

# Anti-emetic drugs

## ▪ Emesis (vomiting) :

<b>Def:</b>	<ul style="list-style-type: none"><li>• <b>protective reflex</b> that removes toxic agents from the gut <b>before</b> absorption.</li><li>• It is frequently <b>preceded by</b> nausea.</li></ul>
<b>Center</b>	<ul style="list-style-type: none"><li>• Vomiting centre is in <b>medulla</b>.</li><li>• This center coordinates a <b>series of events</b> involving pharyngeal, GI, and abdominal wall contractions that lead to <b>expulsion</b> of the gastric contents.</li></ul>

## ▪ There are four important sources of afferent input to the vomiting center:

### 1) Higher cortical centers stimulation (CNS):

- Emotional factors, Nauseating smells, thoughts, sights or pain.

### 2) Disturbance of vestibular system:

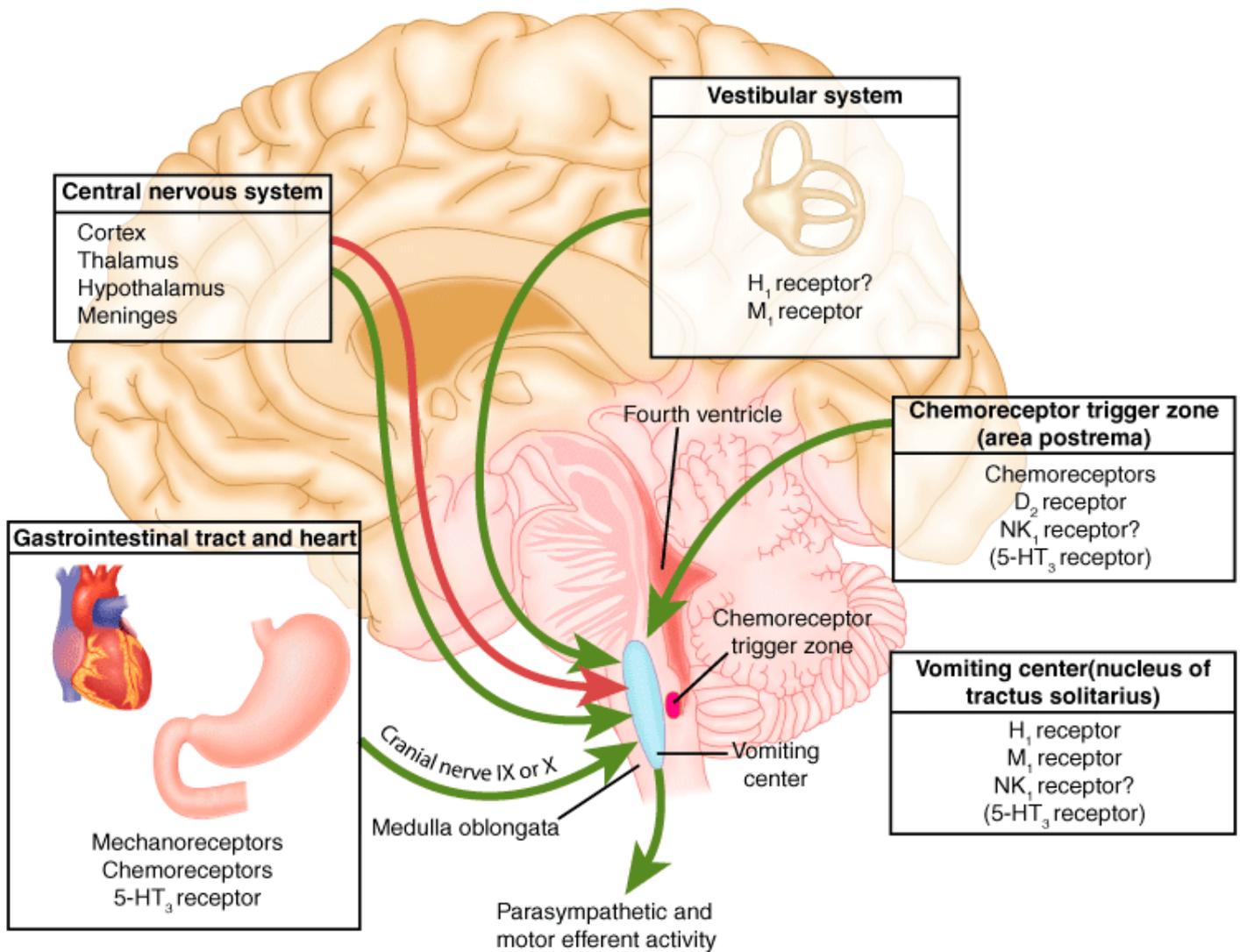
- **Motion sickness** (H1 & M1 receptors).

### 3) The periphery (Pharynx, GIT) via sensory nerves:

- **Noxious substances** in the gut can activate vagal afferent pathways.

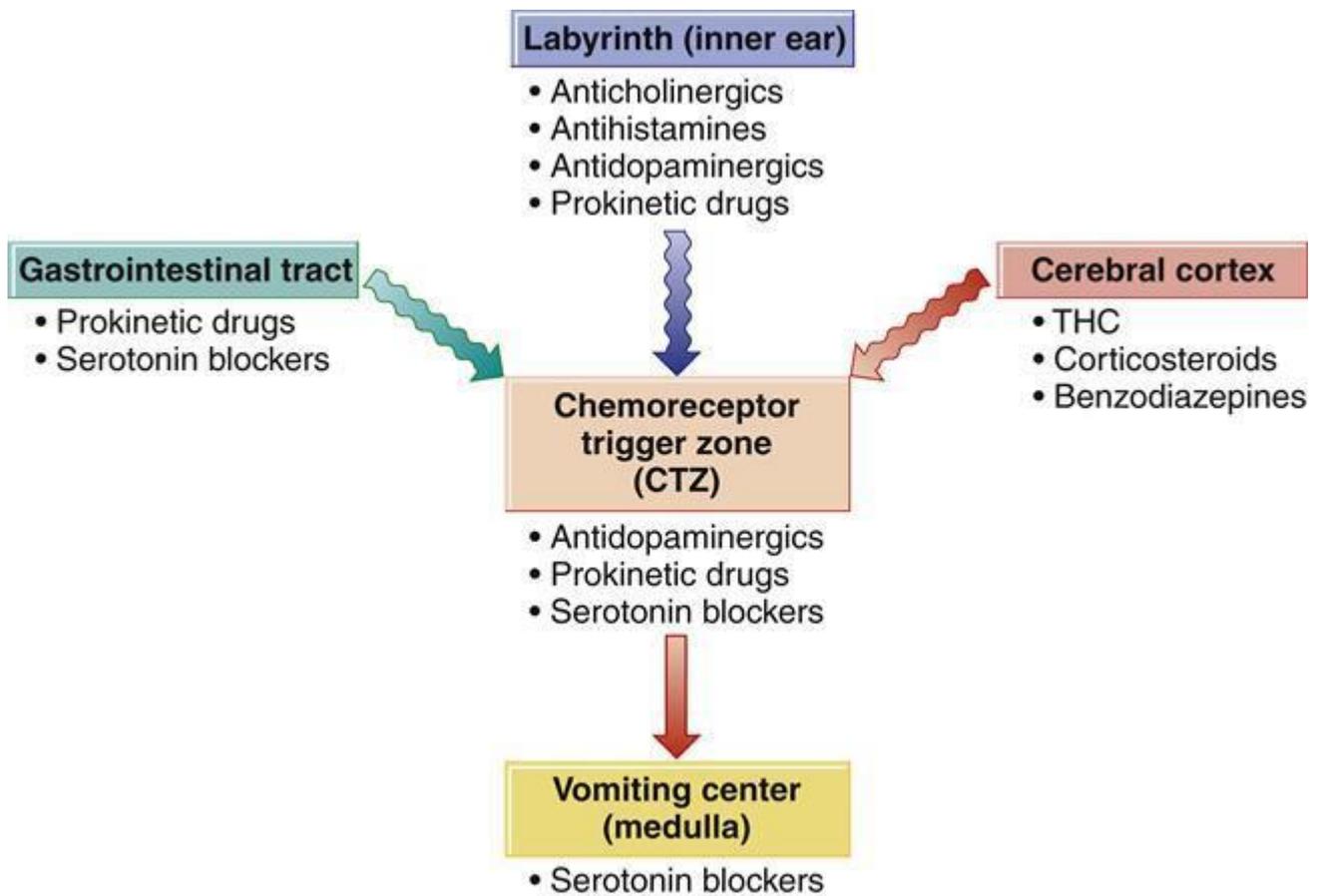
### 4) Chemoreceptor trigger zone (CTZ) stimulation:

- It is **outside** the blood-brain barrier and is accessible to chemical stimuli in the blood or cerebrospinal fluid.
- The D2, 5-HT3, and neurokinin 1 (NK1) receptors have **a major role** in these pathways.



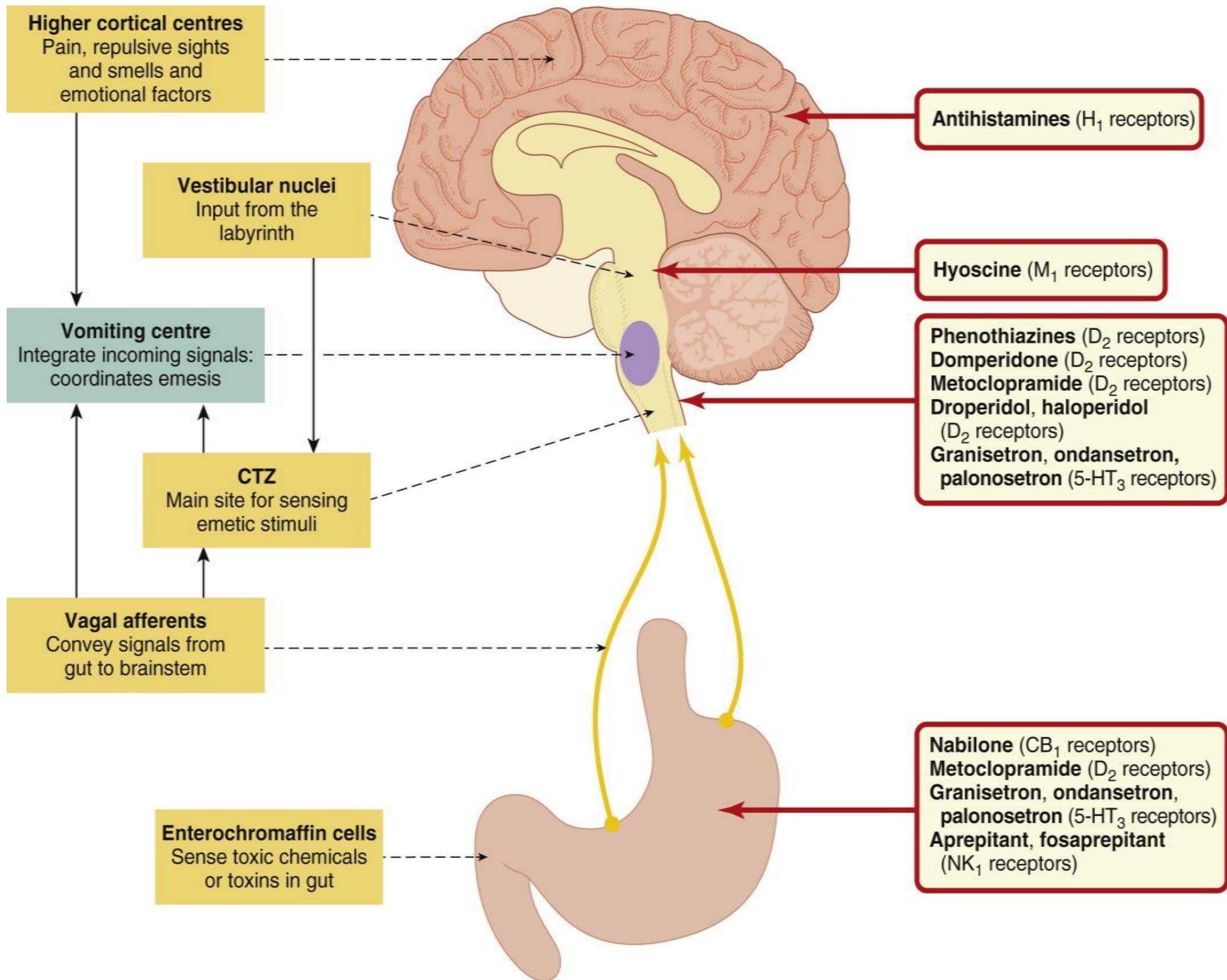
▪ **Classification of antiemetics:**

<b>I. 5-HT<sub>3</sub> blockers:</b>	• e.g., Ondansetron.
<b>II. D<sub>2</sub>-blockers:</b>	• e.g., Prokinetics drugs & Neuroleptics (antipsychotics).
<b>III. Neurokinin-1 receptor blockers:</b>	• e.g., Aprepitant
<b>IV. H<sub>1</sub>-blockers:</b>	• e.g., Diphenhydramine.
<b>V. Muscarinic blockers:</b>	• e.g., Hyoscine.
<b>VI. Cannabinoid derivatives:</b>	• e.g., Nabilone
<b>VII. Others:</b>	• Vitamin B <sub>6</sub> (pyridoxin), Corticosteroids, Benzodiazepines.



	<b>5-HT3 blockers</b>	<b>D2-blockers</b>	<b>H1-blockers</b>
<b>Examples</b>	<ul style="list-style-type: none"> <li>Ondansetron, Granisetron, Dolasetron. <b>MCQ</b></li> </ul>	<ul style="list-style-type: none"> <li><b>Prokinetics drugs:</b> Metoclopramide, Domperidone</li> <li><b>Phenothiazines:</b> chlorpromazine, promethazine</li> </ul>	<ul style="list-style-type: none"> <li>Dimenhydrinate, Meclizine, cinnarizine</li> </ul>
<b>kinetics</b>	<ul style="list-style-type: none"> <li>Orally or parenterally.</li> <li>These drugs are metabolized by <b>cytochrome P450</b>.</li> </ul>		
<b>Mechanism</b>	<ul style="list-style-type: none"> <li>Act by blocking <b>5-HT3 receptor centrally</b> (in vomiting center, CTZ) and <b>peripherally</b> (5HT3 receptors on GI vagal afferents).</li> </ul>	<ul style="list-style-type: none"> <li>They block <b>D2 receptors</b> in the CTZ.</li> <li>Phenothiazines have additional <b>H1 receptor antagonist</b> and <b>antimuscarinic</b> effect.</li> </ul>	<ul style="list-style-type: none"> <li>They block <b>H1 (also M1) receptors</b> in the vestibulo-cerebellar pathway and CTZ.</li> <li>They have <b>sedative action</b>.</li> </ul>
<b>Uses</b>	<ol style="list-style-type: none"> <li><b>Chemotherapy-induced vomiting (CINV).</b> <b>MCQ</b></li> <li><b>Radiation-induced vomiting</b></li> <li><b>Postoperative nausea and vomiting (PONV).</b></li> </ol>	<ol style="list-style-type: none"> <li><b>Vomiting due to drugs</b> (e.g. anesthetics) or fevers.</li> <li><b>CINV.</b></li> <li><b>PONV.</b></li> </ol>	<ol style="list-style-type: none"> <li><b>Vomiting due to motion sickness</b> (Dimenhydrinate)</li> <li><b>Vomiting of pregnancy</b> (Meclizine)</li> <li><b>Vestibular disease</b> (Cinnarizine)</li> </ol>
<b>Adverse effects</b>	<ol style="list-style-type: none"> <li><b>Dizziness, headache</b></li> <li><b>Constipation.</b></li> <li><b>Q–T interval prolongation (torsades de pointes)</b> at high doses</li> </ol>	<ol style="list-style-type: none"> <li><b>Extrapyramidal effects</b> e.g. dystonia and dyskinesia (Not with Domperidone.)</li> <li><b>Hyperprolactinemia</b></li> <li><b>Sedation, Postural hypotension.</b></li> <li>Domperidone can cause <b>Q–T interval prolongation (torsades de pointes)</b> , Its use should be limited to no more than 7 days.</li> </ol>	<ol style="list-style-type: none"> <li><b>Sedation</b> (excitation may occur in children).</li> <li><b>Atropine-like actions</b> (dry mouth, blurred vision, urine retention).</li> <li><b>Postural hypotension</b></li> </ol>

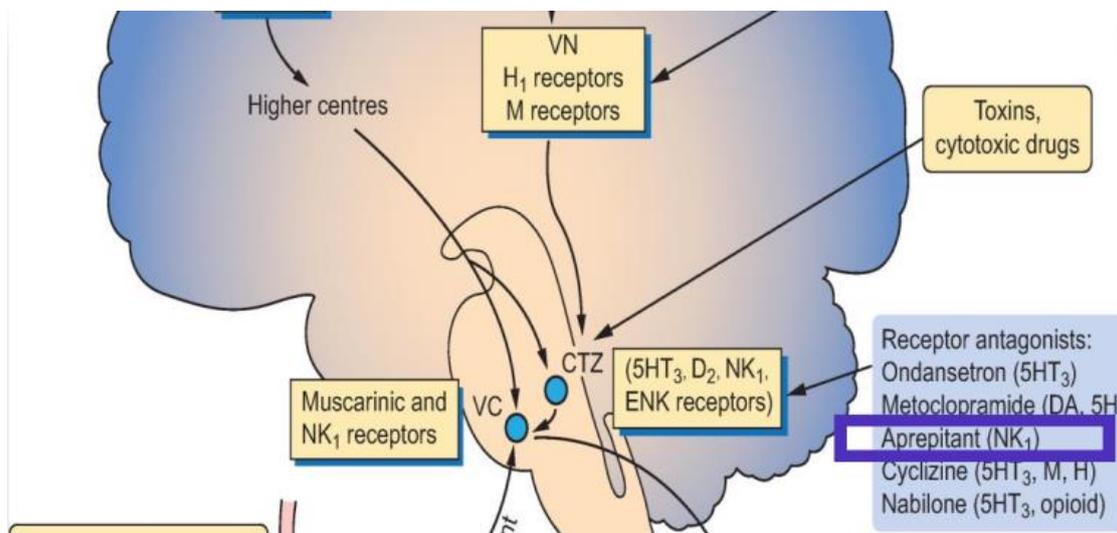
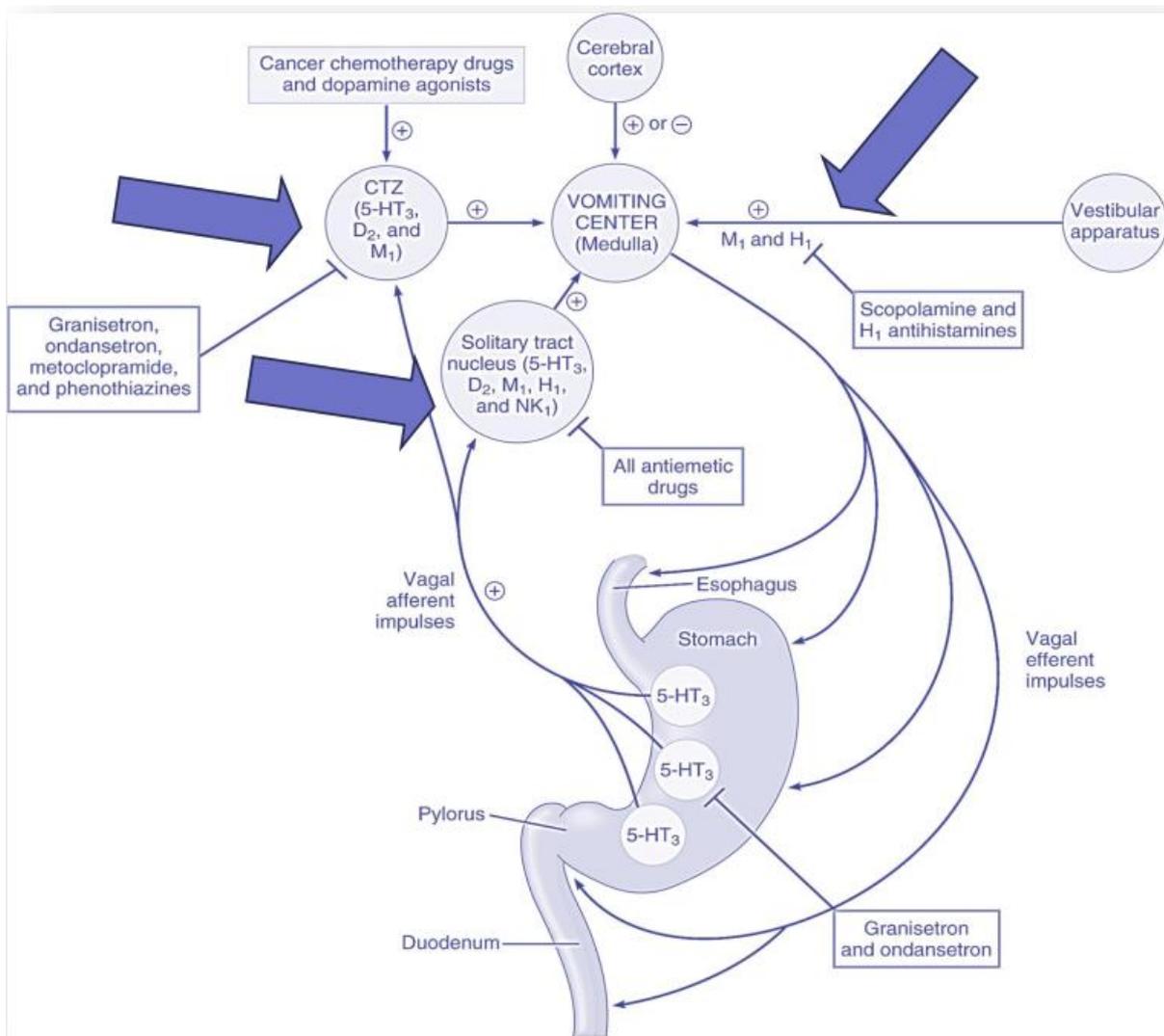
	<b>Muscarinic blockers</b>	<b>Neurokinin-1 receptor blockers</b>	<b>Cannabinoid derivatives</b>
<b>Examples</b>	<ul style="list-style-type: none"> <li>Hyoscine, Scopolamine</li> </ul>	<ul style="list-style-type: none"> <li>Aprepitant. <b>MCQ</b></li> </ul>	<ul style="list-style-type: none"> <li>Nabilone and Dronabinol</li> </ul>
<b>kinetics</b>	<ul style="list-style-type: none"> <li>They are used orally, injection, patches (preferable).</li> <li>Scopolamine is <b>available</b> as a skin patch that slowly releases the drug over 72 hours.</li> </ul>		
<b>Mechanism</b>	<ul style="list-style-type: none"> <li>They block <b>M1 receptors</b> in the vestibulo-cerebellar pathway, solitary tract nucleus &amp; chemoreceptor trigger zone (CTZ).</li> </ul>	<ul style="list-style-type: none"> <li>Acts centrally as <b>substance-P antagonist</b> by blocking NK-1 receptors in vagal afferent fibers in STN and CTZ.</li> </ul>	<ul style="list-style-type: none"> <li>It is a partial agonist at central and peripheral <b>cannabinoid receptors (CB1)</b>.</li> <li>The exact mechanism is <b>unclear</b>.</li> </ul>
<b>Uses</b>	<ul style="list-style-type: none"> <li>Prevention and treatment of vomiting due to <b>motion sickness</b>. <ul style="list-style-type: none"> <li>➤ Patches used in motion sickness before journey by 3-4 hours (<b>prophylactic therapy</b>)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>used in <b>combination with 5-HT3 blockers</b>.</li> <li><b>CINV prophylaxis</b>.</li> </ul>	<ul style="list-style-type: none"> <li><b>CINV</b> (In combination with other antiemetics).</li> <li>Patients who <b>fail to respond</b> to other conventional treat.</li> <li>They are also used as <b>appetite stimulants</b> in patients with advanced HIV.</li> </ul>
<b>Adverse effects</b>	<ol style="list-style-type: none"> <li>Blurred vision</li> <li>Dry mouth</li> <li>Urine retention</li> <li>Mydriasis</li> <li>Tachycardia</li> </ol>	<ul style="list-style-type: none"> <li>Diarrhea and fatigue</li> </ul>	<ol style="list-style-type: none"> <li>Sedation</li> <li>Hallucinations</li> <li>Mood changes</li> <li>Postural hypotension</li> <li>Drug abuse.</li> </ol>



**NB:**

- **5-HT<sub>3</sub> blockers:**

- First choice for prevention of moderate to **severe emesis**
- Their effects is **augmented by** combination with corticosteroids and NK<sub>1</sub> antagonists



## Other adjuvant antiemetics

	<i>I- Vitamin B6 (pyridoxin)</i>	<i>II- Corticosteroids</i>	<i>III- Benzodiazepines</i>
<b>Examples:</b>		<ul style="list-style-type: none"> <li>• Dexamethasone.</li> <li>• Methylprednisolone.</li> </ul>	<ul style="list-style-type: none"> <li>• Lorazepam.</li> <li>• Diazepam.</li> </ul>
<b>Antiemetic mechanism:</b>	<ul style="list-style-type: none"> <li>• May be related to the <b>balance between</b> GABA (CNS inhibitory transmitter) and glutamate (CNS excitatory transmitter).</li> </ul>	<ul style="list-style-type: none"> <li>• The exact mechanism is <b>unclear</b>.</li> </ul>	<ul style="list-style-type: none"> <li>• Allosteric facilitation of <b>central GABA inhibitory transmission</b></li> </ul>
<b>Uses as antiemetic:</b>	<ul style="list-style-type: none"> <li>• Vomiting in <b>pregnancy</b> <b>MCQ</b></li> <li>• Vomiting in <b>children</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Combined with</b> 5-HT-3 antagonists or NK-1 receptor antagonists to treat <b>CINV</b>.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>CINV</b> prophylaxis/treatment</li> </ul>

▪ **The choice of antiemetic according to the etiology:** مهم جدا جدا

Cause of vomiting	Treatment
<b>Motion sickness</b>	<ul style="list-style-type: none"> <li>• Muscarinic antagonists (Hyoscine)</li> <li>• Antihistamines (Dimenhydrinate)</li> </ul>
<b>Vomiting with pregnancy (morning sickness)</b>	<ul style="list-style-type: none"> <li>• Pyridoxine (B6)</li> <li>• Meclizine</li> </ul>
<b>Drug- induced vomiting (CTZ), uremia, gastritis</b>	<ul style="list-style-type: none"> <li>• Dopamine antagonists</li> </ul>
<b>Post operative nausea &amp; vomiting (PONV)</b>	<ul style="list-style-type: none"> <li>• Dopamine antagonists</li> <li>• 5-HT-3 antagonists</li> </ul>
<b>Vomiting due to cytotoxic drugs (CINV)</b>	<ul style="list-style-type: none"> <li>• 5-HT-3 antagonists</li> <li>• NK-1 antagonists</li> <li>• D2- antagonists</li> <li>• Glucocorticoids</li> <li>• Cannabinoid derivatives</li> </ul>