyperresponsiveness of tracheo-bronchial smoth muscle to a variety of stimuli resulting in narrowing of air tubes, often accompanied by increased secretions, mucosal oedema and mucous plugging.

Asthma is categorised into three types:

1) Extrinsic Asthma (Allergic):

The mast cells in the respiratory tract show hyper-responsiveness due to antigen-antibody reaction, resulting in allergic asthma.

2) Intrinsic Asthma (Idiosyncratic):

Cordination between sympathetic and para-sympathetic autonomic nervous system gets disturbed, resulting in neurological imbalance.

Causative agents for extrinsic asthma can be dust, pollen or animal dander and for intrinsic asthma- recurrent respiratory infections, exercise, emotional upset.

3) Mixed Asthma

This type of asthma can be caused by intrinsic factors, extrinsic factors or both.

Symptoms of asthma may be:

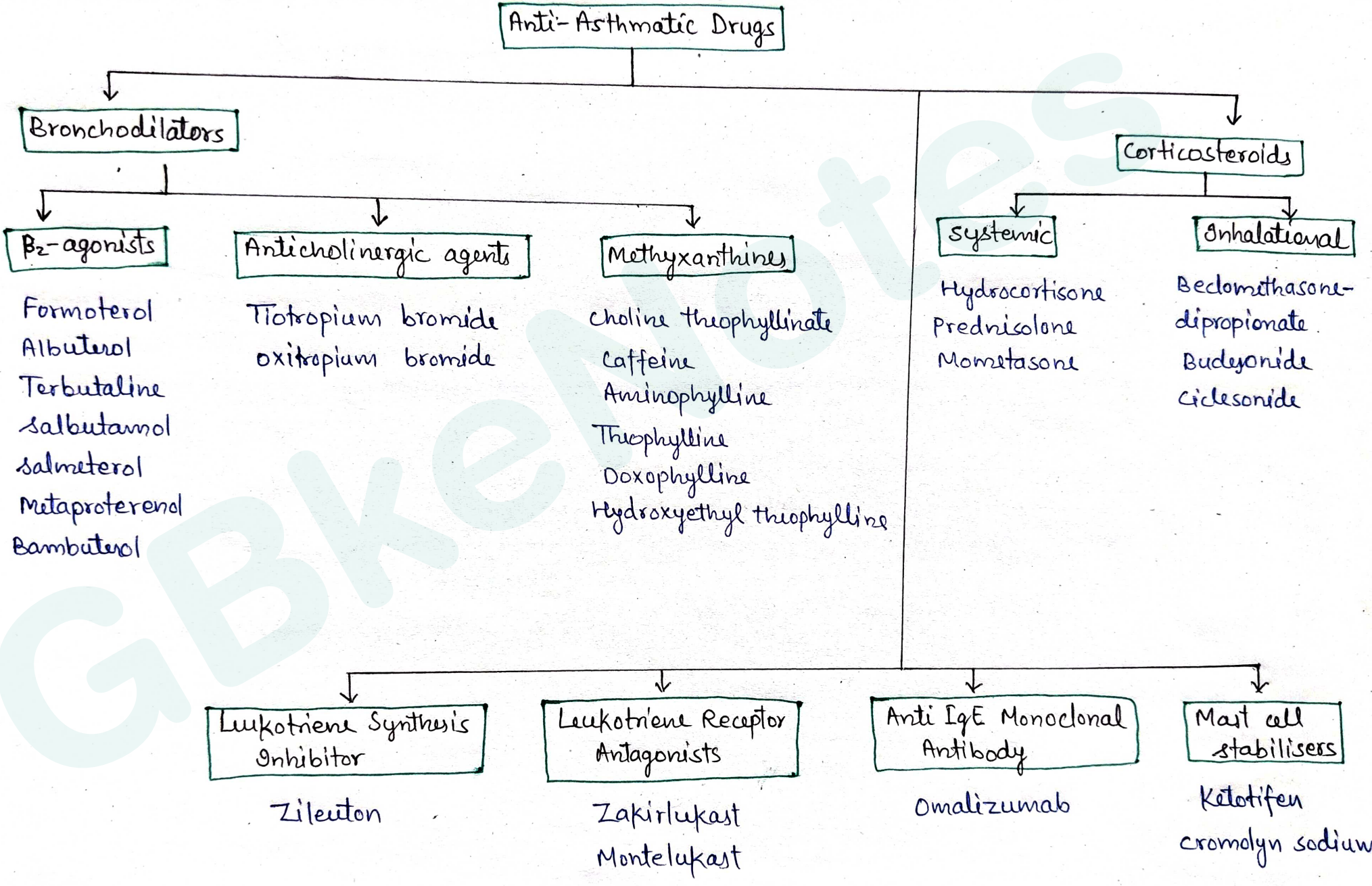
- dyspnoea (shortning of breath, breathing difficulty)
- wheezing (whistle sound during respiration)
- cough

* Status Asthmaticus → This means long-lasting asthma attacks.

Classification of anti-asthmatic drugs

β_2-Agonists (Sympathomimetics)

Sympathomimetics are potent bronchodilators and extensively used in relieving bronchospasm (contractraction in airways).



Activation of β_2-receptors cause relaxation of bronchial smooth muscles. Sympathomimetic agents include salbutamol, adrenaline, terbutaline, and salmeterol.

Further classification of Sympathomimetics

1) short- acting β_2-agonists

These are the fastest acting bronchodilators which reach the peak concentration within 10 minutes and produce their action lasting 6 hours. e.g. salbutamol, terbutline.

2) Long-Acting β_2-agonists

They have slower onset of action but their action remains for 12 hours. e.g. salmeterol, formoterol, bambuterol.

Mechanism of Action

The β_2-agonists cause smooth muscle relaxation of the airways.

β_2-adrenoreceptor agonists are coupled with Gs protein which causes activation of enzyme adenylcyclase thereby resulting in production of cyclic Adenosine Monophosphate (cAMP). This results in relaxing the bronchial smooth muscles.

Major pharmacological actions of β_2-agonists:

1) Increased mucociliary clearance
2) Mediators released from mast cells and monocytes are inhibited.
3) Decreased Ca^{2+} ions release from intracellular stores as well as Ca^{2+} ions entry into smooth muscles cells results in bronchodilation.

Therapeutic uses:

1) Used in the treatment of acute bronchospasm.
2) treatment of asthma
3) COPD, emphysema, chronic bronchitis.

Major Drugs

1) **Salbutamol**

It is a highly selective β_2-adrenergic stimulant having a prominent bronchodilator action. It is given by oral as well as inhalation route by nebuliser. Palpitation, restlessness, nervousness are the common side effects.

2) **Terbutaline**

It is similar to salbutamol and is given by oral, parenteral as well as inhalation.

3) **Salmeterol**

It is a newer long-acting selective α_2-adrenergic agonist with slow onset of action, used for maintenance therapy in asthma, nocturnal asthma and asthma induced by exercise.

Anti-Cholinergic Agents

Anti-cholinergics relax bronchial smooth muscles but response is slower than sympathomimetics. It is more effective in chronic obstructive pulmonary disease (COPD).

Major Drugs

1) **Ipratropium**

It produces bronchodilating effect in asthmatic patients. It is an M_3 receptor antagonist.

MoA

→ When cholinergic neurotransmitter bind with M_3 receptor, it cause activation of phospholipase-C(PLC) because M_3 is a GPCR.

→ Now, due to activation of PLC, it activates IP3 + DAG which further increases the concentration of Ca^{2+} & CAM, which increases the activation of MLCK (Myosin Light Chain Kinase) which cause bronchoconstriction.

Now, when anticholinergics are introduced, they block the M_3 receptor which stop further reaction and cause bronchodilation.

2) **Tiotropium**

Long-acting (upto 24 hrs.)

Methylxanthines

These drugs are used in treating bronchial asthma.

MoA

Normally, cAMP is responsible for bronchodilation. When introduced these drugs block PDE (phosphodiesterase) enzymes which are responsible for degradation of cAMP.

Due to inhibition of PDE, the concentration of cAMP increases which causes the bronchodilation.

Major Drugs

Theophylline

Also known as dimethylxanthine. The drug is used in therapy for respiratory diseases, such as COPD and asthma.

Half life → 7-12 hours (adults)
3-5 hours (children)

Therapeutic uses

→ acute attack of bronchial asthma
→ COPD
→ Infant apnoea

Leukotriene-Synthesis Inhibitors

Leukotrienes are powerful bronchoconstrictor and are long-lasting. Leukotrienes also increase bronchial mucus secretion, increase vascular permeability.

All the leukotrienes are derived from 5-lipoxygenase pathway of arachidonic acid and are synthesized by inflammatory cells in the airways, e.g., eosinophils, mast cells, basophils and macrophases.

The drugs, montelukast and zafirlukast are available for the treatment of asthmatic patients.

Mast Cell Stabilisers

They are highly effective in preventing asthma attacks. They inhibit degranulation of mast cells. These agents do not produce bronchodilation and also do not antagonise the constrictor effect of histamine. Therefore, they are not beneficial in acute attacks of asthma and are used for prophylaxis only.

Corticosteroids

These agents show anti-inflammatory effects. This can ease symptoms of inflammatory conditions like asthma.

MoA

They bind with glucocorticoid receptors and act by inhibiting inflammatory cells which are involved in this inflammatory disease process.

Anti-IgE Antibody

IgE antibodies are found on specific B-lymphocytes in the human body.

MoA

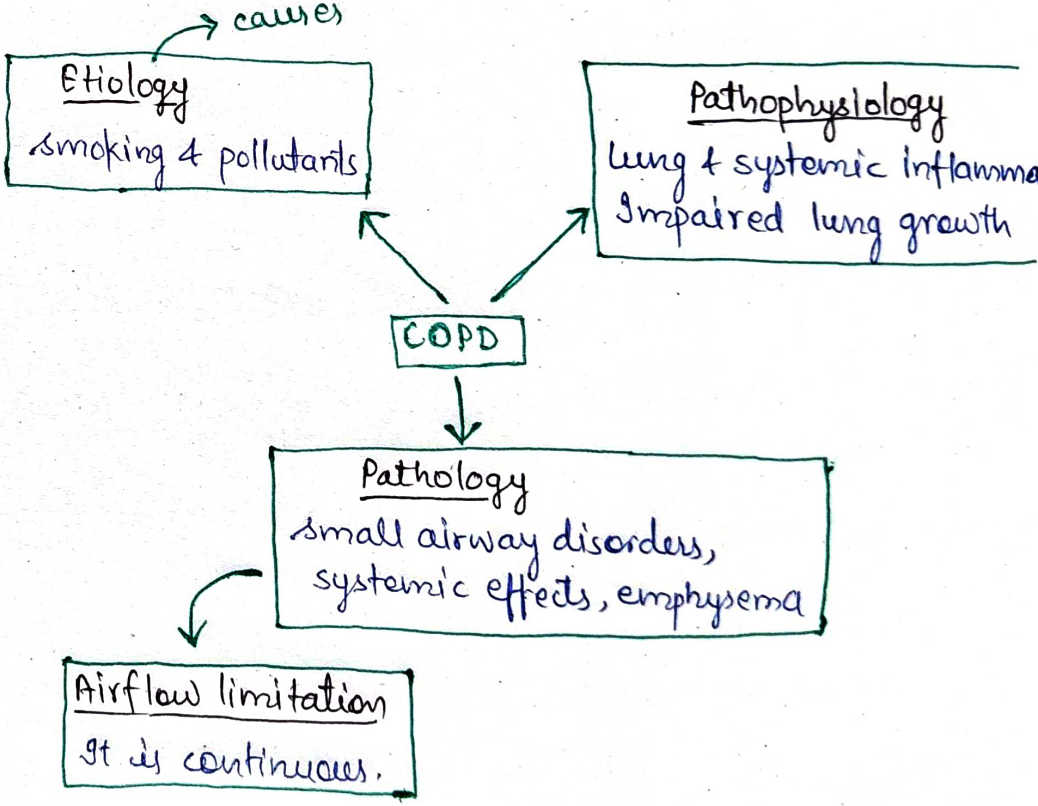
This drug (Omalizumab) bind with free IgE which further cannot bind with mast cells. Due to this, mast cells doesn't activate and not release any other inflammatory mediators, resulting bronchodilation.

Route of administration is subcutaneous.

Drugs used in COPD

Chronic Obstructive Pulmonary Disease is primarily an inflammatory disease of smaller airways of lungs. It is caused by long time exposure and chronic inhalation of harmful, poisonous and toxic substances like smoke from chemical industry, tobacco, noxious particles, gases, etc.

→ It is characterised by irreversible obstruction of airflow and mucous hypersecretion



COPD Therapy

COPD therapy currently in use comprises of:

1) Inhaled bronchodilators
2) Inhaled glucocorticoids
3) Oxygen inhalation
4) Prophylactic antibiotics
5) Prevention of dehydration
6) Physiotherapy, pulmonary rehabilitation, education,

* **Emphysema** → It is a medical condition in which the alveoli of the lungs are destroyed.

Methods of COPD Management

There is no cure for COPD, but treatment can help ease symptoms, lowers the chances of implications and improves quality of life.

→ Guidance for termination of smoking
→ Oxygen therapy
→ Ventilation support
→ exercise therapy, patient counselling,
→ Surgical treatment.

Drugs used

1) **Bronchodilators**

These are those drugs which dilates the bronchi muscles and helps to open the airways of the lungs to make breathing easier.

Mostly used bronchodilators are

a) B_2- agonists
b) Anti-muscaranic drugs

2) **Corticosteroids**

→ These are used as anti-inflammatory agents/drugs.
→ These are used in asthmatic condition produced by COPD.
→ Mostly long-acting bronchodilators are combined with inhaled glucocorticosteroids.

3) **Anti-biotics and Antivirals**

These are given in case of respiratory infections due to pathogens.

Expectorants & Antitussives

Expectorants or mucokinetics

→ These are oral drugs that help in sputum (↗ बलग़म) removal from the respiratory tract either by increasing the bronchial secretion or by reducing its viscosity (increasing the fluidity) to facilitate its removal by coughing.

→ Expectorants basically help in dissolving thick mucus and providing relief in respiratory difficulties.

Classification on the basis of MoA

1) Sedative Expectorants

These expectorants stimulate the gastric reflexes to produce their effects.
e.g. ammonium chloride, potassium iodide.

2) Stimulant Expectorants

These stimulate directly or indirectly the secretory cells of respiratory tract. However, more fluid is secreted in the respiratory tract by these drugs and sputum is diluted.
e.g. eucalyptus, lemon

MoA

Expectorants act by two mechanisms:

1) Reflex stimulation

The drugs produce an irritation of the GIT which causes release and thinning of respiratory trad secretions. e.g. Guaifenesin.

2) Direct stimulation

The secretory glands in the respiratory tract are directly stimulated to cause release of secretions.

Therapeutic Uses

1) Expectorants → used to relieve cough.
side effects are GI upset, nausea, vomitting.

2) Mucolytics → used in cystic fibrosis and bronchiopulmonary disease.
side effects may be:
i) CNS - Dizziness, drowsiness
ii) GI - Nausea, stomatitis, hepatotoxicity, and unpleasant odour.
iii) Respiratory - Bronchospasm, rhinorrhoea.

Major drugs

1) Potassium Iodide - (0.2 - 0.3 gm)
2) Sodium and potassium citrate - (0.3 - 1 mg)
3) Bromhexine → It is an alkaloidal derivative of vasicine obtained from Adhatoda vasica (Vasaka).
4) Acetylcysteine → helps in reducing viscosity of mucus.

Anti-tussives

Anti-tussives are the drugs that suppress cough or act in the CNS to reduce the activity of cough centre.

They control the release of cough/sputum rather than removing it.

Classification

1) Centrally Acting Anti-tussives
   suppress CNS
   a) Opiods/ Narcotics : codeine, Morphine
   b) Non-opiods : Dextromethorphan, Oxeladin

2) Peripherally acting antitussives
   act outside the CNS to inhibit cough,
   a) antihistamines : Promethazine
   b) Hydrating agents : Steam and aerosols

Major Drugs

1) Opioids : The opioids suppress the cough reflex by acting directly on CNS (medulla).
   a) Codeine
   It is an opium alkaloid, less potent than morphine but is more selective for cough centre
   → last for 6 hours
   → dose - 10-30 mg (adults)
   children - 2.5-5 mg (2-6 years)
   5-10mg (6-12 years)

   therapeutic uses
   - cough and cold
   - mild to moderate pain
   - diarrhoea
   - Narcolepsy
   - Irritable bowel syndrome.

b) Pholcodeine

similar in effect as codeine but acts for a longer duration of 12 hours.

dose → 10-15 mg

2) Non-Opiods

These are the agents used in reducing cough without causing any hallcinations. since these are not opiods, they do not have analgesic properties.

a) Dextromethorphan (DXM or DM)

A synthetic central NMDA (N-methyl D-aspartate) receptor antagonist.

→ dose - 10-20 mg

b) Noscapine

It is an benzylisoquinoline alkaloid. It depresses cough but has no narcotic, analgesic properties.

→ dose - 15-30 mg

c) Chlophedianol

It is centrally acting antitusive with slow onset and longer duration of action.

dose - 20-40 mg

Nasal Decongestants

Nasal decongestants are drugs that are used to relieve nasal congestion in the upper respiratory tract.

congestion → blockage

MoA.

Decongestants act by stimulating α_1- adrenergic receptor which causes vasoconstriction of nasal vasculature thereby resulting in reduced inflammation (swelling), mucus formation and decongestion of nasal mucosa.

Classification

1) Adrenal- Releasing Agents

Ephedrine, Pseudoephedrine, Phenylpropanolamine

2) Alpha-Adrenergic Receptor Agonists.

Naphazoline, Oxymetazoline, Phenylephrine

Adverse effects

(i) CVS: hypertension, palpitations, tachycardia

palpitations → irregular heart beat

(ii) CNS: headache, nervousness, restlessness

Major Drugs

1) Ephedrine

It acts as a bronchodilator and decongestant which provides temperary relief in chest tightness, shortness of breath.

It helps in reducing swelling and constricting blood vessels of nasal passages and widening the airways of lung to provide normal breathing.

2) Phenylephrine

It also shrink the blood vessels in the nasal passages, widening it.

Respiratory stimulants

→ These are drugs which stimulate respiration and can have resuscitative effect (property to restore consciousness) in coma or fainting.

→ At low dose, they stimulate respiration but margin of safety is narrow; at a high dose, patient may get convulsions while still in coma.

↳ दौरा पड़ना

Analeptics can be used in following conditions:

1) For providing relief to premature infant suffering from apnoea.

* Apnoea is is a medical condition in which somebody stops breathing for a short time while asleep.

2) Shortness of breath in case of drowning.

3) In case of hypnotic drug poisoning

Major Drugs

1) Naxolone → It helps in stimulating respiration after the overdose of narcotics.

2) Doxapram → It stimulates respiration centre in CNS which in turn stimulates respiratio by carotid and aortic body chemoreceptors and also helps in raising the decreased BP.

3) Prethcamide → MoA similar to Doxapram

4) Yohimbine → It is a respiratory stimulant which acts as an antidote for xylazine overdose.