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!! This is a combination b/w both male& female lectures

Team`s note >> RED

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Causes of Vomiting

Nausea and vomiting may be manifestations of many conditions and may occur due to stimulation of *vomiting center that respond to inputs from:*

1. Chemoreceptor trigger zone (CTZ) stimulation :

- CTZ is an area of medulla that communicate with vomiting center to initiate vomiting.
- CTZ is physiologically outside BBB
- CTZ Contains D_2 & 5 HT_3 receptors. - Dopamine agonists cause vomiting => antagonists are used as antiemetic
- CTZ can be stimulated by drugs, chemicals and toxins in blood, CSF.

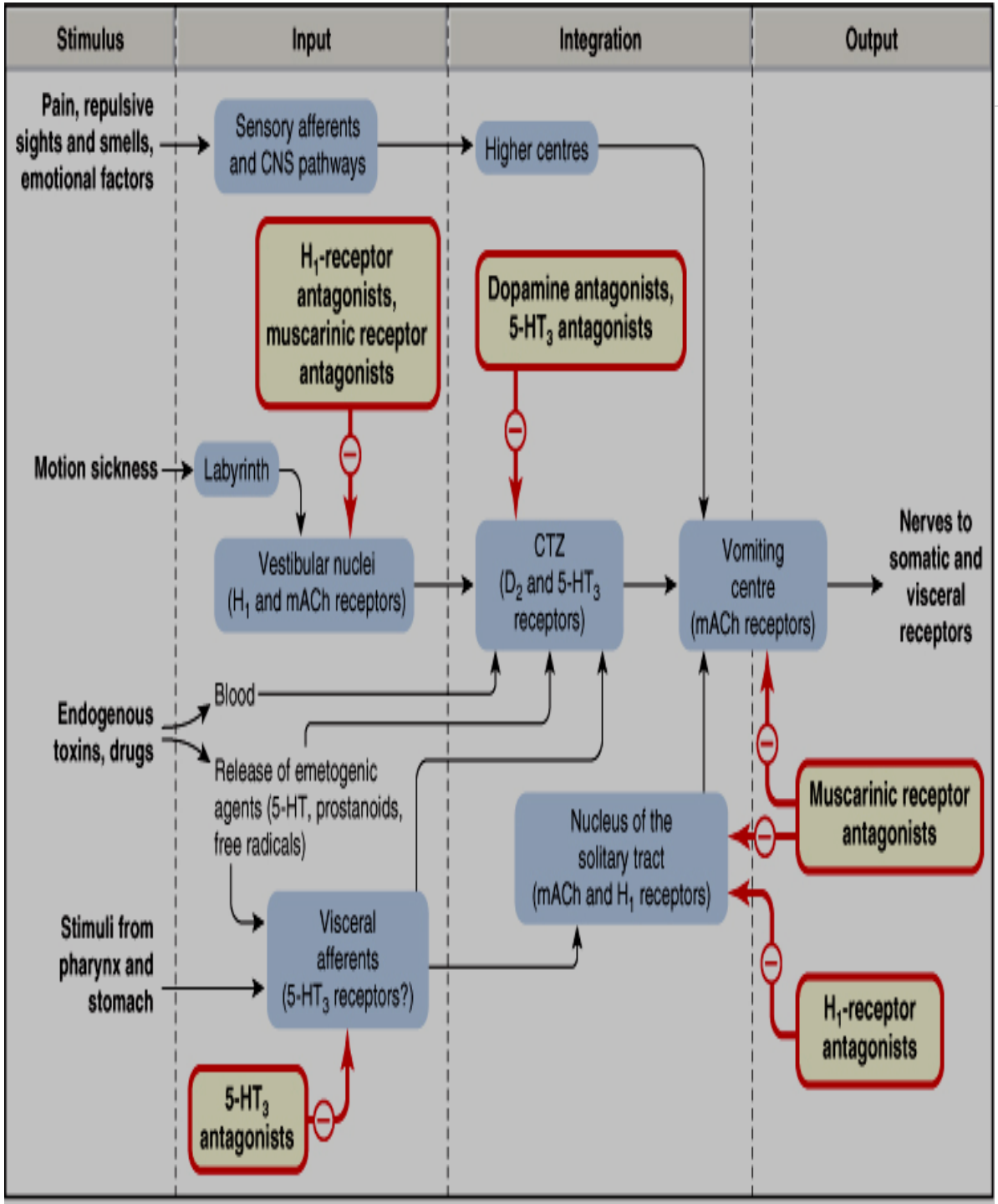
2. Disturbance of vestibular system

3. Higher cortical centers stimulation (CNS) :

emotional factors, nauseating smells or sights.

4. The periphery via sensory nerves :

GIT irritation, myocardial infarction, renal or biliay stones.



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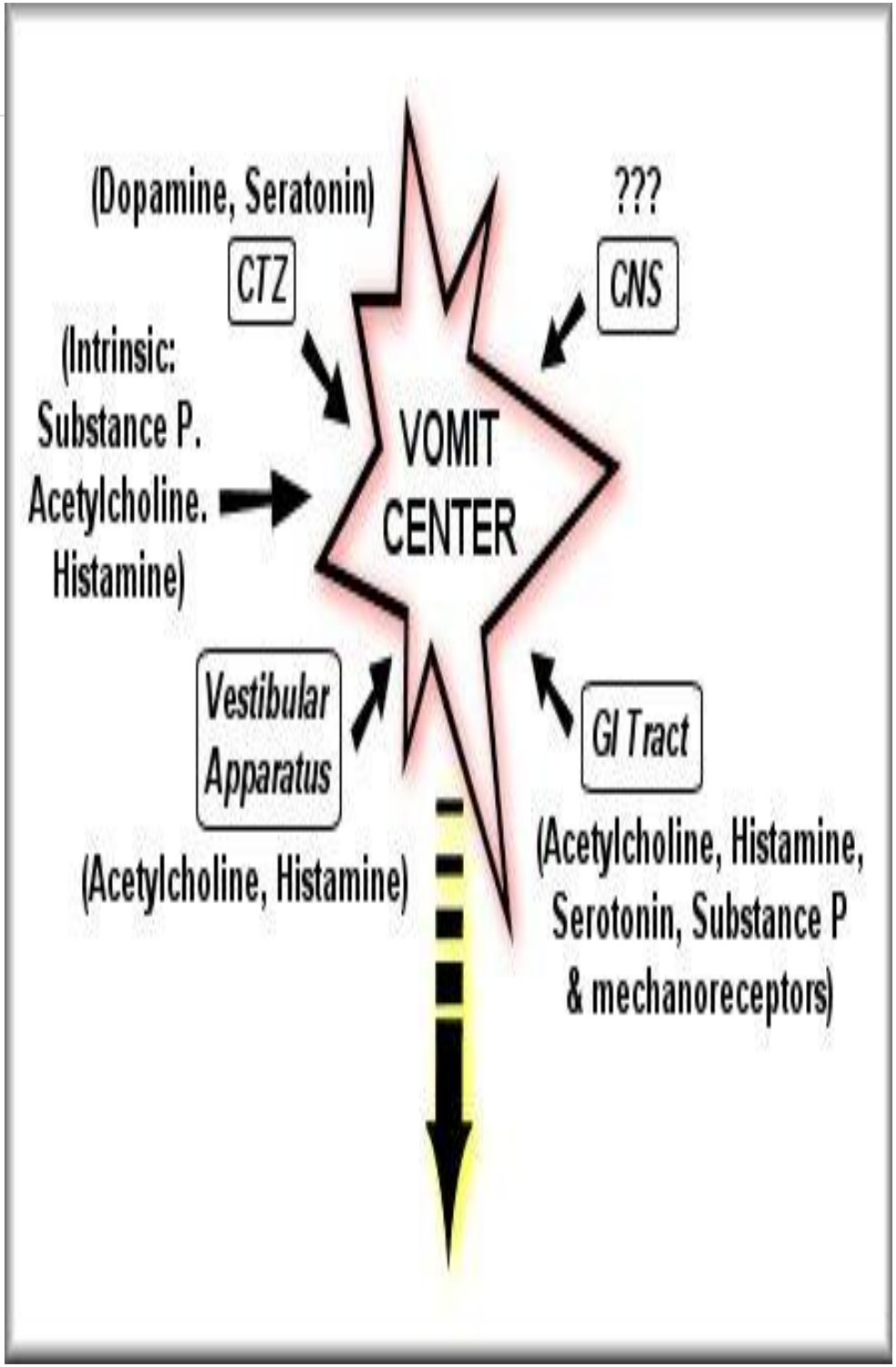

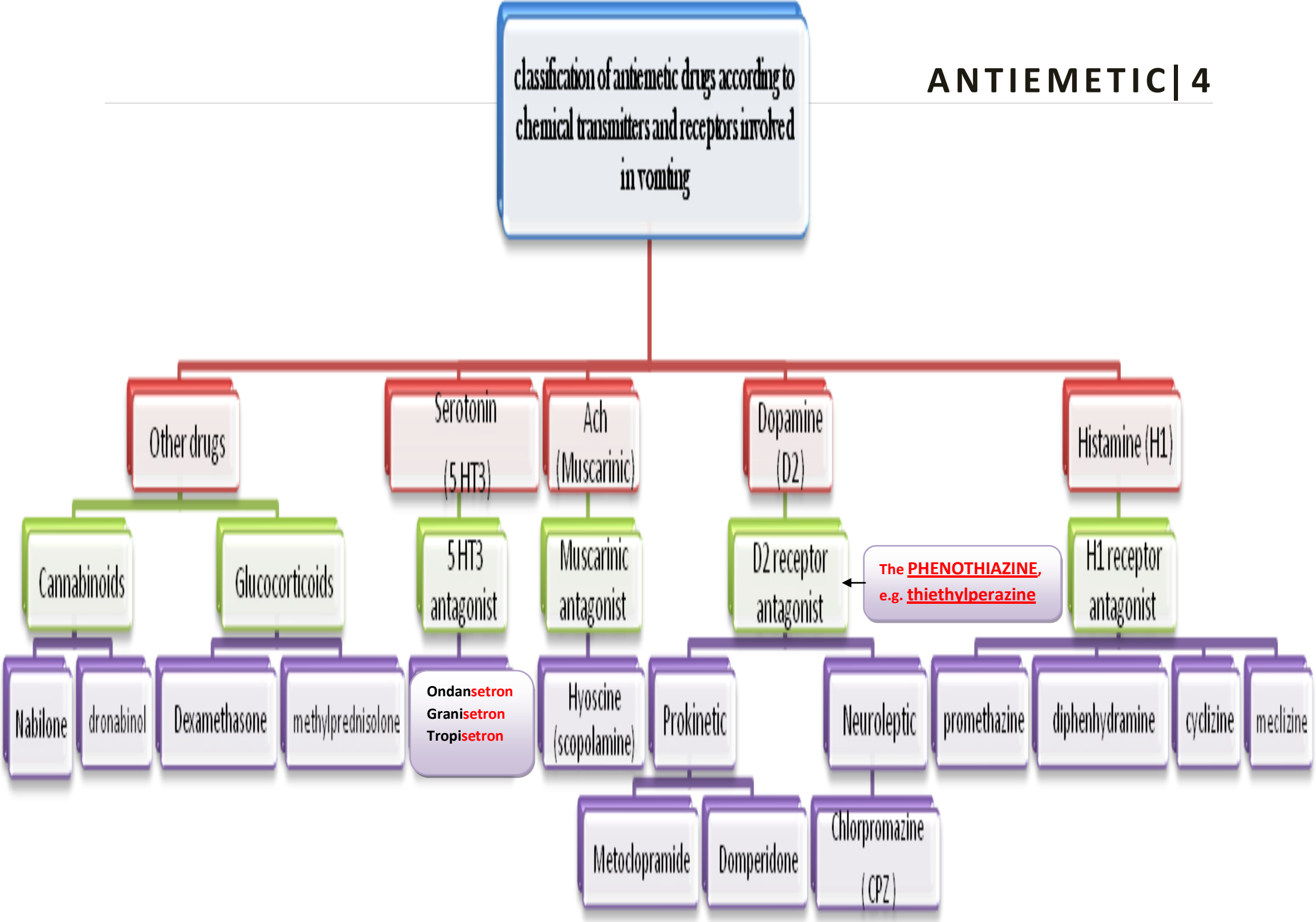
classification of antiemetic drugs according to chemical transmitters and receptors involved in vomiting
Other drugs
Serotonin (5 HT3)
Ach (Muscarinic)
Dopamine (D2)
Histamine (H1)
Cannabinoids
Glucocorticoids
5 HT3 antagonist
Muscarinic antagonist
D2 receptor antagonist
The PHENOTHIAZINE, e.g. thiethylperazine
H1 receptor antagonist
Nabilone
dronabinol
Dexamethasone
methylprednisolone
Ondansetron
Granisetron
Tropisetron
Hyoscine (scopolamine)
Prokinetic
Neuroleptic
promethazine
diphenhydramine
cyclizine
meclizine
Metoclopramide
Domperidone
Chlorpromazine (CPZ)

1st) Anticholinergics:

- Muscarinic receptor antagonists
- Used in motion sickness
- Not used in chemotherapy-induced vomiting
- ADR's: anticholinergic side effects.

2nd) Antihistamines:

- H1-receptor antagonists
- only central antihistaminic are used as antiemetics.

(Loratidine not used because it's peripheral)

- Most centrally acting antihistamines have anticholinergic effect

→ so very effective + ADR's

-Uses:

1) Prophylaxis of motion sickness

2) Vestibular disorders (e.g. Meniere's disease)

Note : In vestibular disorders only antihistamines are used

3) Severe morning sickness of pregnancy.

Not in chemotherapy-induced vomiting.

- ADR's: sedation + most have anticholinergic side effects.

3rd) Dopamine Antagonists:

D2 receptor antagonists (central action on CTZ)

a. Prokinetics:

- Orally, half life 4 -5 h.

- Uses: vomiting due to 1) cytotoxic drugs, gastrointestinal disorders, Postoperative (post-operative cause of anesthesia) , toxins, uremia , radiation

- Differences between Metoclopramide and Domperidone :

1. As side effects, Metoclopromide causes:

a) extrapyramidal symptoms

b) galactorrhea & menstruation disorders due to hyperprolactinemia
c)sedation.

BUT Domperidone does not because it cannot cross BBB

2. Metoclopromide has 5-HT3 antagonizing effect in addition to its D2 antagonizing effect.

3. . Metoclopromide is drug of choice in vomiting due to uremia

b. Neuroleptics:

- Used for vomiting due to: chemotherapy, uraemia, radiation, viral gastroenteritis, severe morning sickness of pregnancy
- orally, parentrally, suppository
- ADR's:
- Hypotension (due to block a- adrenergic receptors)
- Sedation
- Restlesess
- extrapyramidal symptoms.

4th) 5-HT3 antagonists : (ondansetron is the drug of choice.)

- Uses:
  - nausea and vomiting caused by cytotxic anticancer drugs (e.g cisplatin = anticancer drug).
  - postoperative vomiting
  - radiation

- ADR's: constipation

5th) Cannabinoids:

- Used for vomiting by cytotoxic anticancer drugs.

- ADR's:

Sedation, hallucination and dysphoria

6th) Glucocorticoids:

- Highly effective in acute emesis (especially in cancer patients)

- used alone or combined with Phenothiazines or Ondansetron.

- ADR's:

Hyperglycemia , insomnia.

water retention → increase BP, cataracts & osteoporosis)

7th) Vitamin B6 (Pyridoxine): used in morning sickness pregnancy

Mechanism of action	Drugs	Uses	Adverse affect
1. Muscarinic receptor antagonists	- Hyoscine (scopolamine)	- Motion sickness - Not in chemotherapy-induced vomiting	- (Atropine like action) : - dry mouth - constipation & blurred vision
2. H1-receptor antagonists	- Promethazine - Diphenhydramine - Cyclizine - Meclizine (Navidoxine)	- Prophylaxis of Motion sickness - Vestibular disorders *(e.g. Meniere's disease)* - promethazine: severe morning sickness of pregnancy (if only essential). - Not in chemotherapy-induced vomiting.	
3. D2 receptor antagonists	Prokinetics: (increase motility of the upper part of GIT. mostly used to treat vomiting due to gastroesophageal reflux) - Metoclopramide (Plasil^R) - Domperidone (MOtilium^R)	- Orally, half life 4 -5 h. - effective against vomiting due to: drugs, , surgery, gastroenteritis , toxins, uremia and radiation *(central action on CTZ).*	- dystonic reactions (extrapyramidal symptoms), - galactorrhea and menstruation disorders (hyperprolactinemia) - sedation (these ADRs only for Metoclo. cause Domperi. can't cross BBB so no sedation).
	Neuroleptics: - chlorpromazine (CPZ)	- orally, parentrally, suppository - used for vomiting due to chemotherapy- induced emesis	- Hypotension - Restlessness - extrapyramidal symptoms.
	- Phenothiazines (e.g.thiethylperazine)	- severe morning sickness of pregnancy - vomiting caused by uraemia, radiation, viral gastroenteritis	- extrapyramidal symptoms.
4. 5-HT3 antagonists	- Ondansetron	- Orally, long duration of action. - Very effective in vomiting due to cytotoxic drugs (e.g cisplatin = anticancer drug), after radiotherapy, postoperative vomiting.	
5. Cannabinoids	- Nabilone (remember نابليون :) - dronabinol	- used for vomiting by cytotoxic anticancer drugs.	- Sedation, Hallucination , dysphoria.
6. Glucocorticoids	- Dexamethasone - methylprednisolone	- Highly effective in acute emesis alone or combined with CPZ or ondansetron. - vomiting by cytotoxic anticancer drugs	- Hyperglycemia , insomnia. Other side effects : water retention so increase Bp, cataracts ,osteoporosis)
6. Vitamin B6 =Pyridoxine		uses in morning sickness (pregnancy)	

Summary for Therapeutic Choice of Antiemetics

Motion sickness	Vomiting with pregnancy (morning sickness)	Drug- induced vomiting (CTZ)	Vomiting due to cytotoxic drugs	Post-operative vomiting
- For short Journey : Mus-receptor antagonists : Hyoscine - For Long Journey : H1-receptor antagonists: Diphenhydramine	- Because of avoiding all drugs in the first trimester the Pyridoxine (B_6) is given - late pregnancy: H1-receptor antagonists: Promethazine	- D2- antagonists : domperidone & metoclopramide	- 5-HT_3 antagonists : Ondansetron (1st choice) - D2- antagonists. - Glucocorticoids : Dexamethazone - Cannabinoids : Nabilone	- D_2- antagonists : domperidone & metoclopramide