Module 01(a)
Pharmacology of Drugs Acting on Respiratory System

- ANTI -ASTHMATIC DRUGS.
- DRUGS USED IN THE MANAGEMENT OF COPD.
- EXPECTORANTS AND ANTITUSSIVES.
- NASAL DECONGESTANTS.
- RESPIRATORY STIMULANTS

1. Anti -asthmatic drugs.

Asthma is most common respiratory tract infection. It is the reversible obstruction of large and small airways. Bronchial asthma is characterized by hyperresponsiveness of tracheo-bronchial smooth muscle to a variety of stimuli, resulting in narrowing of air tubes, often accompanied by increased secretions, mucosal edema and mucus plugging.

1. Inflammation
2. Hyper reactivity
3. Bronchospasm

T**ypes of Bronchial Asthma**

1. Extrinsic Asthma: (allergic) It is mostly episodic, less prone to status asthmaticus

Atopic (immediate due to IgE antibody).

Nonatopic delayed for some hours, associated with production of precipitating antibodies

2. Intrinsic Asthma

It tends to be perennial, status asthmaticus is more common. Associated with COPD.

Classification

Sympathomimetics :*Short Acting****: Salbutamol, Terbutaline***

*Long Acting****: Formeterol, Salmetrol, Bambuterol***

Mechanism of Action

1. Beta-2 adrenoceptor agonist, when administered binds beta 2 receptors

- ✓ Stimulation of adenylate cyclase
- ✓ Increase cAMP
- ✓ Bronchodilation and decreased muscular tone

Methylxanthine: Aminophylline, Theophylline

Mechanism of Action

1. Inhibit Phosphodiestrase Enzyme (which catalyzes breakdown of cAMP).

- ✓ Increase cAMP
- ✓ Dephosphorylation of MLC

- ✓ Bronchodilation

2. Increased intracellular calcium

3. Blockade of adenosine receptors: Decrease contractility of bronchiolar smooth muscles

Anticholinergics: Ipratropium, Oxytropiu, Tiotropium

Mechanism of Action

- ✓ Blockade of muscarinic receptors present in bronchi and bronchioles
- ✓ Decrease mucus viscosity
- ✓ Increase mucociliary clearance

Leukotriene Receptor Antagonists

- ✓ Montelukast – oral
- ✓ Zafirlukast – (Cingular) oral administration for control of asthma

Leukotrines are products of arachidonic acid metabolism. They are released at the site of inflammation producing bronchoconstriction having contributory effect to inflammation and bronchoconstriction.

Mechanism of Action

Montelukast and Zafirlukast are competitive antagonists.

- ✓ Inhibits cysteinlyl leukotriene Cys LT_1 receptor relieving bronchospasm and bronchoconstriction.
- ✓ Inhibit physiologic actions of LTC_4, LTD_4, LTE_4
- ✓ One drug blocks synthesis of 5 lipooxygenase and is hepatotoxic **Zileuton.** Half like is 2.5 hours

Drug Interactions

Zafirleukast has drug interaction with warfarin sodium, leading to increased prothrombin time, thus dose has to be monitored. Monteleukast is commonly used. ***Mast Cell Stabilizers***

- Na chromoglycate inhalation
- Nedocromil
- Ketotifen- (5HT action) oral

Nedocromil and Ketotifen are not bronchodilators, not having direct effect. They are ineffective once antigen antibody reaction takes place.

Mechanism of Action

1. Inhibit transmembrane influx of Ca provoked by antigen antibody interaction on the surface of mast cells. This is prophylactic use and have to be given before antigen enters.
2. Stabilize mast cells membrane and inhibit release of chemical mediators
3. Depress exaggerated neuronal reflexes triggered by stimulation of irritant receptors
4. Depress axonal reflexes which release inflammatory neuropeptides.
5. Inhibit release of cytokines from T-CELLS

Corticosteroids

- Hydrocortisone **I/V**
- Prednisolone **oral**
- Betamethosone

- Beclomethasone **inhalation**
- Budesonide
- **Flucitasone** having affinity for glucocorticoids receptors in airways

Mechanism of Action

- Anti inflammatory action
- Decrease mucosal oedema, mucus secretion and reduce capillary permeability
- Stabilize mast cells
- Block immune response, decrease antibody formation
- Antagonise histaminergic and cholinergic responses
- Enhance beta-2 adrenoceptor responsiveness to agonists (Catecholamines)

Ciclesonide

Prodrug, when absorbed drug is acted upon by esterases in bronchial epithelial cells, less amount of drug absorbed gets bound to glucocorticoid receptors, bones, skin, eyes, and there are less chances of osteoporosis and cutaneous thinning.

It has some role in people predisposed to cataract and osteoporosis.

Status Asthmaticus Status asthmaticus is an acute exacerbation of asthma that remains unresponsive to initial treatment with bronchodilators. It is a life threatening form of asthma, because it can lead to respiratory failure and cardiac arrest. Status Asthmaticus requires immediate

treatment (corticosteroids are essential as immediate treatment). Air trapping strains on breathing muscle which are fatigue and exhausted. Status asthmaticus is frequently associated with metabolic acidosis, and acidosis reduces the effectiveness of beta agonist.

1. I/V $NaHCo_3$ added if pH is below 7.5 in patient with refractory status asthmaticus, but there is risk of hypercapnia, in children.
2. decrease in PCO_2 level corrected with nasal/Face mask oxygen (Helium)
3. Continuous nebulization of albuterol for the first few hrs
4. Switched to intermittent albuterol very 02 hrs. I/V
5. corticosteroids, inhaled ipratropium every 06 hrs

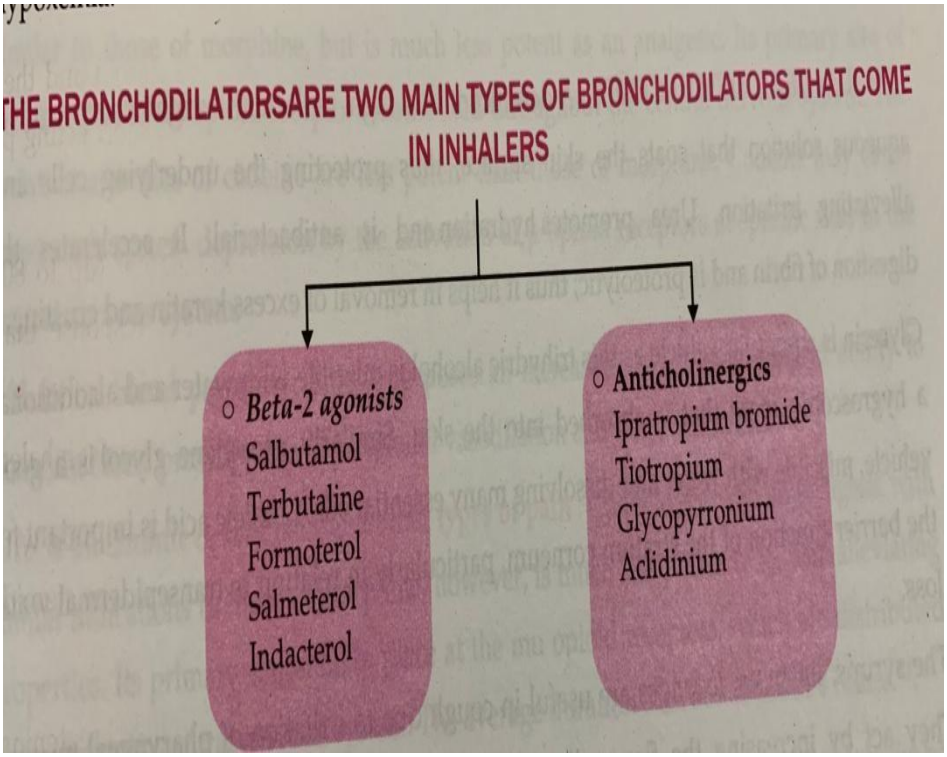
Monoclonal Antibodies: Omalizumab

They bind to IgE antibodies present on mast cells. If administered I/V or subcutaneously, humanized monoclonal antibodies decrease levels of IgE antibodies, decreasing tendency of severe asthma, in both phases (immediate/delayed).

2. Drugs used in the management of COPD.

In chronic obstructive pulmonary disease (COPD), airflow is obstructed during expiration. This increases the work of breathing and causes dyspnoea. In contrast to asthma, the airflow obstruction is not reversible and usually progresses over time. There are several mechanisms of airflow obstruction in COPD. Chronic bronchitis results in hypersecretion of mucus which fills and obstructs the airway lumen.

Beta 2 agonists and anticholinergic drugs are used in COPD



ANTITUSSIVES

The cough reflex occurs when receptors in the airway send impulses to the brainstem and cause contraction of the muscles needed to cough. -The type of cough produced depends on the location of the stimulated receptors and whether or not mucus is brought up with the cough (productive or non productive).

1.Pharyngeal/ demulcents Lozenges, cough linctuses containing syrup, glycerine,

2.Expectorants (Mucokinetics)

a.bronchial secretion enhncers Sodium or Potassium citrate, Potassium iodide, Guaiphenesin, balsum of Tolu,vasaka, Ammonium chloride.

b.Mucolytics: Bromhexine, Ambroxol, Acetyl cysteine, Carbocisteine

3. Antitussives (Cough centre suppressants)

(a) Opioids Codeine, Pholcodeine.

(b) Nonopioids Noscapine, Dextromethorphan, Chlophedianol.

(c) Antihistamines Chlorpheniramine, Diphenhydramine, Promethazine.

4. Adjuvant antitussives

DEMULCENTS AND EXPECTORANTS

Pharyngeal demulcents sooth the throat and reduce afferent impulses from the inflamed/ irritated pharyngeal mucosa, thus provide symptomatic relief in dry cough arising from throat.

Expectorants (Mucokinetics) are drugs believed to increase bronchial secretion or reduce its viscosity, facilitating its removal by coughing.

Mucolytics

Bromhexine A derivative of the alkaloid vasicine obtained from Adhatoda vasica (Vasaka), is a potent mucolytic and mucokinetic, capable of inducing thin copious bronchial secretion.

ANTITUSSIVES Antitussives act centrally by suppressing the neurons located in the brainstem's cough center. Antitussives are often used with tracheitis, tracheobronchitis. When coughing worsens the inflammation that is already present and stimulates more coughing, it needs to be suppressed.

DEMULCENTS AND EXPECTORANTS

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- irritated pharyngeal mucosa, thus provide symptomatic relief in dry cough arising from throat.
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- Sodium and potassium citrate are considered to increase bronchial secretion by salt action.
- Potassium iodide is secreted by bronchial glands and can irritate the airway mucosa. Prolonged use can affect thyroid function and produce iodism. It is rarely used now.
- Guaiphenesin, vasaka, tolu balsum are plant products which are supposed to enhance bronchial secretion and mucociliary function while being secreted by tracheobronchial glands.

Opioids

Codeine: An opium alkaloid similar to but less potent than morphine

It is more selective for cough centre and is treated as the standard antitussive; suppresses cough for about 6 hours.

Non Opioids

Noscapine (Narcotine) An opium alkaloid of the benzoisoquinoline series. It depresses cough but has no narcotic, analgesic or dependence inducing properties

Mucolytics

Bromhexine A derivative of the alkaloid Hysosicine obtained from (Vasaka), is a potent mucolytic and mucokinetic, capable of inducing thin copious bronchial secretion. It depolymerises mucopolvsaccharides directly as well as by liberating lysosomal enzymesnetwork of fibres in tenacious sputum is broken. It is particularly useful if mucus plugs are present.

Side effects are rhinorrhoea and lacrimation, gastric irritation, hypersensitivity.

NASAL DECONGESTANTS

These are a agonists which on topical application as dilute solution (0.05-0.1%) produce local vasoconstriction. The imidazoline compoundsnaphazoline, xylometazoline and oxymetazoline are relatively selective a2 agonist (like clonidine).

They have a longer duration of action (12 hours) than ephedrine. After-congestion is claimed to be less than that with ephedrine or phenylephrine. They may cause initial stinging sensation (specially naphazoline). Regular use of these agents for long periods should be avoided because mucosal

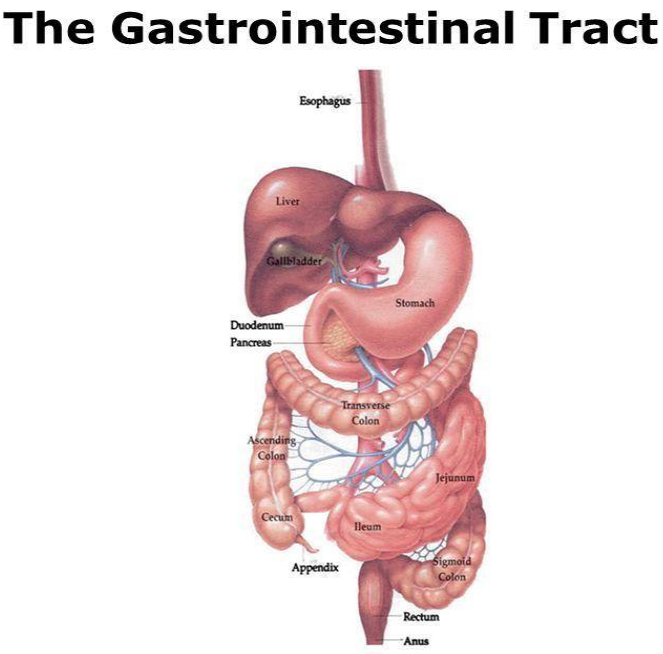
ciliary function is impaired: atrophic rhinitis and anosmia can occur due to persistent vasoconstriction. They can be absorbed from the nose and produce systemic effects-CNS depression and rise in BP. These drugs should be used cautiously in hypertensives and in those receiving MAO inhibitors.

Pseudophedrine A stereoisomer of ephedrine; causes vasoconstriction, especially in mucosae and skin, but has fewer CNS and cardiac effect and is a poor bronchodilator (little 2 agonistic activity). It has been used orally as a decongestant of upper respiratory tract, nose and Eustachian tubes.

Learning Material PHARMACOLOGY-III, BP602.SEM-6TH Module 01(b)

Pharmacology of Drugs Acting on the Gastrointestinal Tract

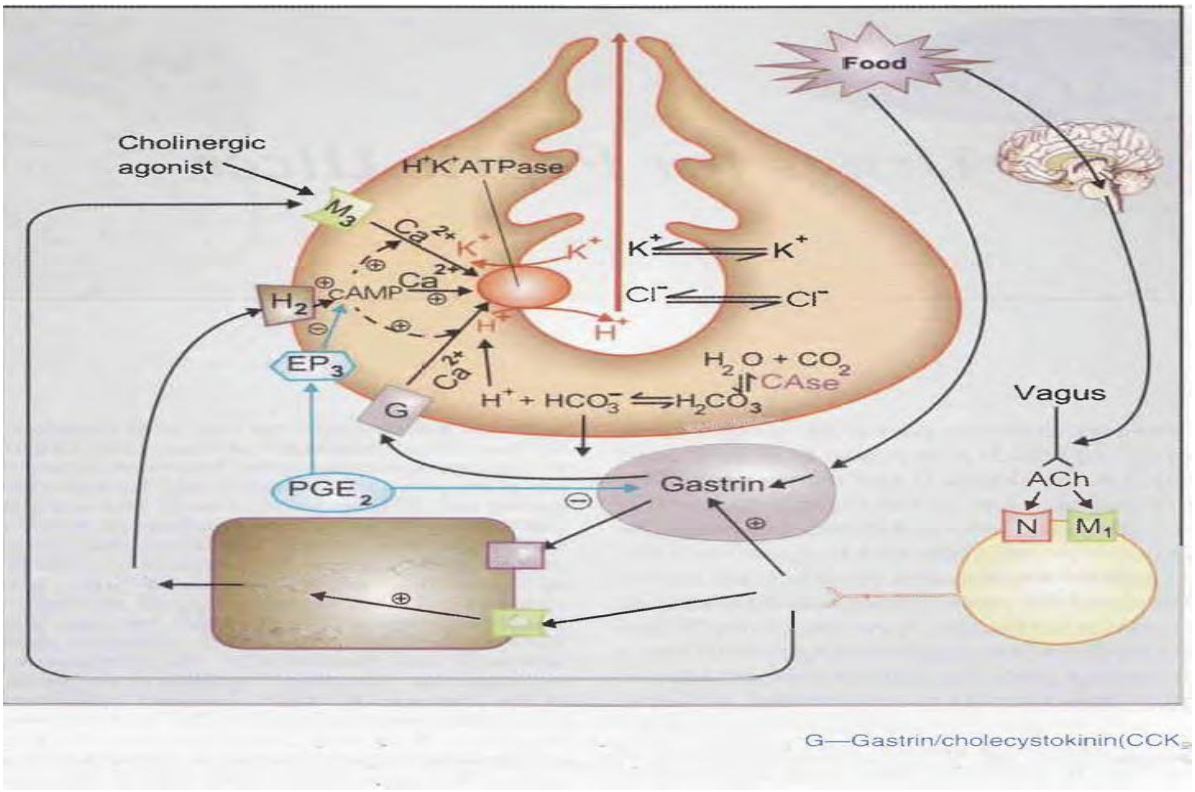
- Antiulcer agents.
- Drugs for constipation and diarrhoea.
- Appetite stimulants and suppressants.
- Digestants and carminatives.
- Emetics and anti-emetics.



1. Anti Ulcer Drugs

Peptic ulcer occurs in that part of the gastrointestinal tract (g.i.t.) which is exposed to gastric acid and pepsin, i.e. the stomach and duodenum. The etiology of peptic ulcer is not clearly known. It results probably due to an imbalance between the aggressive (acid, pepsin, bile and H. pylori) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide, innate resistance of the mucosal cells) factors.

Regulation of gastric acid secretion



1 . Reduction of gastric acid secretion

(a) H2 antihistamines: Cimetidine, Ranitidine, Famotidine, Roxatidine

(b) Proton pump inhibitors: Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole, Esomeprazole

(c) Anticholinergics: Pirenzepine, Propantheline, Oxyphenonium

(d) Prostaglandin analogue: Misoprostol

2. Neutralization of gastric acid (Antacids

(a) Systemic: Sodium bicarbonate, Sodium citrate

(b) Nonsystemic: Magnesium hydroxide, Mag. trisilicate, Aluminiumhydroxide gel, Calcium carbonate

3 . Ulcer protectives: Sucralfate, , bismuth subcitrate (CBS)

4Anti-H. pylori drugs: Amoxicillin,Clarithromycin, Metronidazole, Tinidazole, Tetracyclin

H2 ANTAGONISTS

These are the first class of highly effective drugs for acid-peptic disease. Four H2 antagonists cimetidine, ranitidine, famotidine and roxatidine are available in India; many others are marketed elsewhere. Their interaction with Hz receptors has been found to be competitive in case of cimetidine, ranitidine and roxatidine, but competitive noncompetitive in case of famotidine.

- H2 blockade Cimetidine and all other Hz antagonists block histamine-induced gastric secretion
- Gastric secretion The only significant in vivo action of Hz blockers is marked inhibition of gastric secretion

PROTON PUMP INHIBITORS (PPis)

Omeprazole It is the prototype member of substituted benzimidazoles which inhibit the final common step in gastric acid secretion and have overtaken H2 blockers for acid-peptic disorders. The only significant pharmacological action of omeprazole is dose dependent suppression of gastric acid secretion; without anticholinergic or H2 blocking action. It is a

powerful inhibitor of gastric acid: can totally abolish HCl secretion, both resting as well as that stimulated by food or any of the secretagogues, without much effect on pepsin, intrinsic factor, juice volume and gastric motility.

Zollinger-EIIison syndrome It is a gastric hypersecretory state due to a rare tumour secreting gastrin. H2 blockers in high doses control hyperacidity and symptoms in many patients, but relief is often incomplete and side effects frequent. PPis are the drugs of choice.

ANTICHOLINERGICS

A tropinic drugs reduce the volume of gastric juice without raising its pH unless there is food in stomach to dilute the secreted acid. Stimulated gastric secretion is less completely inhibited. Effective doses (for ulcer healing) of nonselective antimuscarinics (atropine, propantheline, oxyphenonium) invariably produce intolerable side effects.

PROSTAGLANDIN ANALOGUE

PGE2 and PGI2 are produced in the gastric mucosa and appear to serve a protective role by inhibiting acid secretion and promoting mucus secretion. In addition, PGs inhibit gastrin production, increase mucosal blood flow and probably have an ill-defined "cytoprotective" action.

ANTI-HELICOBACTER PYLORI DRUGS

H. pylori is a gram negative bacillus uniquely adapted to survival in the hostile environment of stomach. It attaches to the surface epithelium beneath the mucus, has high urease activity produces ammonia which maintains a neutral microenvironment around the bacteria, and promotes back diffusion of H + ions

Drugs for constipation and diarrhea

Anti-diarrhoeal agents

- Diarrhoea: frequent passage of liquid or semisolid stools is called diarrhoea.
- Causes: enteric infection, food toxins, malnutrition, inflammation, drugs like reserpine, prostaglandins, metoclopramide, domperidome, cholinergic drugs, quinidine and purgatives.
- Dysentery: abdominal pain and passage of bloody stools and mucous due to infection or inflammation.

Management of diarrhea

1. Non-specific therapy:
   a) Oral and parenteral rehydration
   b) Anti-motility and anti-secretory agents:
      i) Opioids: codeine, diphenoxylate, loperaminde
      ii) α-adrenergic receptor agonist: clonidine
      iii) Octreotide.
2. Specific therapy: Antimicrobial agents
3. Antispasmodics: Atropine & oxyphenonium (antrenyl)
4. Adsorbants: Kaolin, pectin and chalk, bismuth subsalicylate

Non-specific therapy

Oral rehydration solution (ORS): 2.6 g NaCl, 1.5 g KCl, 2.9 g sodium citrate, 13.5 g glucose dissolved in 1 liter of water.

Super ORS: (boiled rice powder used instead of glucose)-also decreases frequency of diarrhoea along with rehydration.

Antimotility and antisecretory agents

- Codeine: opium alkaloid, reduces GI motility, also have antisecretory effects.

- Diphenoxylate: structurally related to pethidine, combined with small doses with atropine, side effects are constipation, paralytic ileus, banned in many countries.
- Loperamide: opiate analogue and importantant antidiarroeal than morphine.
- Interact with μ-receptor in the gut, reduces GI motility and increase anal sphincter tone.

Drugs for constipation

LAXATIVES

(Aperients, Purgatives, Cathartics)

These are drugs that promote evacuation of bowels. A distinction is sometimes made according to the intensity of action.

(a) Laxative or aperient: milder action, elimination of soft but formed stools.

(b) Purgative or cathartic: stronger action resulting in more fluid evacuation.

Many drugs in low doses act as laxative and in larger doses as purgative.

CLASSI FICATION

1. Bulk forming:Dietary fibre: Bran, Psyllium (Plantago) Ispaghula, Methylcellulose

2. Stool softener :Docusates (DOSS), Liquid paraffin

3. Stimulant purgatives (a) Diphenylmethanes, Phenolphthalein, Bisacodyt Sodiumpicosulfate

(b) Anthraquinones (Emodins) Senna, Cascara sagrada

(c) 5-HT4 agonist Tegaserod (d) Fixed oil, Castor oil

4. Osmotic purgatives Magnesium salts: sulfate, hydroxide , Sodium salts: sulfate, phosphate Sod. pot. Tartrate Lactulose

M ECHANISM OF ACTION

All purgatives increase the water content of faeces by:

(a) A hydrophilic or osmotic action, retaining water and electrolytes in the intestinal lumen-increase volume of colonic content and make it easily propelled.

(b) Acting on intestinal mucosa, decrease net absorption of water and electrolyte; intestinal transit is enhanced indirectly by the fluid bulk.

(c) Increasing propulsive activity as primary action-allowing less time for absorption of salt and water as a secondary effect.

Laxatives modify the fluid dynamics of the mucosal cell and may cause fluid accumulation in gut lumen by one or more of following mechanisms:

(a) Inhibiting Na+K+ATPase of villous cellsimpairing electrolyte and water absorption.

(b) Stimulating adenylyl cyclase in crypt cellsincreasing water and electrolyte secretion.

(c) Enhancing PG synthesis in mucosa which increases secretion.

(d) Structural injury to the absorbing intestinal mucosal cells

Appetite Stimulants and suppressants

Appetite Stimulants **:** May help promote appetite and weight gain in elderly with unintentional weight loss or poor P.O. intake Drugs should not be considered as first-line treatment Even if successful in inducing weight gain, long-term effects on quality of life are unknown The following appetite stimulants Dronabionol (Marinol) Mirtazapine (Remeron) Megestrol Acetate (Megace) Metoclopraminde (Reglan) Cyproheptadine (Periactin) Anabolic Steroids (Oxandrolone; Oxandrin) Ghrelin Recombinant Human Growth Hormone (Serostim) Testosterone

Dronabinol Drug name: Marinol. A tetrahydrocannabinol Use: Weight gain in cancer-related anorexia patients Side Effects: Lightheadedness Sleepiness Blurred vision Can't think clearly Dizziness Sedation Fatigue Hallucinations

Mirtazapine • Drug Name: Remeron. A serotonergic norepinephrine uptake inhibitor used to treat depression in older adults • Use: • Appetite stimulant for cachexia and treats underlying depression in older adults • Side Effects: • Sedation • Dry mouth • Constipation • Fatigue • Weight gain • Dizziness • Other studies show causes hepatotoxicity, bone marrow suppression, restless legs syndrome, arthralgia, and coagulopathy

Megestrol Acetate Drug Name: Megace. A progestational agent Use: Weight gain in Anorexia, AIDS, Cachexia, and Cancer patients Side Effects: Edema Constipation & delirium Diarrhea Flatulence Rash Hypertension Fluid retention Glucose intolerance Nausea Insomnia • Gastrointestinal upset • Impotence •

Metoclopramide Drug Name: Reglan. Prokinetic agent Use: Relieves nausea-induced anorexia (Hoffman, 2002) Side Effects: Dystonia & Parkinsonian symptoms in elderly Many drug interactions such as B12, D3, Lipitor, Fish oils, Aspirin, Crestor Can cause GI obstruction,

perforation or hemorrhage Causes GI obstruction, perforation or hemorrhage; pheochromocytoma; history of seizures or concomitant use of other agents likely to increase movement disorder reactions May increase risk of seizures and movement disorders (extrapyramidal reactions)

Cyproheptadine Drug name: Periactin. Antihistaminic and serotonin-blocking drug Use: Weight gain in children with anorexia nervosa & cancer Elderly in nursing homes Side Effects: Blurred vision Dry mouth Urinary retention Constipation Tachycardia and delirium in older patients **Anabolic Steroids** Drug Name: Oxandrolone (Oxandrin), Ornithine What it is: Synthetic anabolic steroids Use: Treats wasting in AIDS & Cachexia in Cancer Side Effects Carpal tunnel syndrome Headache Arthralgias Myalgias, & gynecomastia Risk of prostate hyperplasia, fluid retention, and transaminase elevations

Ghrelin • Drug Name: None .Growth hormone produced from the fundus of the stomach increases food intake by stimulating nitric oxide in the hypothalamus • Use: Appetite stimulant in oncology patients and older adults

Recombinant Human Growth Hormone Drug Name: Serostim Anabolic Growth Hormone Use: Increase lean body mass in HIV patients with wasting or cachexia Side Effects: Carpal Tunnel Syndrome Headache Arthralgia Myalgias Gynecomastia Edema Arthralgia Impaired fasting glucose

Testosterone • Drug name: None • A steroid hormone from the androgen group and is found in mammals, reptiles, birds, and other vertebrates • Use: Treat cachexia and weight loss in HIV Patients • Side Effects: • Higher hematocrit • Leg edema • Prostate events (exacerbation of prostate cancer) • Lower HDL levels • Possible metabolic syndrome in men

Appetite suppressant

An **anorectic** or **anorexic** is a drug which reduces appetite, resulting in lower food consumption, leading to weight loss. By contrast, an appetite stimulant is referred to as orexigenic. The term is (from the Greek *ἀν-* (an-) = "without" and (órexis) = "appetite"), and such drugs are also known as **anorexigenic**, **anorexiant**, or **appetite suppressant**.

Amfepramone, Bupropion and naltrexone (combination), Dexfenfluramine, Fenfluramine,Mazindol, Phentermine, Sibutramine, Topiramate, Benfluorex, Butenolide, Diethylpropion, Phenmetrazine' Phentermine, Phenylpropanolamine, Sibutramine, Lorcaserin

Sibutramine is a monoamine reuptake inhibitor (MRI) that, in humans, reduces the reuptake of norepinephrine (by ~73%), serotonin (by ~54%), and dopamine (by ~16%),[21] thereby increasing the levels of these substances in synaptic clefts and helping enhance satiety; the serotonergic action, in particular, is thought to influence appetite

Phentermine (phenyl-tertiary-butylamine), sold under the brand name **Ionamin** among others, is a medication used together with diet and exercise to treat obesity. The primary mechanism of phentermine's action in treating obesity is the reduction of hunger perception, which is a cognitive process mediated primarily through several nuclei within the hypothalamus

Orlistat is a drug designed to treat obesity. It is marketed as a prescription drug under the trade name **Xenical.** Orlistat is the saturated derivative of lipstatin, a potent natural inhibitor of pancreatic lipases isolated from the bacterium *Streptomyces toxytricini*. However, due to its relative simplicity and stability, orlistat was chosen over lipstatin for development as an anti- obesity drug.

CARMINATIVES

These are drugs which promote the expulsion of gases from the g.i.t. and give a feeling of warmth and comfort the epigastrium.

Commonly used drugs are:

Sodium bicarbonate 0.6--1.5 g

Oil Peppermint 0.06--0.1 ml

Tincture Cardamom Co. 1-2 ml

Oil of dil 0.06--0.2 ml

Tincture ginger 0.6--1 ml

Sodium bicarbonate reacts with gastric HCl, which rapidly distends stomach, relaxes

The others are condiments and spices, contain volatile oils, which by their mild irritant action and flavour and increase g.i.t. motility. They give a feeling of warmth and comfort in the abdomen.

DIGESTANTS

These arc substances intended to promote digestion of food. A number of proteolytic, amylolytic and lipolytic enzvmes are marketed in combination formulations and more vigorously promoted for dyspeptic symptoms, and appetite stimulants or health tonics.. Their routine use in tonics and appetite improving mixtures is irrational.

Hydrochloric acid It may be used in achlorhydria;10 ml of dilute HCl (10%) should be further diluted to 100-200 ml with water and sipped with a straw (to prevent contact with teeth) during meals.

Pepsin May be used along with HCl due to atrophic gastritis, gastric carcinoma, pernicious anaemia, etc.

Papain It is a proteolytic enzyme obtained from raw papaya. Its efficacy after oral ingestion is doubtful

Pancreatin It is a mixture of pancreatic enzymes obtained from hog and pig pancreas. It contains amylase, trypsin and lipase; indicated in chronic pancreatitis and other exocrine pancreatic deficiency states. Fat and nitrogen content of stools may be reduced and diarrhoea/ steatorrhoea may be prevented. It has to be used as enteric coated tablets or capsules to protect the enzymes from being themselves digested in stomach by pepsin. Nausea, diarrhoea and hypen:ricaernia are the occasional side effects.

Diastase and Takadiastase These are amylolytic enzymes obtained from the fungus Aspergillus. They have been used in pancreatic insufficiency.

EMETICS AND ANTI-EMETICS

Emesis Vomiting occurs due to stimulation of the emetic (vomiting) centre situated in the medulla oblongata. Multiple pathways can elicit vomitingThe chemoreceptor trigger zone (CTZ) located in the area postrema and the nucleus tractus solitarius (NTS) are the most important relay areas for afferent impulses arising in the g.i.t, throat and other viscera. The CTZ is also accessible to blood-borne drugs, mediators, hormones, toxins, etc. because it is unprotected by the blood-brain barrier.

EMETICS

These are drugs used to evoke vomiting.

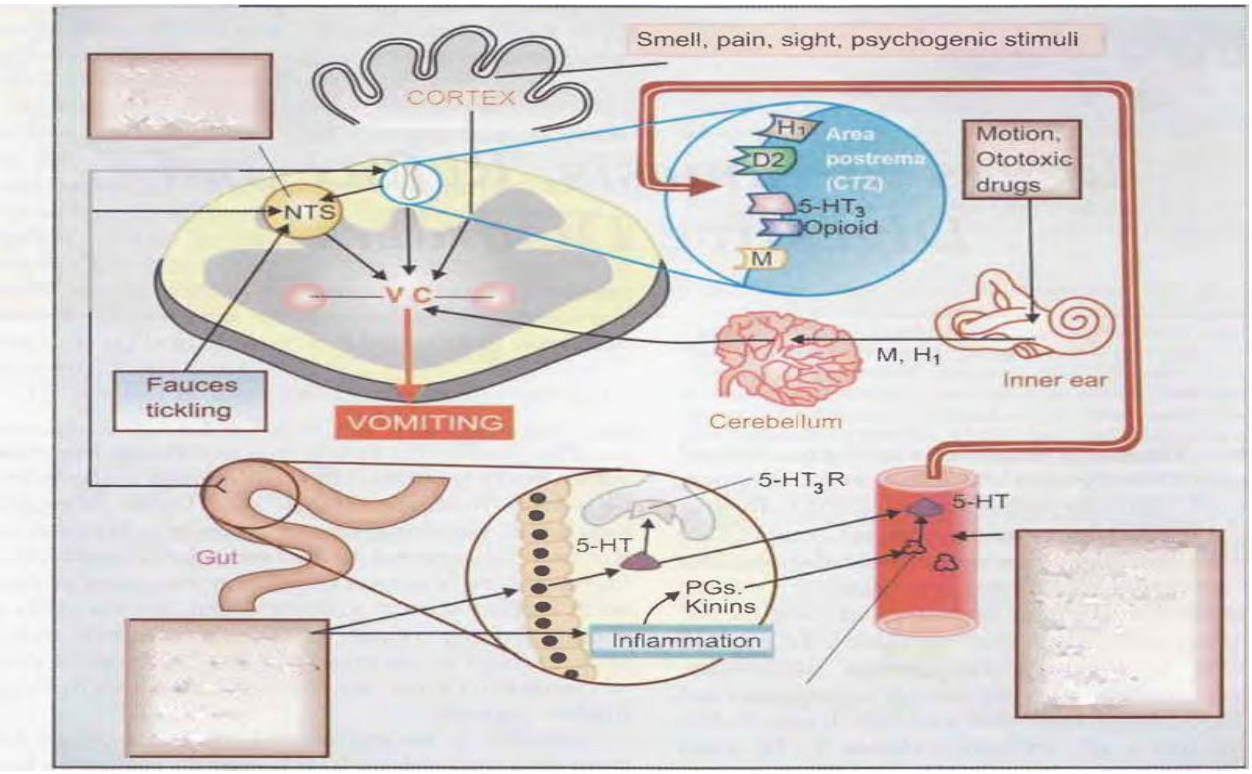
1 . Act on CTZ : Apomorphine

2 . Act reflexly and on CTZ : Ipecacuanha

Vomiting needs to be induced only when an undesirable substance (poison) has been ingested. Powdered mustard suspension or strong salts solution may be used in emergency. They act reflexly by irritating the stomach.

Apomorphine It is a semisynthetic derivative of morphine; acts as a dopaminergic agonist on the CTZ. Injected i.m./s.c. in a dose of 6 mg, it promptly (within 5 min) induces vomiting.

Ipecacuanha The dried root of Cephne/is ipecncunnha contains emetine and is used as surup ipecac (15-30 ml in adults, 10-15 ml in children, 5 ml in infants) for inducing vomiting



ANTI EMETICS

These are drugs used to prevent or suppress vomiting.

CLASSIFICATION

1. Anticholinergics Hyoscine, Dicyclomine
2. H1 antihistaminics: Promethazine, Diphenhydramine, Dimenhydrinate, Doxylamine, Cyclizine, Meclozine, Cinnarizine.
3. Neuroleptics Chlorpromazine,Prochlorperazine, Haloperidol, etc
4. Prokinetic drugs Metoclopramide, Domperidone, Cisapride, Mosapride, Tegaserod
5. 5-HT3 antagonists Ondansetron, Granisetron
6. Adjuvant antiemetics Dexamethasone, Benzodiazepines, Cannabinoids.

ANTICHOLINERGICS

Hyoscine (0.2-0.4 mg oral, i.m.) is the most effective drug for motion sickness. However, it is a brief duration of action; produces sedation and other anticholinergic side effects; suitable

for short brisk journies. It acts probably by blocking conduction of nerve impulses across cholinergic link in the pathway leading from the vestibular apparatus to the vomiting centre and is not effective in vomiting of other etiologies.

H1 ANTI HISTAMINICS

Some antihistaminics are antiemetic. They are useful mainly in motion sickness and to a lesser extent in morning sickness, postoperative and some other forms of vomiting. Their antiemetic effect appears to be based on anticholinergic, antihistaminic and sedative properties. Promethazine, diphenhydramine, dimenhydrinate These drugs afford protection of motion sickness by their central anticholinergic action they block the extrapyramidal side effects
of metoclopramide while supplementing its antiemetic action. Their combination is used in chemotherapy induced vomiting.

NEUROLEPTICS

These are potent antiemetics; act by blocking D2 receptors in the CTZ; antagonize apomorphine induced vomiting and have additional antimuscarinic as well as H1 antihistaminic property.

PROKINETIC DRUGS

These are drugs which promote gastrointestinal transit and speed gastric emptying by enhancing coordinated propulsive motility.

Metoclopramide

Metoclopramide is chemically related to procainamide, but has no pharmacological similarity with it. Introduced in early 1970s as a 'gastric hurrying' agent, it is now a widely used antiemetic. Metoclopramide blocks D2 receptors and has an opposite effect fasting gastric emptying and

5-HT3 ANTAGONISTS

Ondansetron It is the prototype of a new class of antiemetic drugs developed to control cancer chemotherapy I radiotherapy induced vomiting, and later found to be highly effective in postoperative nausea and vomiting as well. It blocks the depolarizing action of 5-HT through 5-HT3 receptors on vagal afferents in the g.i.t. as well as in NTS and CTZ.

ADJUVANT ANTIEMETICS

Cannabinoids Tetrahydrocannabinol (D. THC) is the active principle of the hallucinogen Cannabis indica. It possesses antiemetic activity against moderately emetogenic chemotherapy. It probably acts at higher centres or at vomiting centre itself by activating CB1 subtype of cannabinoid receptors. The disorienting and other central effects of THC limit its clinical utility.