Emetics & Anti emetics

B.Pharmacy : III Year II Semester

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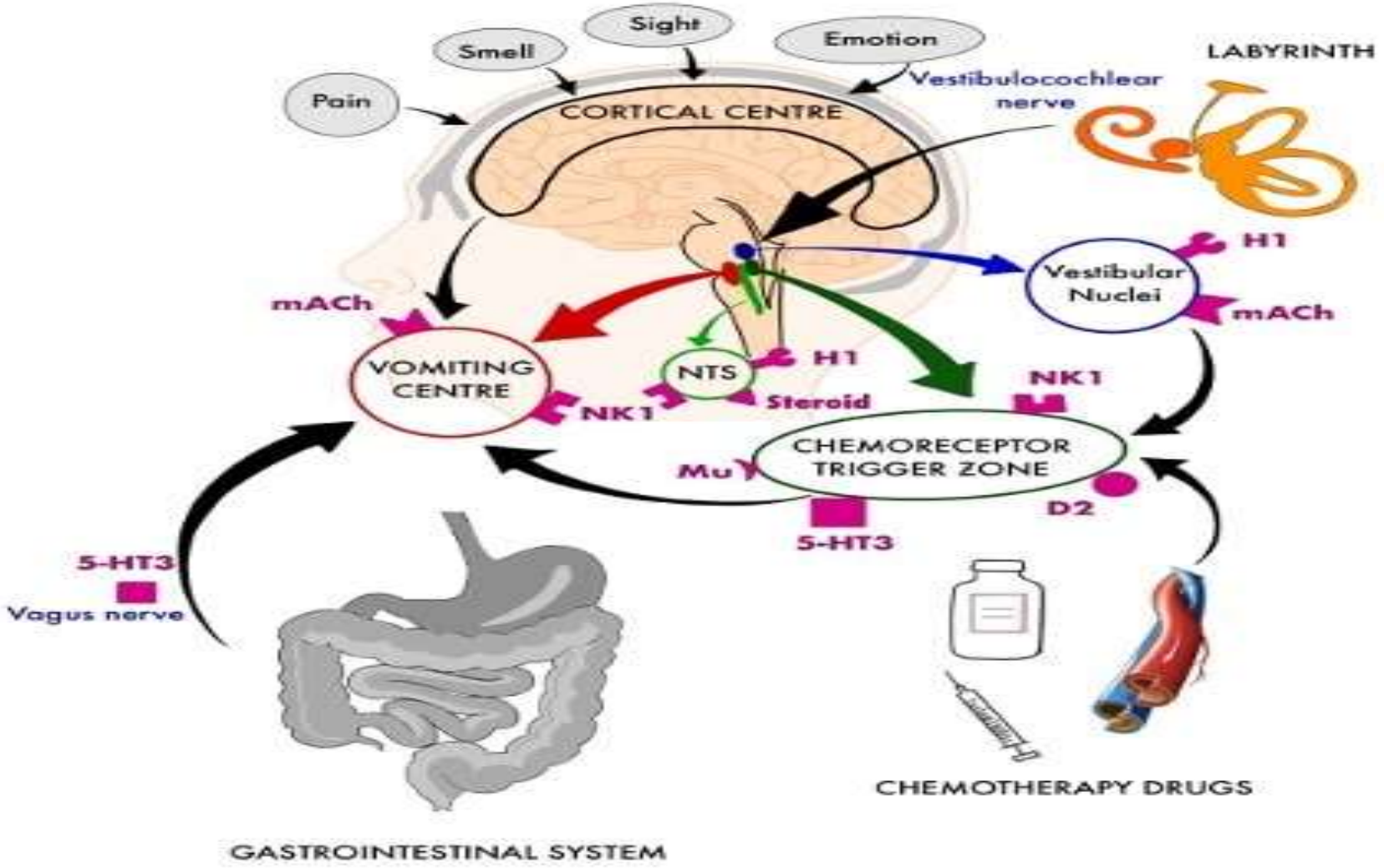
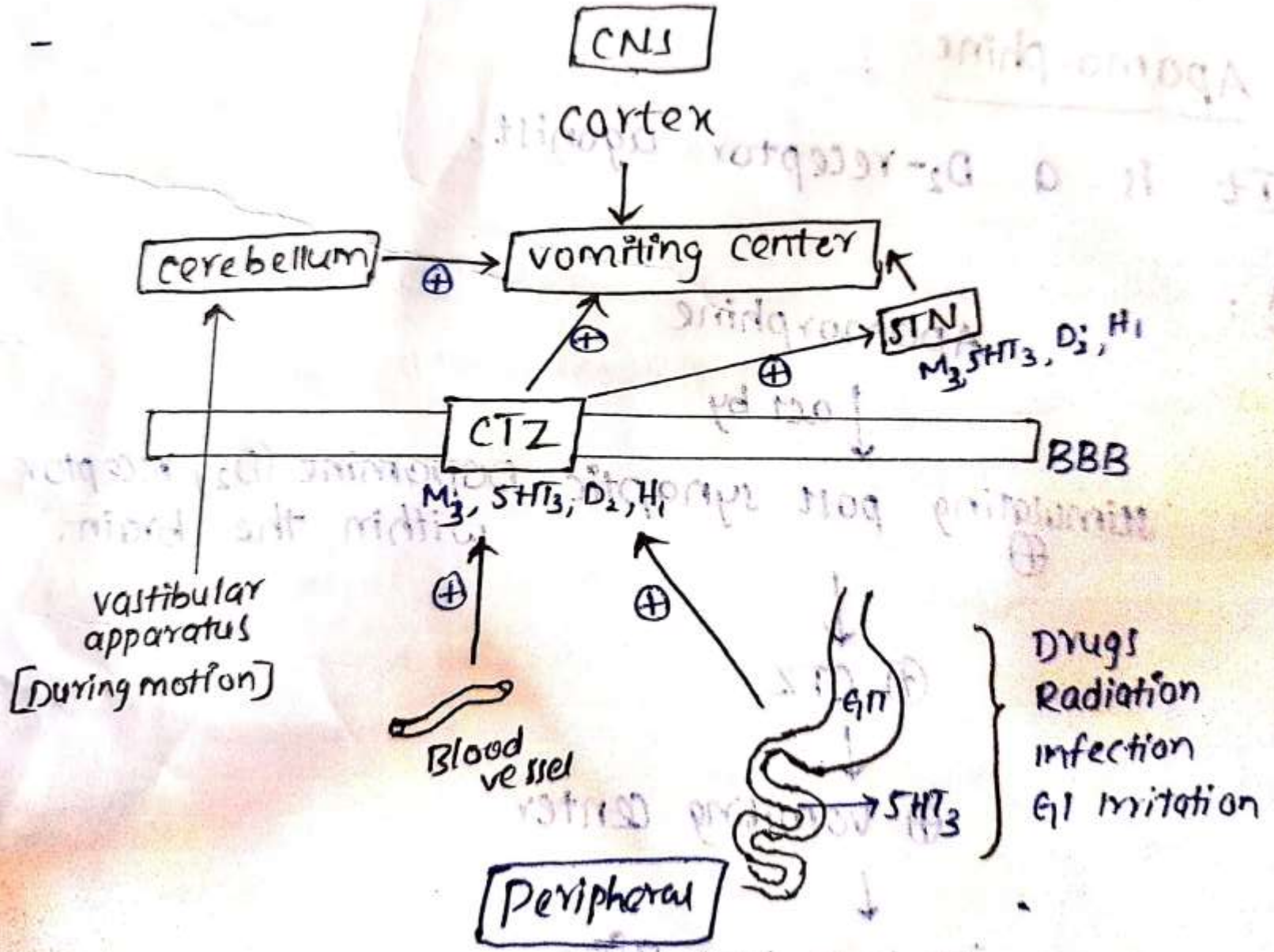
Emetics

- Drugs that induce vomiting are called Emetics.
- Emetics are substances or medications that are capable of inducing vomiting when ingested or administered.
- They work by irritating the stomach lining or by stimulating the vomiting center in the brain, triggering the reflex to expel the stomach contents.
- Emetics are primarily used in medical settings for the purpose of removing toxic substances from the stomach in cases of poisoning or overdose. **Vomiting**: Vomiting is the forceful ejection of the contents of your stomach and upper digestive system through your mouth.

Physiology


Sight
Smell
Emotion
Pain
CORTICAL CENTRE
LABYRINTH
Vestibulocochlear nerve
H1
Vestibular Nuclei
mACh
mACh
VOMITING CENTRE
NTS
H1
NK1
Steroid
NK1
CHEMORECEPTOR TRIGGER ZONE
Mu
D2
5-HT3
5-HT3
Vagus nerve
GASTROINTESTINAL SYSTEM
CHEMOTHERAPY DRUGS

Physiology of vomiting



CLASSIFICATION OF EMETICS

1. Stimulants of CTZ

- Apomorphine
- Morphine

2. Irritants of gastric mucosa

- Mustard
- Sodium chloride

3. Both CTZ stimulant and irritant effect

- Pecacuanha
- Digitalis

Centrally acting agents
eg:Apomorphine

- Apomorphine is a dopamine agonist medication that primarily acts on dopamine receptors in the brain.
- Its mechanism of action involves binding to and activating both D1 and D2 subtypes of dopamine receptors.
- However, its affinity for D2 receptors is higher than for D1 receptors.
- Apomorphine is a medication primarily used in the treatment of Parkinson's disease and, to a lesser extent, for acute treatment of opioid overdose and certain other medical conditions.

Mechanism of action

Apomorphine

Act by ↓

+ Post synoptic D2 receptors within the brain

↓

+CTZ

↓

+VC

↓

Induce vomiting

Pharmacokinetics

- Route : s.c, i.v and oral sublingual
- B.A : 100%
- Onset of action : Rapid (10 – 20 min)
- Duration of action :short (60-90min)
- Plasma half life : 40min
- Cross : BBB
- Peak plasma con: 5 – 10 min
- PPB : 99.9%
- Metabolism : Liver
- Excretion : urine

Adverse effects

- Dizziness
- Confusion
- Hallucination
- Increase heart rate
- Palpitation
- Erectile dysfunction
- Respiratory depression
- Convulsion
- Sedation
- Hypotension
- Coma, N,V

Drug interactions

- Apomorphine+Benzodiazepine→ severity of CNS depression
- Apomorphine+Acetazolamide→ severity of CNS depression

Uses

- Uses as emetic agent
- Apomorphine injection is used to treat ''off'' episodes (times of difficulty moving, walking, and speaking that may happen as medication wears off or at random) in people with advanced Parkinson's disease

Ipecacuanha

- The actions of ipecac are mainly those of major alkaloids, emetine (methylcephaeline) and cephaeline.

Ipecacuanha

act

locally by irritating the gastric mucosa

centrally by stimulating the medullary chemoreceptor triggerzone

induce vomiting.

Pharmacokinetics

- Route : oral
- B.A : 67%
- Onset of action : 30min
- Duration of action : 20min
- Plasma half life : 20min
- Peak plasma con: 20min
- Metabolism : Liver
- Excretion : urine

Adverse effects

- Diarrhea.
- fast or irregular heartbeat.
- nausea or vomiting (continuing more than 30 minutes)
- stomach cramps or pain.
- troubled breathing.
- unusual tiredness or weakness.
- weakness, aching, and stiffness of muscles, especially those of the neck, arms, and legs

Drug interactions

- Ipecac + activated charcoal→ reduce ph effect

Uses

- ❖Ipecac is used in the emergency treatment of certain kinds of poisoning.
- ❖It is used to cause vomiting of the poison.
- ❖Used in treatment of dysentery
- ❖Used as expectorant
- ❖Used as potent emetic

Anti emetics

- Anti-emetics are medications used to prevent or relieve nausea and vomiting. They work by targeting different receptors and pathways involved in the emetic (vomiting) reflex.

Classification

- **Serotonin (5-HT3) Receptor Antagonists**

  eg:Ondansetron, Granisetron, Palonosetron, Dolasetron

- **Dopamine Receptor Antagonists**

  eg: Metoclopramide,Domperidone ,

  Prochlorperazine, Promethazine

- **Muscarinic Receptor Antagonists**

  eg: Scopolamine, Dicyclomine

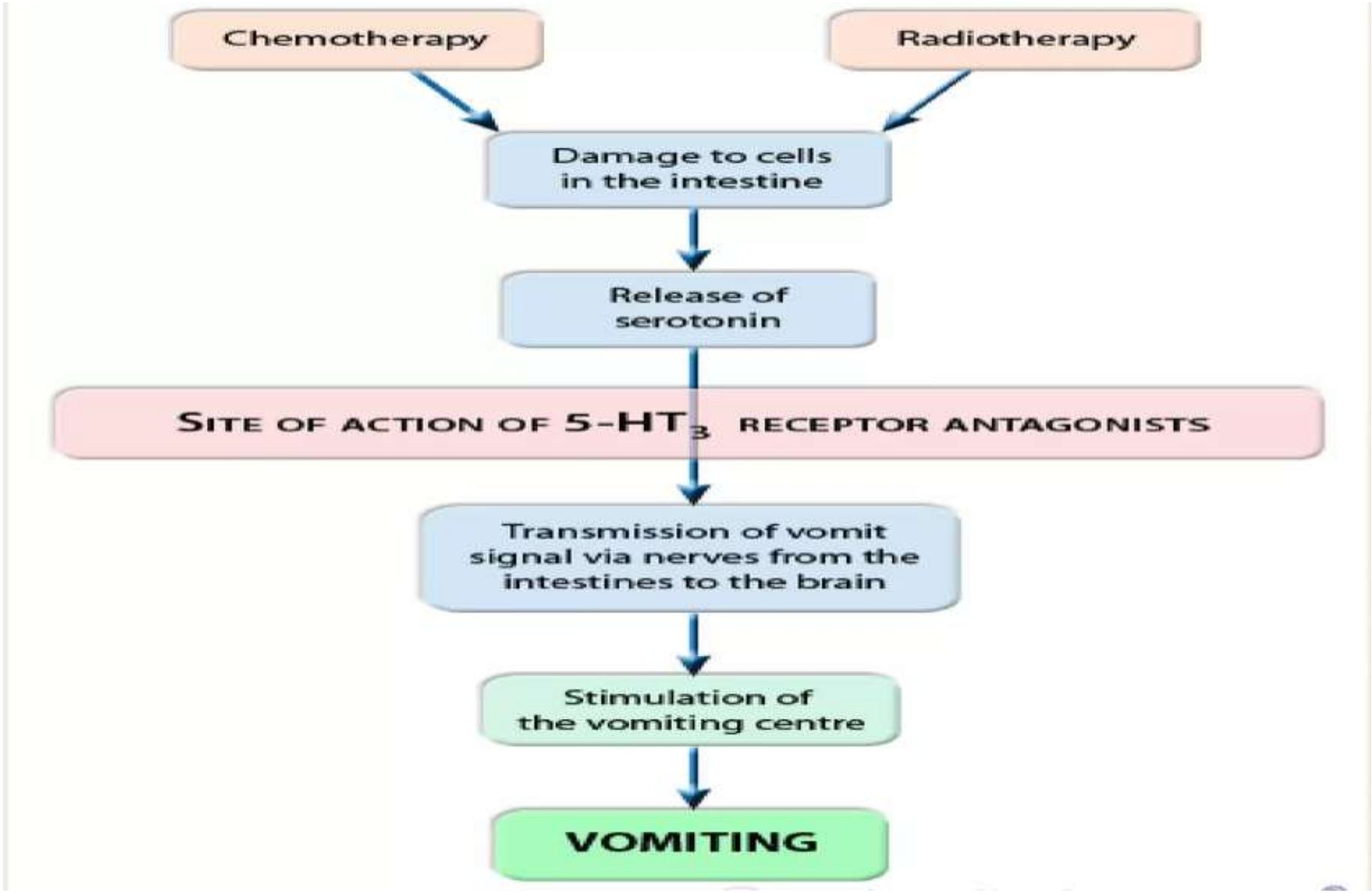
- **Neurokinin-1 (NK1) Receptor Antagonists**

  eg: Aprepitant, Fosaprepitant, Netupitant

- Neuroleptics
  - eg: Chlorpromazine, prochlorperazine
- Cannabinoid
  - eg:Dronabinol, Nabilone
- Glucocorticoid
  - eg:Dexamethasone, Betamethasone, Methylprednisolone
- Benzodiazepines
  - eg: Lorazepom , Alprazolam
- H1 receptor antagonist
  - eg: Diphenhydramine , cyclizine , Promethazine

Serotonin (5-HT3) Receptor Antagonists

eg: Ondansetron Mechanism of action



Pharmacokinetics

- Route : oral
- B.A : 50 -60%
- Onset of action : 30min
- Duration of action : 8Hrs
- Plasma half life : 4hrs
- Cross : BBB
- Peak plasma con: 5 – 10 min
- PPB : 70-75%
- Metabolism : Liver
- Excretion : urine

Side effects

- Headache
- Constipation
- Abdominal discomfort
- skin rashes
- Dizziness
- Diarrhoea
- sedation
- Anxiety
- urihary retention
- Fever
- chest pain
- Hypotension

Drug interactions

- Ondansetron + phenytoin →↓pharmacological action.
- Ondansetron +CBZ= decrease in pharmacological action .
- Ondansetron + Rifampin= decrease of pharmacological action.
- ondansetron + Tramadol toxicity of tramadol.

Uses

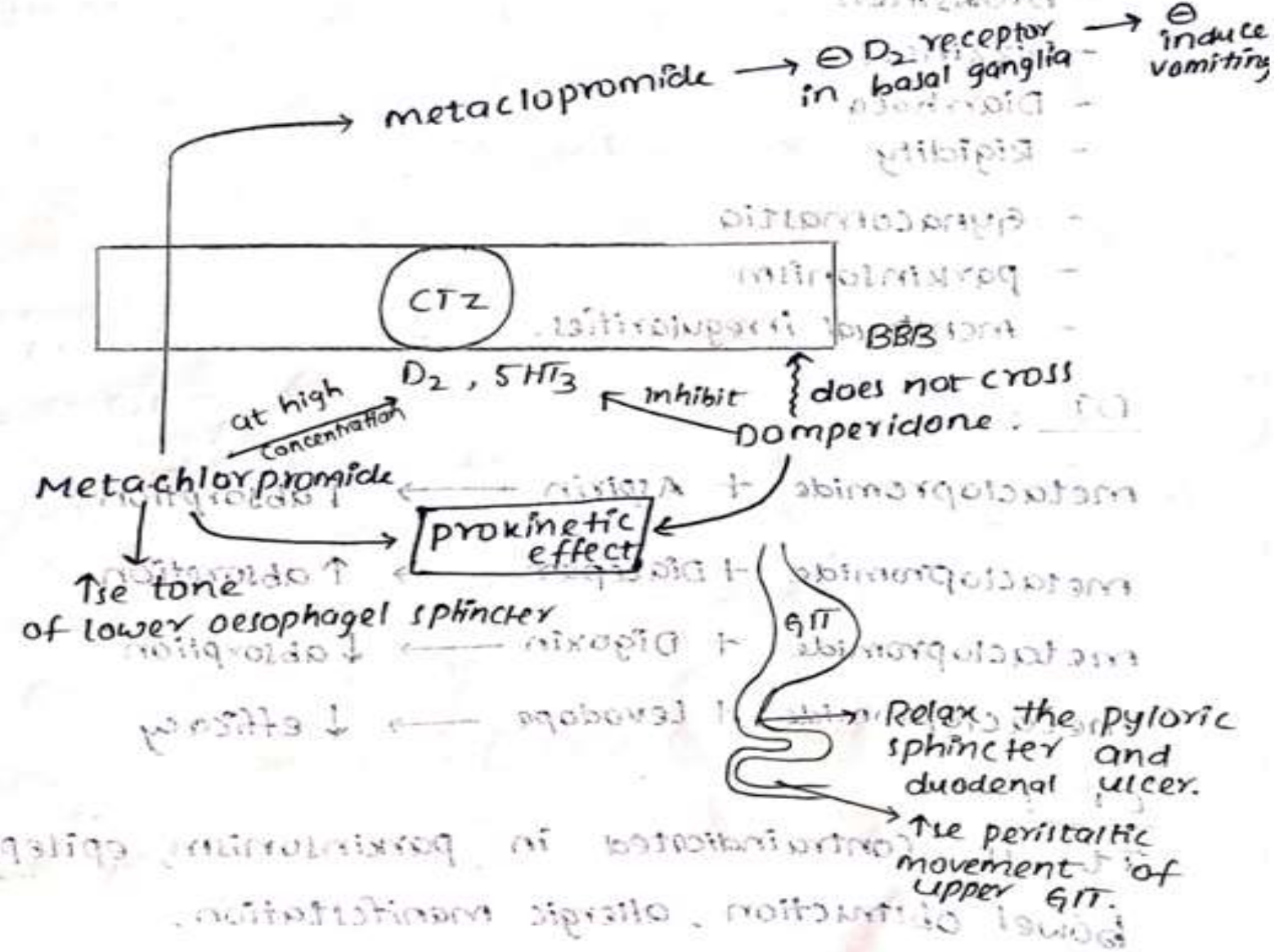
- It is used in to prevention of chemotherapy induced nausea and vomiting.
- It is used in the prophylactic treatment of postoperative nausea and vomiting.
- - They are also effective in hyper emelis past operative, and post radiation vomiting.
- They are used in drug induced vomiting motion sl ineffective against motion sickness.

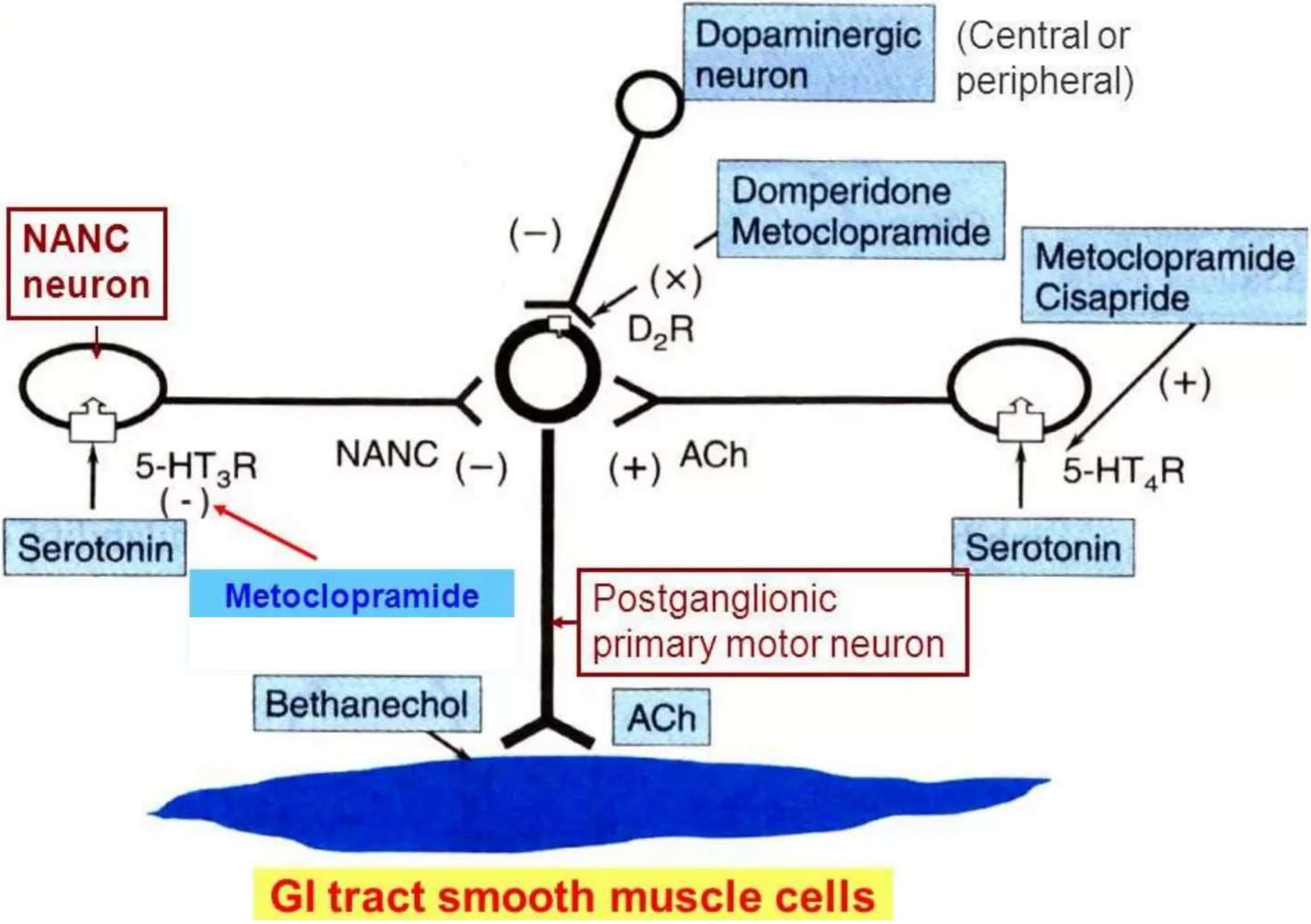
D2 Receptor Antagonists

eg: Metoclopramide, Domperidone

- These drugs block D2receptors, and inhibit release of dopamine.
- They prevent the transfer of emetic impulses and thus emesis.
- It is Structurally similar to procainamide and and pharmacologically related to phenothiazine
- -It shows D_2 and SHI_3 receptor antagonist and 5Hiy agonist activity.

MOA :


metaclopromide
⊖ D2 receptor in basal ganglia
⊖ induce vomiting
CTZ
BBB
D2 , 5HT3
at high concentration
inhibit
does not cross
Domperidone
Metachlorpromide
prokinetic effect
↑se tone of lower oesophagel sphincter
GIT
Relax the pyloric sphincter and duodenal ulcer.
↑se peristaltic movement of upper GIT.


Dopaminergic neuron
(Central or peripheral)
Domperidone
Metoclopramide
(−)
(×)
D2R
NANC neuron
Metoclopramide
Cisapride
(+)
5-HT3R
(-)
NANC (−)
(+) ACh
5-HT4R
Serotonin
Metoclopramide
Serotonin
Postganglionic primary motor neuron
Bethanechol
ACh
GI tract smooth muscle cells

D2 Antagonism : Dopamine (D2 Receptor) an inhibitory transmitter in g.i.t .

Delay gastric emptying when food is present in the stomach. It causes gastric dilation and LES relaxation attending nausea and vomiting.

Metaclopramide blocks D2 receptor- hastens gastric emptying, enhances LES tone by augmenting Ach release. Secondary action , $5HT_4$ Being primary mechanism.

Central antidopaminergic action on CTZ is responsible for antiemetic property.

D2 blockade : Antagonism of Apomorphine induced vomiting, CPZ like extrapyramidal Effects and Hyperprolactinaemia.

$5HT_3$ Antagonism.

$5HT_3$ receptors present on inhibitory myenteric interneurons and in NTS and CTZ.

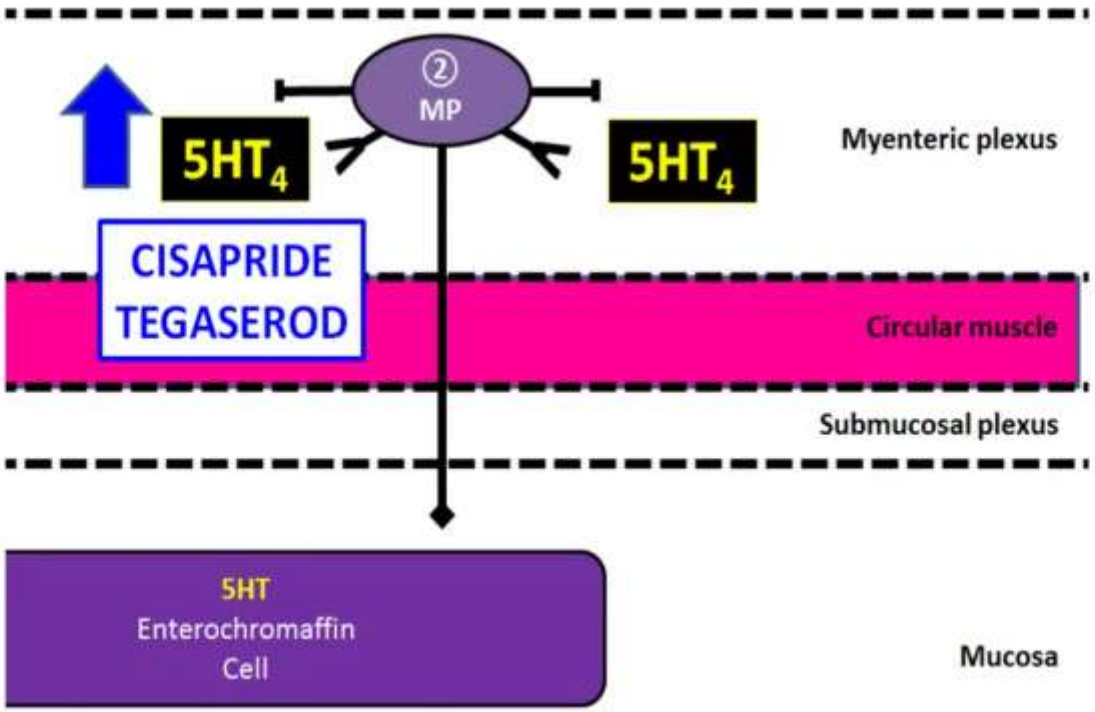
Metaclopramide at high concentrations blocks $5HT_3$ receptors , This augments Ach release in the gut which is very minor.

Its central action is significant only when large doses are used to control Chemotherapy induced nausea and vomiting.

$5HT_4$ Agonism

$5HT_4$ Receptor activation on Primary afferent neurons of Enteric nervous system which activates excitatory interneurons which enhances Ach release from myenteric motor neurons.

Gastric hurrying and LES tonic effects of metaclopramide are mainly due to this action . Synergised by Bethanechol and attenuated by atropine.



Pharmacokinetics

- Route : oral , i.v & i.m
- B.A : 80%
- Onset of action : 30 - 60min
- Duration of action : 1-2Hrs
- Plasma half life : 5-6hrs
- Cross : BBB
- Peak plasma con: 10 - 30min
- PPB : 30%
- Metabolism : Liver
- Excretion : urine

Adverse effect

- Drowsiness
- Dizziness
- Diarrhoea
- Rigidity
- Gynecomastia
- parkinsonism
- menstrual irregularities.

Drug intercations

- metoclopramide + Aspirin= increase absorption
- metoclopramide + Diazepam =↑ absorptión.
- metoclopramide + Digoxin=↓ absorption
- metoclopramide + Levodopa=↓efficacy

Uses

- It is used as an antiemetic in
  - diseased associated vomiting
  - drug induced vomiting
  - post operative vomiting.
  - Cancer chemotherapy
  - Radiation sickness induced vomiting


Thank you!