



# Lecture 1

## Antiemetic drugs

### Learning objectives

- ★ Classify the main different classes of antiemetic drugs according to their mechanism of action.
- ★ Know the characteristic pharmacokinetics & dynamics of different classes of antiemetic drugs.
- ★ Identify the selective drugs that can be used according to the cause of vomiting.
- ★ Learn the adjuvant antiemetics.
- ★ Describe the major side effects for the different classes of antiemetics.

- Additional Notes
- Explanation –Extra-
- Important

before starting, please check our [GIT block correction](#)

For any correction, suggestion or any useful information do not hesitate to contact us: [Pharmacology434@gmail.com](mailto:Pharmacology434@gmail.com)

# Vomiting:



**Definition:** Is a complex series of integrated events culminating in the forceful expulsion of **gastric contents** through the mouth.

**Why vomiting can be a valuable, life-saving physiological response ?**

Vomiting is an **adaptive** behavior that can work to eliminate **toxic** substances that have been ingested.

**Consequences of vomiting if severe :**

- **Dehydration**
- **Acid-base imbalance**
- **Electrolyte depletion**
- **Aspiration, pneumonia**

## Causes of Vomiting:

Nausea and vomiting may be manifestations of many conditions and diseases.

**Vomiting center respond to inputs from:**

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

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

**2)Disturbance of vestibular system:**

motion sickness (**H1 & M1** receptors)”H1 is different than H2 which we will take in the next Lec”.

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

GIT irritation, myocardial infarction, renal or biliary stones (5 HT<sub>3</sub> receptors)

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

\*CTZ is an area of medulla that communicate with vomiting center to initiate vomiting.

\*CTZ is physiologically **outside** BBB “ not completely covered by BBB”

\*CTZ contains **D<sub>2</sub> receptors, 5 HT<sub>3</sub> receptors, opioid receptor and Substance p.**

**stimulated by:**

- 1)Emetogenic drugs (opioids, general anesthetics, digitalis, L-dopa).
- 2)chemicals and toxins (blood, CSF).
- 3) Radiation.
- 4)Uremia.

The vomiting center is in Medulla which receive all the vomiting stimulation signals

we want to antagonize these receptors

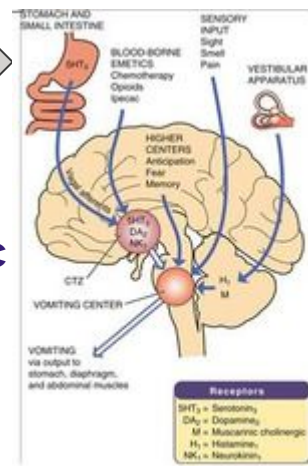
## Chemical transmitters & receptors involved in vomiting include:

- Ach (**Muscarinic receptors**)
- Dopamine (**D2**)
- Histamine (**Histaminergic receptors H1**)
- Serotonin (**5-HT3**)
- Substance P (**Neurokinin receptors, NK1**)
- Opioid (**Opioid receptors**)

## Classification of Antiemetic Drugs:

“from strongest to weakest “

1. 5-HT<sub>3</sub> antagonists
2. D<sub>2</sub> receptor antagonists
3. NK<sub>1</sub> antagonists
4. H<sub>1</sub>-receptor antagonists
5. Muscarinic receptor antagonists
6. Cannabinoids “ derived from marijuana which cause addiction so not used clinically nowadays”
7. Glucocorticoids



# Serotonin (5-HT<sub>3</sub>) antagonists

<b>Drugs</b>	Ondansetron, Granisetron
<b>pharmacodynamic and kinetic</b>	<ul style="list-style-type: none"><li>•Orally or parenterally,</li><li>•have <b>long</b> duration of action, first pass effect</li><li>•The most <b>potent</b> antiemetic drugs</li><li>•Act by blocking 5-HT<sub>3</sub> receptor centrally (<b>in vomiting center, CTZ</b>) and <u>peripherally</u> (5HT<sub>3</sub> receptors on GI vagal afferents).</li></ul>
<b>Uses</b>	<ul style="list-style-type: none"><li>● <u>First</u> choice for prevention of moderate to severe emesis:</li><li>● Their effects is <b>augmented</b> by combination with corticosteroids and NK<sub>1</sub> antagonists "if vomiting did not stop for the patient we mix"</li><li>● Post-radiation NV &amp; Post-operative NV "NV = nausea and vomiting"</li><li>● Chemotherapy-induced nausea and vomiting (<b>CINV</b>) especially <b>cisplatin</b> <small>Cisplatin is anti-cancer drug which is a potent NV</small></li></ul>
<b>Side effects</b>	Well tolerated, Headache, dizziness and constipation, minor ECG abnormalities ( <b>QT prolongation</b> )

# D<sub>2</sub> receptor antagonists

types	<p><b>Prokinetics drugs</b></p> <p>Drugs increase kinesis الحركة (increased GI motility &amp; gastric emptying)</p>		<p><b>Neuroleptics</b> ( antipsychotics)</p>	
Drugs	<p><b>Domperidone</b> Oral</p>	<p><b>Metoclopramide</b> Oral, I.V</p>	<p><b>Chlorpromazine</b> (CPZ)</p>	<p><b>Droperidol</b></p>
MOA	<p><b>block D<sub>2</sub> dopamine receptors in the CTZ</b></p>			
Uses	<p><b>Antiemetics (blocking D2 receptors in CTZ)</b></p> <ul style="list-style-type: none"> <li>• Effective against vomiting due to cytotoxic drugs, gastroenteritis, surgery, toxins, uremia, radiation</li> </ul> <p><b>Prokinetic (5 HT4 agonist activity)</b></p> <ul style="list-style-type: none"> <li>• <b>Gastroesophageal reflux disease (GERD)</b></li> <li>• <b>Gastroparesis</b> (impaired gastric emptying after surgery)</li> <li>• Diabetic</li> </ul>		<p><b>1-postoperative vomiting</b> <b>2-chemotherapy-induced emesis</b></p>	

# D<sub>2</sub> receptor antagonists

<p>types</p>	<p><b>Prokinetics drugs</b></p> <p>Drugs increase kinesis الحركة (increased GI motility &amp; gastric emptying)</p>	<p><b>Neuroleptics</b> <b>(Antipsychotic)</b></p>
<p>Side effects</p>	<p><b>Dyskinesia (extra-pyramidal side effects)</b></p> <p>Galactorrhea, menstrual disorders, impotence</p> <p>Postural hypotension (<math>\alpha</math>-blocking action)</p> <p>Sedation, drowsiness</p>	<ul style="list-style-type: none"><li>● <b>Extra pyramidal symptoms</b></li><li>● Sedation</li><li>● Postural hypotension</li></ul>
	<p><b>Metoclopramide <u>crosses</u> BBB but domperidone <u>cannot</u> (both have antiemetic effects as CTZ has incomplete blood brain barrier)</b></p>	

## Neurokinin1 (NK1) receptor antagonists

Drug	<b>Aprepitant</b> Orally
MOA	Acts centrally as <b>substance P antagonist</b> by blocking neurokinin 1 receptors in vagal afferent fibers in STN and area postrema
Uses	Usually combined with 5-HT <sub>3</sub> antagonists and corticosteroids in <b>prevention of chemotherapy-induced nausea and vomiting and post-operative NV</b> Better to be combined

## H<sub>1</sub>-receptor antagonists

Drugs <small>1<sup>st</sup> generation anti histaminic</small>	<b>Diphenhydramine</b>	<b>Promethazine</b>	<b>Meclizine</b>	<b>Cyclizine</b>
Uses	<b>Motion sickness</b> Morning sickness in pregnancy <b>Promethazine:</b> severe morning sickness of pregnancy (if only essential) ★ can be used to treat <b>extrapyramidal side effect</b> especially <b>diphenhydramine</b>			
Side effects	Prominent sedation , Hypotension , Anticholinergic effects or atropine like actions ( <b>dry mouth, dilated pupils, urinary retention, constipation</b> ).			

# Muscarinic receptor antagonists

<b>Drug</b>	<b>Hyoscine (scopolamine)</b> <div data-bbox="1387 175 1856 328" style="border: 1px solid black; padding: 5px; background-color: #e0e0e0;">Non selective. prominent CNS effect. Antiemetics action more than atropine</div>
	<b>Orally, injection, patches (preferable)</b> <b>Patches used in motion sickness before journey by 3-4 hours (prophylactic therapy)</b>
<b>Uses</b>	<b>Transdermal patches in motion sickness (applied behind the external ear).</b> <b>Reduce impulses from vestibular apparatus</b> <b>Not in chemotherapy-induced vomiting</b>
<b>Side effects</b>	<b>Sedation</b> <b>Tachycardia, blurred vision, dry mouth, constipation, urinary retention (atropine-like action)</b>



# Glucocorticoids

Drug	Dexamethasone	Methylprednisolone
Uses	<p><b>chemotherapy-induced vomiting (cancer patients)</b> Treatment of asthma, immune diseases, during transplantation (decrease rejection of organ), antiemetics</p>	
	<p><b>combined with 5-HT<sub>3</sub> antagonists or NK1 receptor antagonists</b></p>	
Side effects	<p><b>Hyperglycemia, Hypertension (due to salt retention), Cataract, Osteoporosis, Increased intraocular pressure, Increased susceptibility to infection (due to decrease immunity), Increased appetite &amp; obesity, increase body weight (due to water &amp; fluid retention)</b> <b>Avoid giving these drugs in women who has high risk of osteoporosis</b></p>	

# The choice of antiemetic depends on the etiology

<b>Motion sickness</b>	<b>Muscarinic antagonists</b> <b>Antihistaminics</b>
<b>Vomiting with pregnancy (morning sickness)</b>	<b>avoid all drugs in the first trimester</b> <b>Pyridoxine (B6)</b> <b>Promethazine (late pregnancy).</b>
<b>Drug- induced vomiting (CTZ), uremia, gastritis, post surgery</b>	<b>Dopamine antagonists</b>
<b>Post operative nausea &amp; vomiting</b>	<b>Dopamine antagonists</b>
<b>Vomiting due to cytotoxic drugs</b>	<b>5-HT<sub>3</sub> antagonists</b> <b>NK<sub>1</sub> antagonists</b> <b>D<sub>2</sub>- antagonists</b> <b>Glucocorticoids</b>

# MCQ,s

1- All the following combination are used in 5-HT<sub>3</sub> antagonists except?

- A) Corticosteroides
- B) NK<sub>1</sub> antagonists
- C) 5-HT<sub>3</sub>
- D) Histamine

2- A patient is under treatment plan for cancer was complaining of constipation, which of the following drugs cause this symptom?

- A) Ondansetron
- B) Chlorpromazine
- C) Domperidone
- D) Droperidol

3- A pregnant woman came to the clinic with a severe morning sickness which of the following is the best drug of choice in this case?

- A) Diphenhydramine
- B) Promethazine
- C) Meclizine
- D) Cyclizine

4- Which of the following drugs NOT used in chemotherapy induced vomiting?

- A) Aprepitant
- B) Hyoscine
- C) Dexamethasone
- D) Neuroleptics

5- A woman has high risk of osteoporosis, which of the following drugs is contraindicated in her case?

- A) Metoclopramide
- B) Methylprednisolone
- C) Meclizine
- D) Chlorpromazine

6- Ahmed is going on a journey with his friends but he has motion sickness. Which of the following is a prophylactic therapy in his case?

- A) Hyoscine
- B) Cyclizine
- C) Droperidol
- D) Aprepitant

4- B

5- B

6- A

# Good luck!

## Done by Pharmacology team

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For any correction, suggestion or any useful information do not hesitate to contact  
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