

Pharmacology-III

UNIT-I

Pharmacology of Emetics and anti-emetics Drugs

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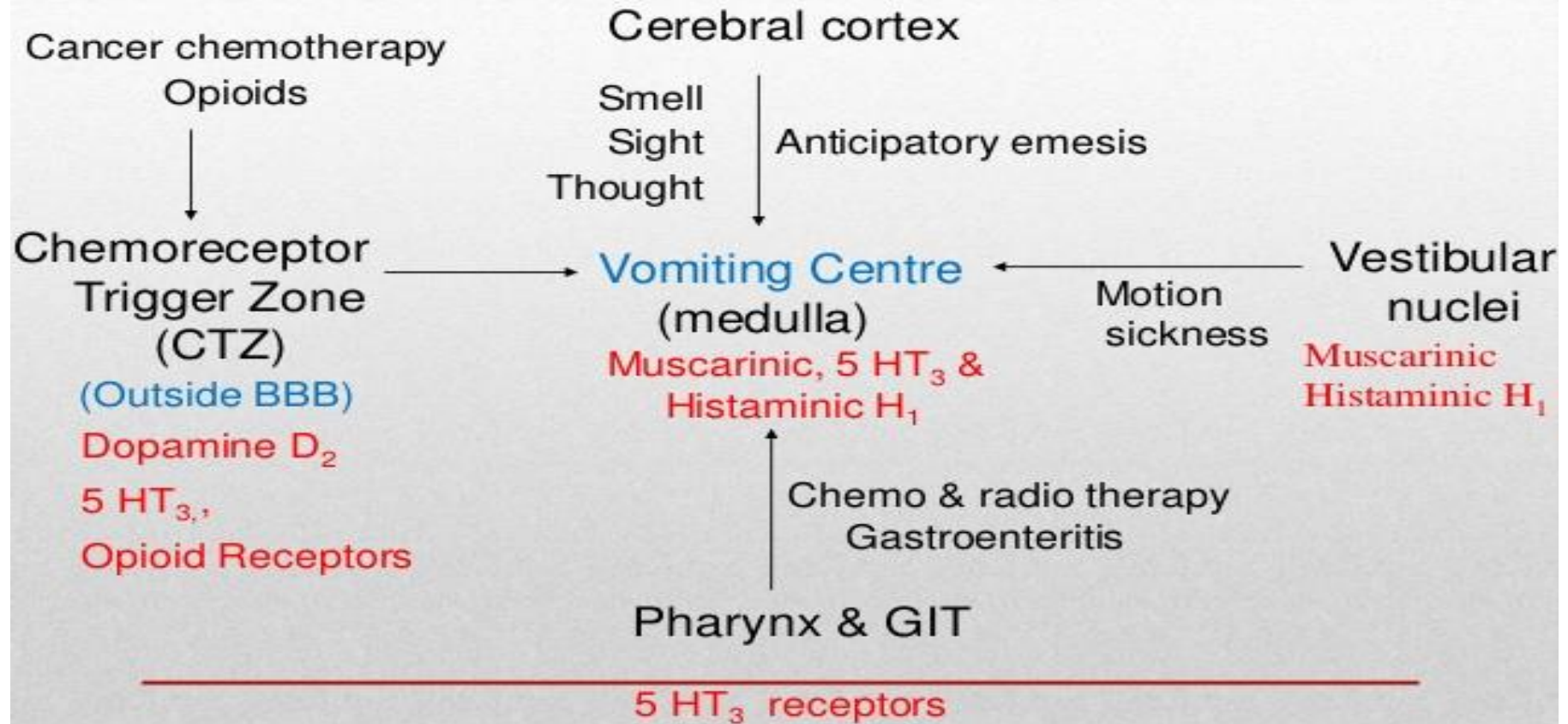
School of Pharmacy and Life Sciences



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Pathophysiology of Emesis



MANAGEMENT :

- Treatment of cause : relief of pain, treatment of GI inflammation
- Symptomatic treatment : Antiemetic drug
- Supportive treatment : Rehydration, electrolytes balance

1. Anticholinergics

Hyoscine, Dicyclomine

2. H1 antihistaminics

Promethazine, Diphenhydramine, Dimenhydrinate, Doxylamine, Meclozine (Meclizine), Cinnarizine.

3. Neuroleptics

Chlorpromazine, (D2 blockers) Triflupromazine, Prochlorperazine, Haloperidol, etc.

4. Prokinetic drugs

Metoclopramide, Domperidone, Cisapride, Mosapride, Itopride

5. 5-HT3 antagonists

Ondansetron, Granisetron, Palonosetron, Ramosetron

6. Adjuvant Dexamethasone, antiemetics Benzodiazepines, Dronabinol, Nabilone

ANTICHOLINERGIC DRUGS :

Hyoscine, Dicyclomine

- **Muscarinic cholinergic receptor:**
- **Motion sickness is mediated by ACh receptor**
- **Hyoscine can cross BBB , antiemetic action due to blocking of central ACh receptor**
- **Peripheral reduction of salivary & gastric secretion**
- **And spasmodic activity , prevention of relaxation of sphincters**
- **Side effects : ABC, sedation**
- **Dose 0.25 mg orally**

H1 anti-histaminic drugs : Promethazine, Diphenhydramine, Dimenhydrinate, Doxylamine, Meclozine (Meclizine), Cinnarizine

- H1 antagonist effectively block : histamine induced contraction of intestinal muscle (useful of antiemetic)
- Useful in : motion sickness, morning sickness, Post operative vomiting
- Action is based on: anticholinergic , antihistaminic , weak-antidopaminergic , sedative propertive
- Promethazine : give protection from motion sickness
- Shouldn't drive after taking this medication

Neuroleptics : Chlorpromazine, (D2 blockers) Triflupromazine, Prochlorperazine, Haloperidol, etc

- **D2 blockers / antipsychotic drugs**
- **Action: block D2 receptor at CTZ**
- **Antagonize action of Apomorphine**
- **Additional properties: antimuscarinic + H2 histaminic**
- **Uses : drug induced and post operative- nausea & vomiting**
- **Disease induced: gastroenteritis, liver disease, migraine**
- **Chemotherapy induced : radiation sickness, morning sickness**
- **Side effects : sedation, hypotension, acute muscle dystoxia,**
- **Dose : antiemetic dose is lower than the antipsychotic drugs**

Prokinetics drugs : Metoclopramide, Domperidone, Cisapride, Mosapride, Itopride

- Promote GI Transit
- Speed up gastric emptying
- Increase motility

Metoclopramide :

a substituted benzamide, is chemically related to procainamide

Metoclopramide has more prominent effect on upper g.i.t.;
increases gastric peristalsis while relaxing the pylorus and the first part of
duodenum → speeds gastric emptying,

- Metoclopramide acts through both dopaminergic and serotonergic receptors
- The central antidopaminergic (D2) action of metoclopramide on CTZ is clearly responsible for its antiemetic property

Domperidone

- It is a D2 receptor antagonist, chemically related to haloperidol
- pharmacologically related to metoclopramide
- The antiemetic action is exerted mainly through CTZ which is not protected by blood-brain barrier
- Domperidone is absorbed orally, but bioavailability is only ~15% due to first pass metabolism
- completely biotransformed and metabolites are excreted in urine
- Dry mouth, loose stools, headache, rashes, galactorrhoea are generally mild

5-HT₃ antagonists : Ondansetron, Granisetron, Palonosetron, Ramosetron

- **5HT₃ receptor blockade on intestinal vagal afferents**
- **Central 5HT₃ receptor blockade in the vomiting centre & CTZ**
- **High first pass metabolism**
- **Excreted by liver**
- **Uses : post radiation nausea & vomiting**

Ondansetron

- It is the prototype of a distinct class of antiemetic drugs
- developed to control cancer chemotherapy/radiotherapy induced vomiting
- Oral bioavailability of ondansetron is 60–70% due to first pass metabolism
- eliminated in urine and faeces, mostly as metabolites
- headache and dizziness. Mild constipation and abdominal discomfort occur in few patients
- Hypotension, bradycardia, chest pain and allergic reactions are reported, especially after i.v. injection.