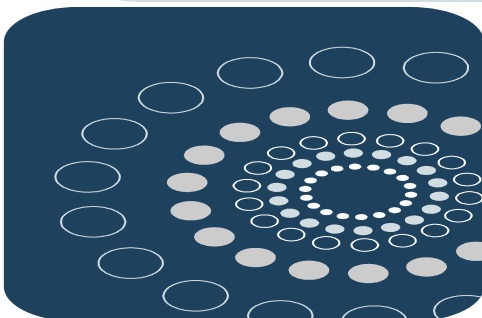
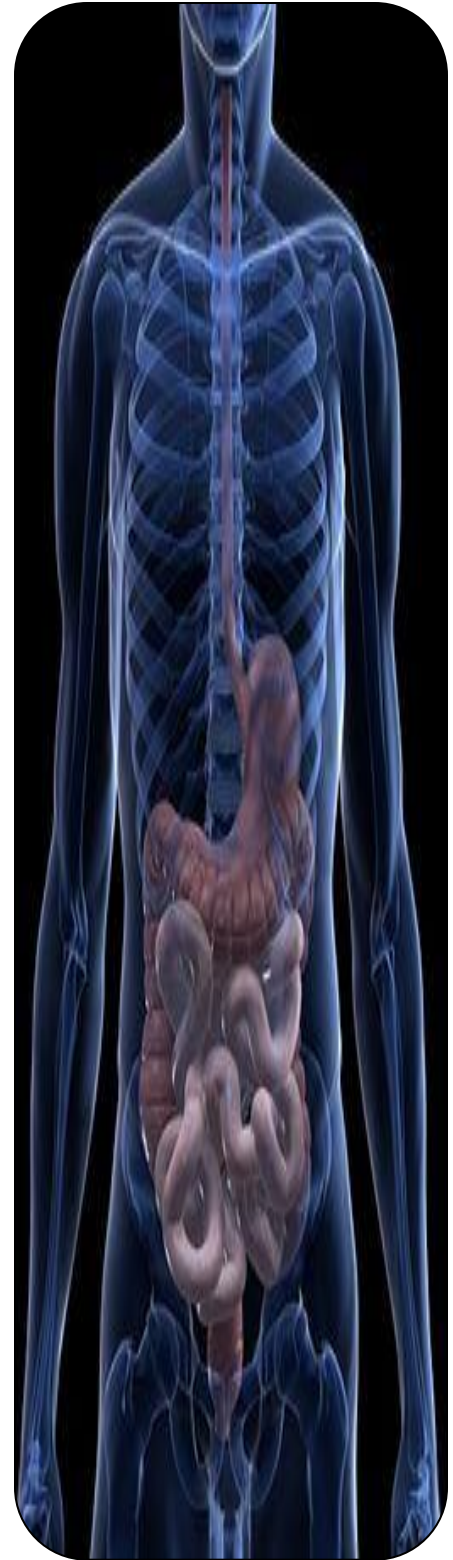


Pharmacology Team
Antiemetic drugs



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Introduction

-Vomiting : it's not a disease its indication of certain diseases
Vomiting occur due to stimulation of vomiting center that respond to inputs from:

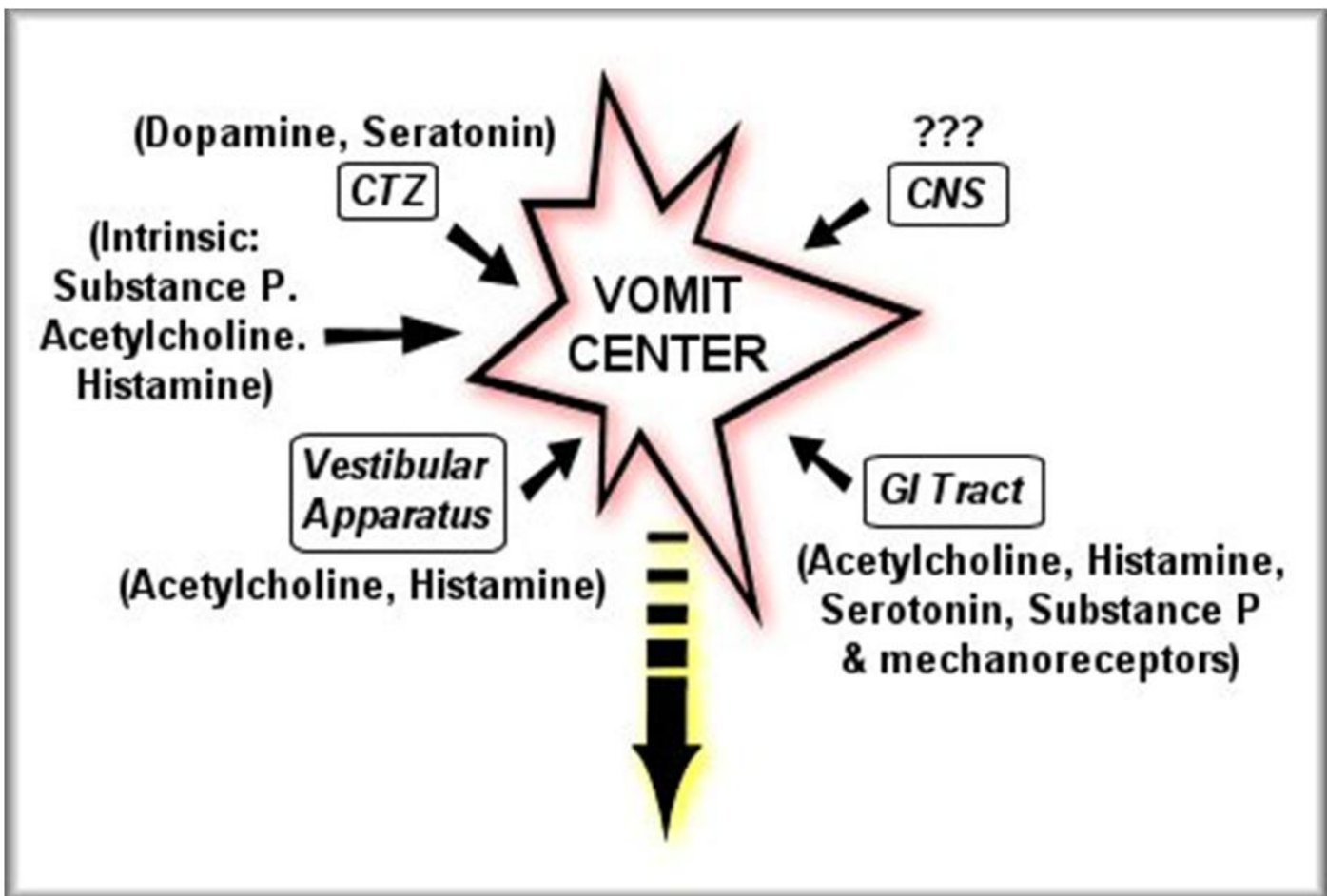
1. **Chemoreceptor trigger zone (CTZ) stimulation**
2. **Disturbance of vestibular system**
3. **Higher cortical centers stimulation (CNS)**
4. **The periphery (Pharynx, GIT) via sensory nerves**

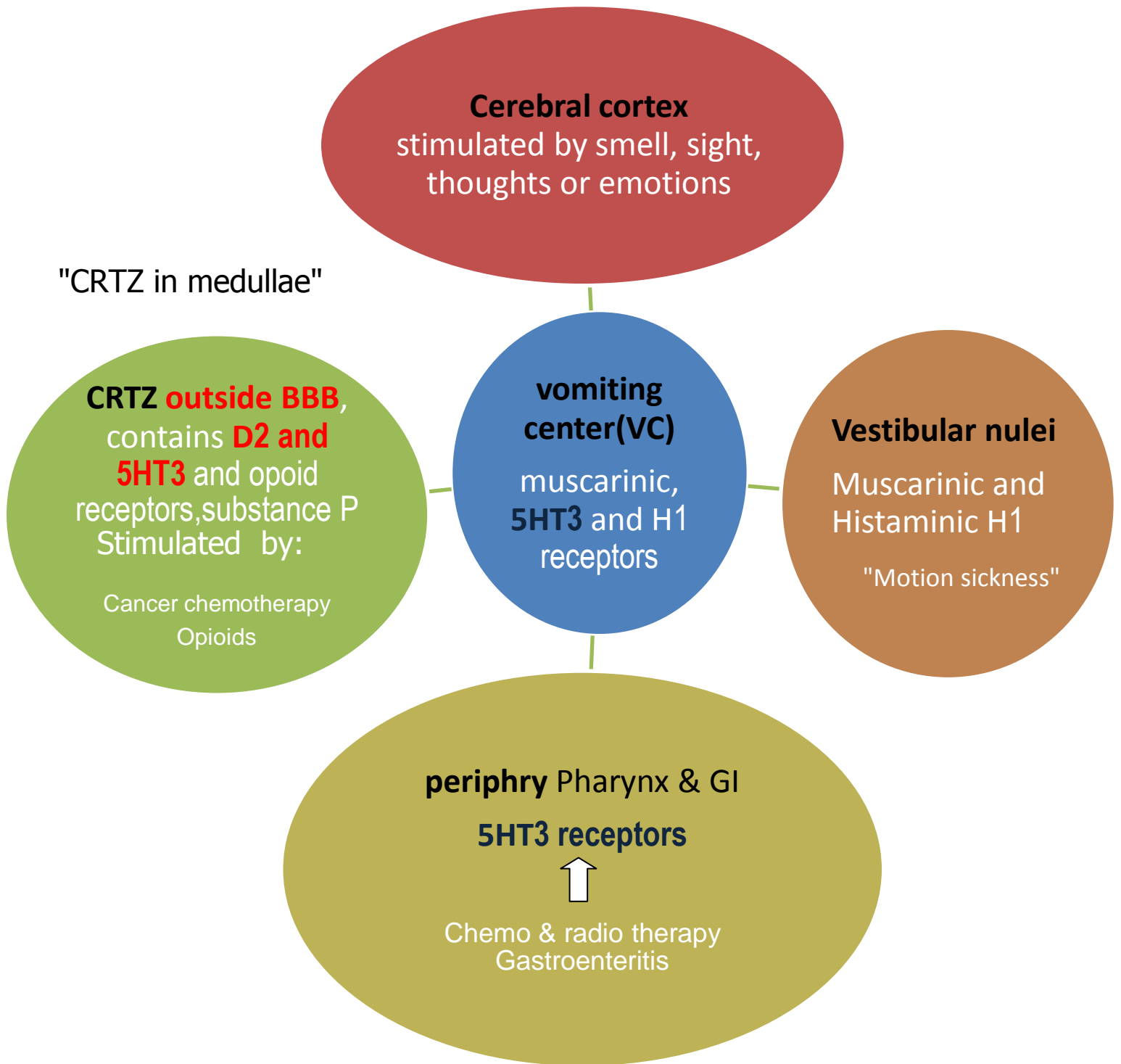
-Vomiting sometimes is a life-saving to get rid of toxins in the stomach.

-CRTZ stimulated by **Uremia** or drugs like: Morphine, Emetine or L-dopa, and periphery stimulated by GI irritation, MI or renal stones.

-Antiemetic drugs should only used when the cause of vomiting is known

-The drug of choice depend on the etiology; post-operative, chemotherapy..etc





Neurotransmitters and receptors involved in vomiting;

- | | |
|--|-----------------------|
| 1-Histamine (Histaminergic receptors H1) | 2- Serotonin (5-HT3), |
| 3- Ach (Muscarinic) | 4-Dopamine (D2) |
| 5-Substance P (Neurokinin receptors) | 6-Opioid Receptors. |

1-5HT₃ antagonist:

Ondansetron , Granisetron

B/C they block 5HT₃ so it affects VC, CRTZ & GI → most potent one
Oral/IV → long duration

#Effective in nausea & vomiting caused by;

Cytotoxic drugs (Cisplatin), post-operative or post-radiation

2-D₂ Antagonist:

A-Prokinetics drugs:

Dom-peridone (orally) , **Metoclo-peramide** (Orally/I.V.) the latter cross BBB

-Both are **Gastroprokinetics**; B/C both are **5HT₄ agonist**

5HT₄→release Ach→GI motility ↑↑

-Effective in vomiting caused by;

Gastroenteritis, uremia, toxins, post-operative, **radiation** (90%) and drugs

-Which one is better Domperidone or metocloperamide?

Clearly the first is better B/C the second cross BBB causing extrapyramidal S/E "dyskinesia", Galactorrhea, menstruation disorders or sedation.

-So what're the uses of metocloperamide?

Facilitate endoscopy, Diagnostic radiology of gut → ↓ time required for barium to reach caecum → ↓ No. of films required

***Clears gastric contents in emergency anaesthesia (I.V.)**

B-Antipsychotic drugs" for example **Chlorpromazine or Droperidol** due to their potent effect on D₂, but 5HT₃ blockers replace them due to their S/E such as extrapyramidal symptoms or hypotension "α-1 blocking effect".

3-Neurokinin1 (NK1) blockers:

Apre-pitant; prevent effect of Substance P on NK1 receptors.

Used as **adjuvant therapy** in chemo induced vomiting

*Usually don't used by doctors.

4-H1 receptors antagonist:

Diphenhydramine, Meclizine, Cyclizine and Promethazine

#Effective against;

***Motion sickness**, Opioid's nausea

Morning sickness in pregnancy

Sever morning sickness in pregnancy → **Promethazine**

Not USED IN CHEMOTHERAPY, POST-OPERATIVE OR UREMIA INDUCE VOMITING

5-Muscarinic receptors antagonist:

Hyoscine "**Scopolamine**", used in:

***Motion sickness**, trans-dermal patches behind external ear

NOT IN CHEMOTHERAPY-INDUCED VOMITING, "like H1 antagonist"

6- "psychoactive drugs:

Nabilone, as **adjuvant therapy** in chemo induced vomiting "like **Apre-pitant** "
S/E; Hallucination & dysphoria

7-Glucocorticoids

Dexamethasone, Methyl-predni-solone

Used alone or in combination with Ondansetron in acute emesis, cytotoxic drugs induce vomiting

S/E:

Hyperglycemia "diabetes"

Hypertension "Activate aldosterone → water retention"

Cataract, Osteoporosis

ICP ↑↑, Infection ↑↑, Appetite ↑↑

NOTE :most of antiemetic drugs are antagonist except Cannabinoids

Classification of Antiemetic Drugs	Drugs	MAO	Uses	Side effects
5-HT ₃ antagonists	<p>Ondansetron Granisetron "Orally or parenterally</p>	<p>Block 5-HT₃ receptor in vomiting center, CTZ and 5HT₃ receptors on intestinal vagal afferents.</p>	<p><u>First choice for prevention of:</u> 1-Chemotherapy-induced nausea and vomiting (CINV) especially cisplatin. 2-Post-radiation NV& Post-operative NV 3-Their effects is increased by combination with corticosteroids and NK1 antagonists</p>	<p>1-Well tolerated 2-mild headache, dizziness and constipation 3-minor ECG abnormalities (QT prolongation)</p>
D ₂ receptor antagonists	<p><u>1-Prokinetics drugs</u> -metoclopramide -domperidone</p>	<p>Both are prokinetic agents due to their 5 HT₄ agonistic activity</p>	<p>1-used in GERD (gastroesophageal reflux disease), gastroparesis 2-Used as antiemetics (blocking D₂ receptors) 3- Metoclopramide crosses BBB but domperidone cannot (both have antiemetic effects as CTZ is outside BBB).</p>	<p>Side effects (only for metoclopramide): 1-Dyskinesia (<i>extra-pyramidal side effects</i>), 2-Galactorrhea, menstrual disorders, impotence. 3-Sedation, postural hypotension.</p>
	<p><u>2-Neuroleptics (antipsychotics):</u> -Chlorpromazine(CPZ) - droperidol</p>		<p>postoperative vomiting and chemotherapy-induced nausea & vomiting.</p>	<p>1-extrapyramidal symptoms 2-sedation, postural hypotension</p>

NK ₁ antagonists	Aprepitant "Orally"	Is a substance P antagonists that acts by blocking neurokinin 1 receptor	1-Used in prevention of acute and delayed chemotherapy-induced nausea and vomiting and for prevention of postoperative nausea and vomiting. 2-Usually combined with 5-HT ₃ antagonists and corticosteroids.	
H ₁ -receptor antagonists	1- Diphenhydramine 2-Mecizine - Cyclizine 3-Promethazine		<u>Promethazine</u> severe morning sickness of pregnancy (<i>if only essential</i>)	prominent sedation, hypotension, anticholinergic effects (dry mouth, dilated pupils, urinary retention, constipation).
Muscarinic receptor antagonists	Hyoscine (scopolamine) "Orally, injection, patches"		1-Used as transdermal patches in motion sickness (applied behind the external ear). 2-Not in chemotherapy-induced vomiting	tachycardia, blurred vision, dry mouth, constipation, urinary retention (atropine-like actions).
Cannabinoids	1-Nabilone 2--dronabinol	act at central cannabinoid receptors	1-Used in vomiting due to cytotoxic anticancer drugs (adjuvant therapy). 2-Not commonly used.	euphoria, dysphoria, sedation, hallucination.
Glucocorticoids	1-Dexamethasone 2-methylprednisolone	.	1-chemotherapy-induced vomiting 2-combined with 5-HT ₃ antagonists or NK1 receptor antagonists	-Hyperglycemia, Hypertension -Cataract, Osteoporosis -Increased intraocular pressure -Increased susceptibility to infection -Increased appetite & obesity

Summary

Motion sickness

- Muscarinic antagonists
- Antihistaminics

Vomiting with pregnancy (morning sickness)

- avoid all drugs in the first trimester
- Pyridoxine (B6)
- Promethazine (late pregnancy).

Drug- induced vomiting (CTZ)

Dopamine antagonists

Post operative nausea & vomiting

**Dopamine antagonists
5-HT₃ antagonists
NK1 antagonists**

Vomiting due to cytotoxic drugs

**5-HT₃ antagonists
NK1 antagonists
D2- antagonists
Glucocorticoids
Cannabinoids**

Questions

1- A 53 year old female patient receiving chemotherapy for the treatment of ovarian cancer. Currently, she is suffering from severe vomiting. which one of the following would be most effective to counteract her emesis ?

A-Chlorpromazine

B-Hyoscine

C- Ondansetron

D-Promethazine

2- A patient on an antiemetic drug therapy. She suddenly developed extrapyramidal symptoms and galactorrhea. Which one of the following drug is responsible for these side effects ?

A- Hyoscine

B- Metoclopramide

C- Nabilone

D- Ondansetron

Answers :

1-C

2-B