



## 2: Antiemetics

### 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.

### Color index

● extra information and further explanation

● **important**

● **doctors notes**

● **Drugs names**

● **Mnemonics**



[Kindly check the editing file before studying this document](#)

# Introduction

## Vomiting

**What is vomiting?** Sometimes, It is a protective mechanism

is forceful expulsion of gastric contents through the mouth.

**Can vomiting be considered as a disease?**

It is a manifestation of many conditions and diseases. **it is a sign of disease**

**Consequences of vomiting Severe vomiting may result in :**

- Dehydration
  - Acid-base imbalance
  - Electrolyte depletion
  - Aspiration, pneumonia
- one of the serious complication, aspiration while lying down especially common in children**

**How is vomiting induced?**

**Vomiting center respond to inputs from:**

### 1. Higher cortical centers stimulation

**(CNS):**

- ✓ Emotional factors **happiness or sadness**
- ✓ Nauseating smells or sights

### 2. Disturbance of vestibular system:

**Remember the two M's**

- ✓ Motion sickness (H1 & M1 receptors)
- Morning sickness (especially in pregnancy)

### 3. The periphery (Pharynx, GIT) via sensory nerves it is stimulated by:

- ✓ GIT irritation **e.g. gastritis**
- ✓ Myocardial infarction
- ✓ Renal or biliary stones
- post surgery: as side effect of anesthetic drugs**
- ✓ Cancer
- ✓ food poisoning

We have this receptor in two place where they can induce the vomiting  
- GI tract. - CTZ

**Add a point:**  
✓ **Estrogen and hormonal fluctuation, especially in pregnancy**

### 4. Stimulation of chemoreceptor trigger zone (CTZ)

- CTZ is an area of medulla that communicate with vomiting center to initiate vomiting.
- CTZ is physiologically outside BBB. (so any changes in the contents of the CSF or the blood will trigger this receptors, such as antihypertensive drugs. that's why some drugs can't cross BBB and still can block the receptors of the CTZ -because they are distributed in the blood-)
- CTZ contains D<sub>2</sub> receptors, 5HT<sub>3</sub> receptors & opioid receptors.
- **stimulated by:**
  - ✓ Emetogenic drugs **Can cross BBB** (opioids stimulate the opioid receptors, general anesthetics, digitalis, L-dopa stimulates D2 receptors, anticancer drugs
  - ✓ chemicals and toxins 'chemical substance (including drugs) cannot cross BBB' (blood, CSF).
  - ✓ Radiation.
  - ✓ Uremia urea inside blood.

# To understand !

This slide is NOT extra

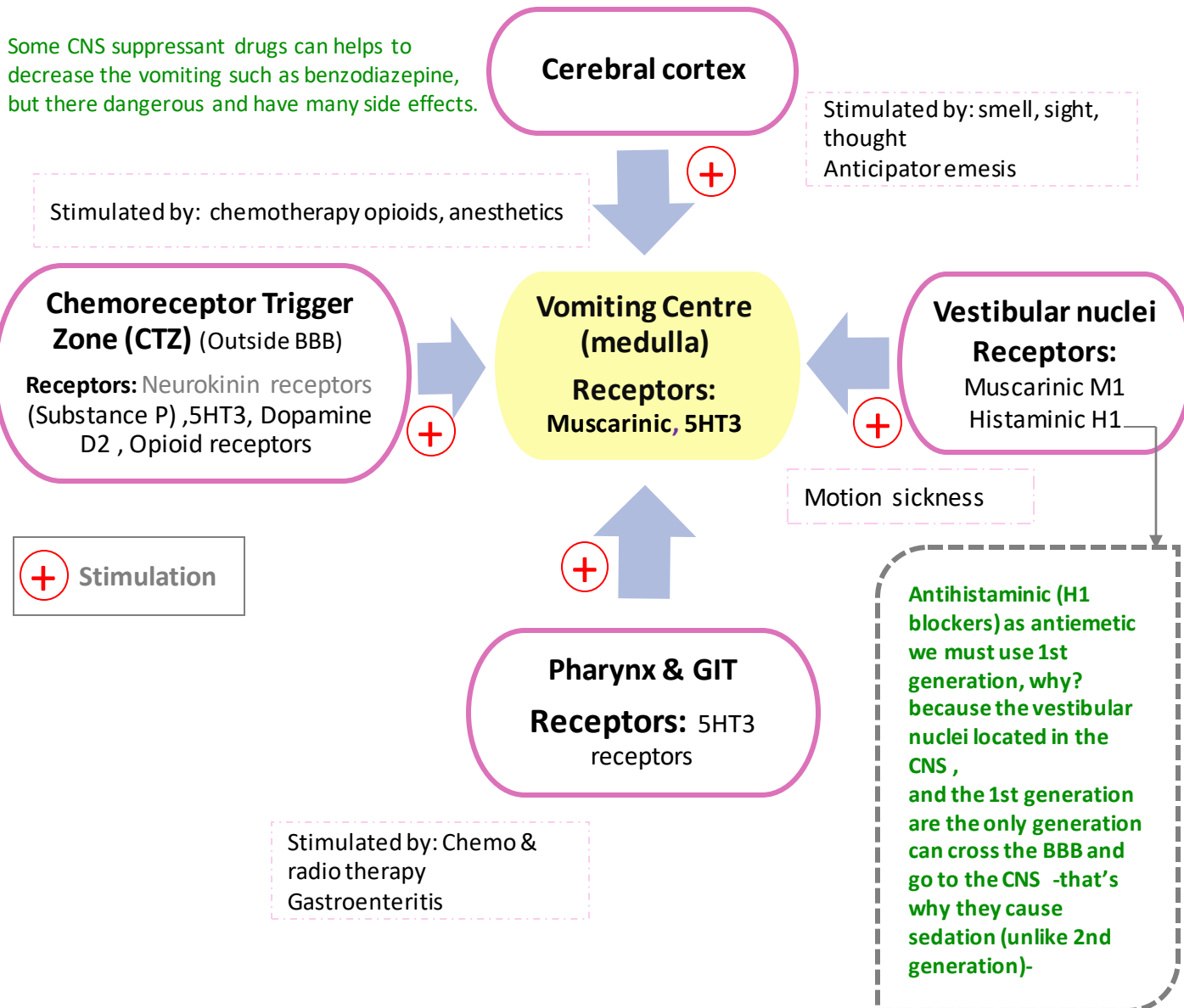
## Pathophysiology of Emesis



Helpful  
video 15:53

- Antiemetics are all blockers
- you can noticed that many places inducing vomiting has 5HT3 receptors

Some CNS suppressant drugs can helps to decrease the vomiting such as benzodiazepine, but there dangerous and have many side effects.



المقصود هنا إن أي جزء من الأجزاء اللي باللون البنفسجي (مثلاً cerebral cortex أو CTZ) لمن يتحفز بواسطة أي محفز لها مثل ما هو مذكور في المربعات الوردية- تحفيزها راح يؤدي إلى تحفيز vomiting center بالتالي الشخص راح يبدا يصير عنده vomiting

Dr. ishfaq is highly recommend us that after studying this lecture, to get back to this slide and write down every single drugs in a correct place to examine ourselves.

# Overview on antiemetic drugs




Classification	Receptors	Neurotransmitter	Drugs
5-HT3 antagonists	5-HT3	Serotonin	<b>Ondansetron</b> <b>Granisetron</b> Setron = serotonin ممكن نقرأ اخر مقطع منهم (الست الحديدية) فهم أقوى مجموعة هنا
D2 receptor antagonists	Dopaminergic receptors (D2)	Dopamine نوم دن نوم دن.. كأنه صوت شيء يتحرك	Prokinetics drugs: <b>Domperidone, Metoclopramide</b> Neuroleptics: <b>Chlorpromazine (CPZ), droperidol</b>
NK1 antagonists	Neurokinin receptors (NK1 receptors)	Substance P	متى صار كلو برا المعدة! يعني استقرغ أو رجع <b>Aprepitant</b> Apparently (Aprepitant) this drug <u>Nice Kind</u> (NK1) to be <u>added</u> to other drugs ( <u>adjuvant</u> )
H1-receptor antagonists*	(Histaminergic receptors H1)	هاي يا ستى (hi-sta-mine) دي فينها وفيها الدراما- phenhy-dramine Histamine	<b>Diphenhydramine, Promethazine, Meclizine, Cyclizine</b> حسبنا ان اخوي متحسن عن اول My bro=Pro - Methazine أحس أول (H1) السبيل كان زين أحس أول (H1) كان يلعب ميسي زين
Muscarinic receptor antagonists	(Muscarinic receptors)	Ach	<b>Hyoscine (scopolamine)</b>
Glucocorticoids	-	-	<b>Dexamethasone, methylprednisolone</b> نفس اخر مقطع من الكورتيزون
Cannabinoids	Cannabinoid receptors		They are not clinically use as antiemetic
Opioid	Opioid receptors	Opioid	

\* We do not prefer to use the 2<sup>nd</sup> generation of Antihistamine such as loratidine because they do not have sedative effect so they are use in allergy rather than antiemetic drugs

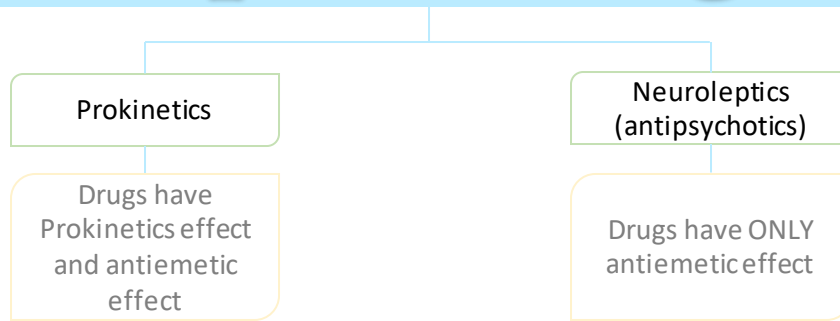
\*\* EXTRA :

Receptor	Function
5-HT3	vomiting
5-HT4	Gut motility
D2	Involved in many action e.g. motor , info processing ..etc.
H1	mitigate certain inflammatory processes in associated cells

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

Drug	<p><b><u>Granisetron , Ondansetron</u></b>      Setron = serotonin</p> <p>My grandpa is one of the oncology team</p>
Action/Mech. of action	<p><b>Act by blocking 5-HT<sub>3</sub> receptor:</b>      5-HT antagonist drugs are potent because they have dual action on both stomach and brain.</p> <ul style="list-style-type: none"> <li>centrally (in vomiting center, CTZ)</li> <li>peripherally (5HT<sub>3</sub> receptors on GI vagal afferents).</li> </ul>
Pharmacokinetics	<ul style="list-style-type: none"> <li>Orally or parenterally (<b>used parenterally for pts with chemotherapy</b>).</li> <li>have long duration of action, first pass effect</li> <li><b>The most potent antiemetic drugs</b>      <b>Set iron = (الست الحديدية) يمكن نقرأ اخر مقطع منهم</b></li> </ul> <p>(However we will combine it with corticosteroids and NK<sub>1</sub> antagonists. To have better and stronger effect)</p>
Indications	<p><b>First choice for prevention of moderate to severe emesis :</b></p> <ul style="list-style-type: none"> <li><b>Chemotherapy-induced nausea and vomiting (CINV)</b> especially <b>cisplatin</b> (it is a chemo drugs which cause sever vomiting because it acts on the vomiting center or CTZ)</li> <li><b>Post-radiation NV</b> (nausea and vomiting) &amp; <b>Post-operative NV</b> (nausea and vomiting) because the anesthetic drugs cause vomiting as a side effect.</li> </ul> <p>Their effects is augmented by combination with <b>corticosteroids and NK<sub>1</sub> antagonists.</b> (we use this combination if 5-HT<sub>3</sub> isn't effective with the patient)</p> <p>We will not combine it with H1 blockers here, why? So In the case which does not control with 5-HT<sub>3</sub>, for sure it will not ne controlled with H1 blockers Because it very weaker than them. So the best choice is corticosteroids.</p>
ADRs	<ul style="list-style-type: none"> <li>○ Are minimal as they are well tolerated.</li> <li> Headache, dizziness</li> <li> constipation.</li> <li> Minor ECG abnormalities (QT prolongation) <b>it is produced by the action of 5-HT<sub>4</sub> not 3</b> and it is very minor, so these drugs are not contraindicated in patients with heart disease</li> </ul>

# D2 receptor antagonists



Drug	Prokinetics	
	Metoclopramide	Domperidone <i>it's safer.</i>
M.O.A	<ul style="list-style-type: none"> <li>As Prokinetics: 5-HT4 agonist activity</li> <li>As Antiemetics: blocking D2 receptors in CTZ</li> <li>Both has antiemetic effect as CTZ has incomplete BBB</li> </ul>	
P.K	Oral, I.V	Oral
Pharmacodynamic	Are prokinetic agents, they increase: <ul style="list-style-type: none"> <li>Upper GI motility <i>that's why we can't use it for constipation</i></li> <li>Gastric emptying).</li> </ul>	
	Can cross BBB <i>So may have high risk of toxicity</i>	Can not cross BBB in significant amount (it has antiemetic effect as CTZ has incomplete brain barrier)
Indications	<ul style="list-style-type: none"> <li>As Prokinetic:               <ul style="list-style-type: none"> <li>Gastroesophageal reflux disease (GERD) <i>it increase the motility to get rid of the food that's will decrease the acidity.</i></li> <li>Gastroparesis (impaired gastric emptying after surgery, or in diabetic patients with peripheral neuropathy)</li> </ul> </li> <li>As Antiemetics               <ul style="list-style-type: none"> <li>Effective against vomiting due cytotoxic drugs, gastroenteritis, surgery, toxins, uremia, radiation</li> </ul> </li> </ul>	
	<ul style="list-style-type: none"> <li><i>Meta u close il pyramids Metoclopramide = extrapyramidal</i></li> <li>Dyskinesia (extra-pyramidal side effects) parkinsonism like effect</li> <li>Galactorrhea, menstrual disorders, impotence, hyperprolactinemia <i>which can cause infertility in female</i></li> <li>Postural hypotension (<math>\alpha</math>-blocking action).</li> <li>Sedation, drowsiness</li> </ul>	<ul style="list-style-type: none"> <li><i>Not of them because it can not cross BBB</i></li> <li><i>So if we have patient with parkinsonism and he has vomiting we can use this drug</i></li> </ul>
ADRs	<ul style="list-style-type: none"> <li><i>Especially if it combine with antihypertensive drugs</i></li> </ul>	

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

Drug	<b>Neuroleptics (antipsychotics)</b> <p style="color: green; font-size: small;">Not commonly use Usually psychotic patients , So we use prokinetics instead</p>
M.O.A	Chlorpromazine(CPZ), Droperidol
M.O.A	block D <sub>2</sub> dopamine receptors in the CTZ
Indications	<ul style="list-style-type: none"> <li>• Postoperative vomiting</li> <li>• Chemotherapy-induced emesis.</li> </ul> <div style="border: 1px solid green; border-radius: 10px; padding: 5px; width: fit-content; margin-left: 100px; color: green; font-size: small;">             Just we can use them in sever and resistant cases, although it is not a good choice due to its side effects         </div>
ADRs	<ul style="list-style-type: none"> <li>🌧️ Extra pyramidal symptoms <span style="color: green;">because they block D<sub>2</sub> centrally.</span></li> <li>🌧️ Sedation</li> <li>🩸 Postural hypotension</li> </ul>

# Neurokinin1 (NK1) receptor antagonists

Drug	<div style="border: 1px dashed cyan; border-radius: 10px; padding: 5px; display: inline-block; color: cyan; font-size: small;">Is he <u>A</u> pre patient ?</div> <span style="font-size: large; color: blue; margin-left: 20px;"><b>Aprepitant</b></span>
M.O.A	Acts centrally as <u>substance P antagonist</u> by blocking neurokinin 1 receptors in vagal afferent fibers in substantial nigara (STN) and area postrema.
P.K	Orally
Notes	Usually combined with 5-HT <sub>3</sub> antagonists and corticosteroids in prevention of chemotherapy-induced nausea and vomiting and post- operative NV. <span style="color: green;">we use this combination if the patient is not response to 5-TH3 antagonist drugs</span>

As antiemetic drug can help if it is combine with other drugs because it has a different Mechanism of action . But it is not that stronger to be given alone.

# H1-receptor antagonists








Drug	Promethazine, Diphenhydramine, Meclizine, Cyclizine (meclizine and cyclizine has teratogenic effect)
Indications	<ul style="list-style-type: none"> <li>▪ Motion sickness</li> <li>▪ Morning sickness in pregnancy</li> <li>▪ Promethazine: severe morning sickness of pregnancy (if only essential).</li> </ul> <p>Ideally we don't give pregnant lady Antihistaminic because it has teratogenic effect, but she has sever morning sickness she may develop dehydration so we should give her the safest Antihistaminic which is Promethazine in combination with vitamin B6 which has antiemetic effect</p>
ADRs	<ul style="list-style-type: none"> <li>🧠 Prominent sedation</li> <li>🫀 Hypotension (<math>\alpha</math>-blocking action).</li> <li>🚽 Anticholinergic effects or atropine like actions (dry mouth, dilated pupils, urinary retention, constipation). (glaucoma and prostatic hypertrophy are contraindications)</li> </ul>

# Muscarinic receptor antagonists

Drug	Hyoscine (scopolamine) <small>هذا الخير السكوب لمين؟ This scope-lamine</small>
M.O.A	Reduce impulses from vestibular apparatus
P.K	Orally, injection, patches
Indication	<ul style="list-style-type: none"> <li>▪ Used as transdermal patches in <b>motion sickness</b> (applied to the postauricular area). <b>Better to take it before the induction of vomiting</b> يعني لو عنده دوار من الطيران يأخذ الدواء قبل رحلة الطيران</li> <li>▪ <b>Not in chemotherapy-induced vomiting</b></li> </ul>
ADRs	<ul style="list-style-type: none"> <li>🧠 Sedation</li> <li>🚽 Tachycardia, blurred vision, dry mouth, constipation, urinary retention (atropine –like actions). (glaucoma, prostatic hypertrophy are contraindications)</li> </ul>



# Glucocorticoids

Drug	Dexamethasone - methylprednisolone	
Indications	chemotherapy-induced vomiting (combined with 5-HT <sub>3</sub> antagonists or NK1 receptor antagonists. <b>Sometimes we combine all the 3 drugs together</b> )	
ADRS	<ul style="list-style-type: none"> <li> Hyperglycemia</li> <li> Hypertension <b>because glucocorticoids can cause water retention</b></li> <li> Cataract</li> <li> Osteoporosis <b>it effect the Ca absorption, women should be careful</b></li> <li> Increased intraocular pressure <b>cause glaucoma</b></li> <li> Increased susceptibility to infection <b>glucocorticoids are immunosuppressant drugs</b></li> <li> Increased appetite &amp; obesity (patients who are on glucocorticoids therapy gain weight, why? Because these drugs cause water retention and increase appetite)</li> </ul>	Most of side effects are hyper or increased

## Choices of antiemetic :

Motion sickness	Vomiting with pregnancy (morning sickness)	Drug- induced vomiting (CTZ), uremia, gastritis	Post operative nausea & vomiting	Vomiting due to cytotoxic drugs (Chemotherapy-induced nausea and vomiting)	
Antihistaminic	Avoid all drugs in the first trimester	Dopamine antagonists	Dopamine antagonists	5-HT <sub>3</sub> antagonists	أول واحد هو أفضل خيار ثم اللي بعده وهكذا ↓
Muscarinic antagonists	Pyridoxine (B6)			NK1 antagonists	
	Promethazine (late pregnancy).			D2- antagonists	
				Glucocorticoids	

# Summary

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

Ondansetron , Granisetron .

The **most potent** antiemetic drugs.  
-Their effects is augmented by combination with **corticosteroids** and **NK<sub>1</sub> antagonists**.

**First choice for prevention of moderate to severe emesis:**

- 1- Chemotherapy-induced nausea and vomiting (CINV) especially **cisplatin**.
- 2- Post-radiation NV& Post-operative NV.

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

**Prokinetics drugs:**

**Metoclopramide**,  
**Domperidone**

**Uses:**

- 1- antiemetic (**blocking D<sub>2</sub> receptors in CTZ**)
- 2- prokinetic (**5-HT<sub>4</sub> agonist**)

**Metoclopramide** crosses BBB while **Domperidone** cannot

**Neuroleptics**

**(antipsychotics):**

**Chlorpromazine (CPZ)**,  
**droperidol**

-used for postoperative vomiting and chemotherapy-induced emesis

## 3-NK<sub>1</sub> antagonists : Aprepitant .

-Usually combined with **5-HT<sub>3</sub> antagonists** and **corticosteroids** in prevention of chemotherapy-induced nausea and vomiting and post-operative NV.

**4-H<sub>1</sub>-receptor antagonists** : **diphenhydramine**, **promethazine**, **meclizine**, and **cyclizine** .

**-Uses :**

- 1-Motion sickness.
- 2-Morning sickness in pregnancy.
- 3-Promethazine: severe morning sickness of pregnancy (**if only essential**).

## 5-Muscarinic receptor antagonists:

**Hyoscine**

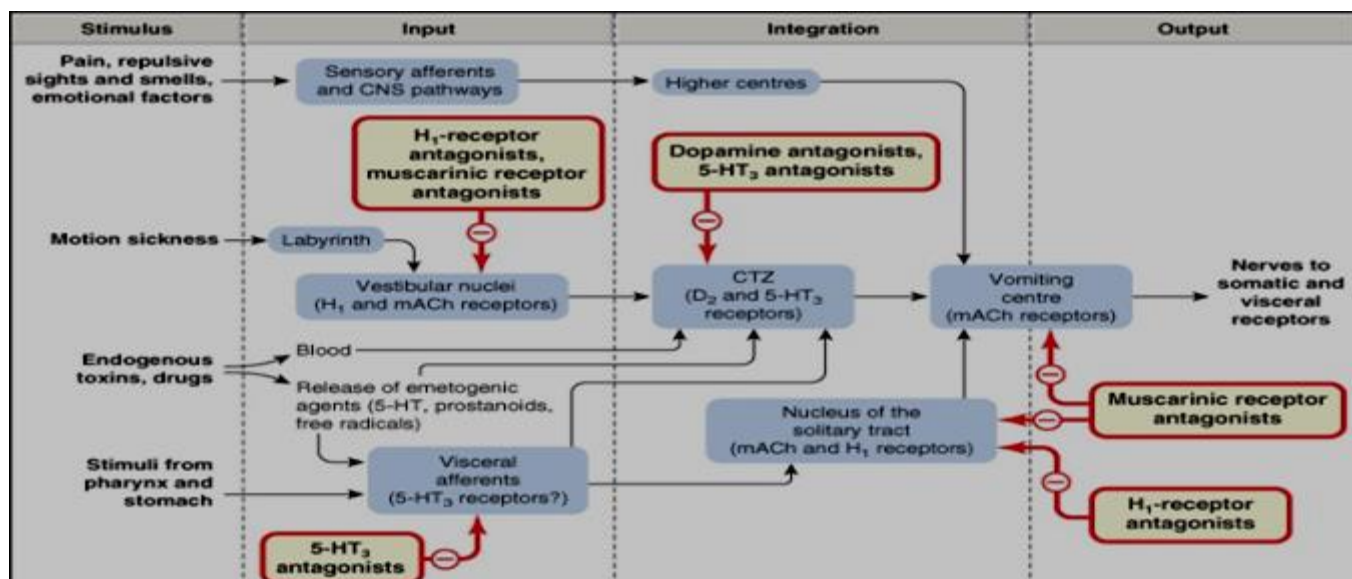
Used as **transdermal patches** in motion sickness

ADRs: Sedation, tachycardia, blurred vision (atropine like effect)

**7-Glucocorticoids:** **Dexamethasone** - **methylprednisolone** .

-Used in chemotherapy-induced vomiting.

**-combined with 5-HT<sub>3</sub> antagonists or NK<sub>1</sub> receptor antagonists.**



# MCQs

1. A 68-year-old patient is diagnosed with ovarian cancer. She begins using cisplatin but becomes nauseous and suffers from severe vomiting. Which of the following medications would be most effective to counteract the emesis in this patient ?

- A. Droperidol.                                      B. Ondansetron .                                      C. Aprepitant .

2. A patient is receiving treatment with paracetamol prior to headache to help him to relief his pain, later he develop nausea and vomiting after overdose toxicity. Which of the following antiemetic drug can be used in this patient?

- A. Ondansetron                                      B. Domperidone.                                      C. Aprepitant

3. Domperidone can increase the upper G.I motility and doesn't cause diarrhea by acting as?

- A. 5-HT3 antagonist.                                      B. 5-HT4 agonist                                      C. D2 Antagonist

4. Which one of the following is the target of Ondansetron as antiemetic drugs?

- A. 5-HT3 antagonist.                                      B. H1 Antagonist                                      C. D Antagonist

5. 42 years old diabetic man had an appendectomy , after surgery he had an impaired gastric emptying. Which of the following is the best drug for him ?

- A. Domperidone                                      B. Granisteron                                      C. hyoscine

6. Which of the following Antiemetic drugs is contraindicated for Parkinson patient due to its Extrapyrimalid symptoms ?

- A. Metoclopramide                                      B. Domperidone                                      C. Aprepitant

7. A patient who is on chemotherby have sever nausea and vomiting, and he was initially be given ondansetron but it does not control his case, Which of the following could be the best additive drug?\*\*\*

- A. Aprepitant                                      B . Methylprednisolone                                      C. Cyclizine

8. 40 years old man with a history of glaucoma complains of nausea and vomiting. Which of the following should be avoided ?

- A. Meclizine                                      B. Domperidone                                      C. Dexamethasone

9. 28 years old lady visited planning to go on vacation , she visited a local clinic asking for something to help with her motion sickness. What would you recommend ?

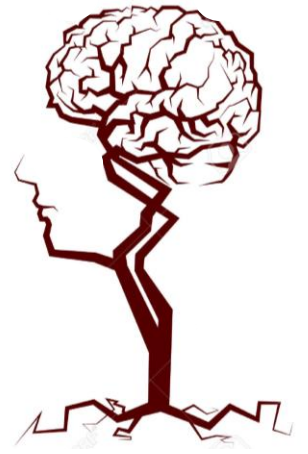
- A. Hyoscine                                      B. Dexamethasone                                      C. Chlorpromazine

10. 35 years old pregnant women visited her O.B. complaining of sever nausea in the morning. What would you recommend for her?

- A. Promethazine                                      B. Cyclizine                                      C. Hyoscine

\*\* Dr. Ishfaq said, although both of them is correct. But in the exam if you have the both A & B the most potent is Glucocorticoid and you have to choose it.

1) B  
2) B  
3) B  
4) A  
5) A  
6) A  
7) B  
8) A  
9) A  
10) A



إِنَّ فِي ذَلِكَ لَآيَاتٍ لِّقَوْمٍ يَتَفَكَّرُونَ ﴿٣٦﴾

## قادة فريق علم الأدوية :

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### References :

- 1- 436 Prof.Hanan's slides & notes
- 2- 436 Dr.Ishfaq notes



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