



PASSION ACADEMIC TEAM



Sheet# 6

*YU - MEDICINE*

# GASTROINTESTINAL SYSTEM

Lec. Title : Antiemetics .

Written By : Assem A Khatatbeh  
Maram Alkhaldi

IF YOU COME BY ANY MISTAKE , PLEASE KINDLY REPORT IT TO  
[SHAGHAFBATCH@GMAIL.COM](mailto:SHAGHAFBATCH@GMAIL.COM)

**#note :antibiotic usually cause mixed jaundice but erythromycin cause cholestatic jaundice**

## **Pharmacology -Antiemetic**

### **What is an Antiemetic?**

**Emesis:** The involuntary expulsion of the stomach's contents through the mouth. It serves as a protective function to rid the body of harmful substances that have been ingested, rather than allowing them to be retained and absorbed by the intestine. An antiemetic is a drug that completely inhibits or reduces vomiting and nausea.

### **Common Uses of Antiemetics**

- Used before and after surgery to prevent nausea after administration of anesthesia
- Motion sickness
- Nausea associated with Chemotherapy and Chemoradiation patients
- Prevent dehydration with gastroenteritis; more harmful in younger and older age groups

**#slide 5 very important**

### **What is the Physiological Process of Emesis?**

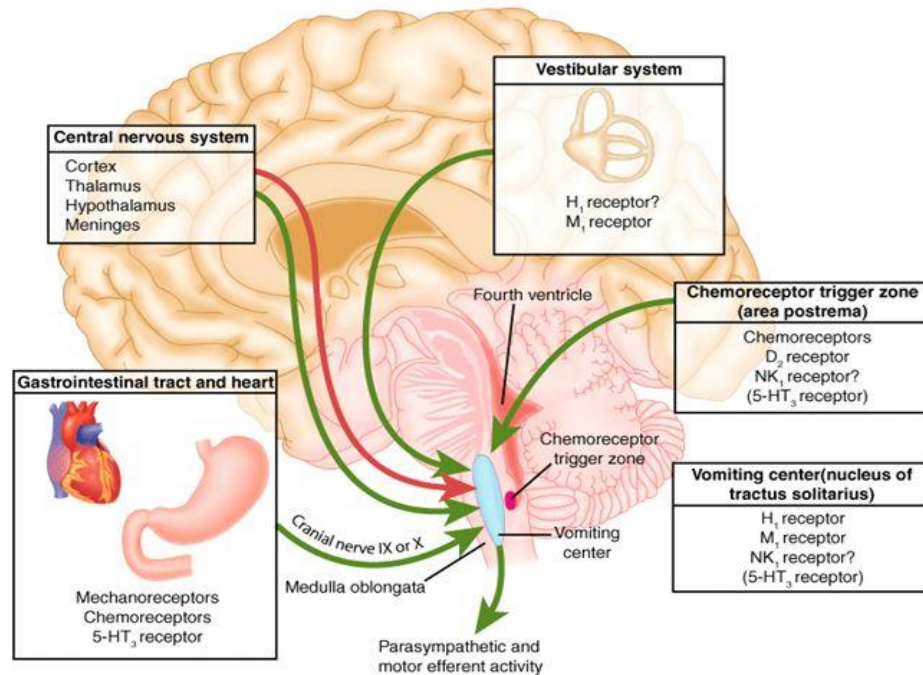
**#look at the pic below**

**# Vomiting Center- Coordinates activities of the nearby neural structures to produce a complex patterned response, resulting in the processing and action of the vomiting reflex. The center is located in the medulla. The motor component is controlled by both somatic and autonomic systems, meaning that both voluntary and involuntary systems are involved in the process. located in the nucleus solitary tract (blue color)**

**#near to the vomiting center there is Chemoreceptor Trigger Zone (red color)- Located in the medulla of the brain. It has a defensive blood-brain barrier for detecting circulating toxins in the blood and cerebrospinal fluid (CSF), and is sensitive to a number of circulating emetic agents, including morphine. When**

activated, the CTZ does not initiate vomiting itself, but relays stimuli to the integrative vomiting center which produces the actual act of emesis. it is affected by chemicals (drugs /toxin)these chemicals stimulate CTZ which will stimulate the vomiting center

## Chemoreceptor Trigger Zone (CTZ)



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology*, 11th Edition: <http://www.accessmedicine.com>  
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**#substance that stimulate CTZ and cause vomiting:**

**1-digoxin**(cardiac glycoside)

**2-dopamine** :also the drugs that have dopamine like action :**1-l-dopa**

**2-bromocriptine**

**3-opioids:morfine and its derivative /apomorphone** (morfine is emetic because it stimulate the CTZ)

**4-cholenergetic agonist :acetyline**

**5-cytotoxic drugs:anticancerdrugs:chemotherapy**

**####all these are emetics**

**#vomiting center is affected by signals from**

**1-CTZ**

**2-signals from cortex**

senses such as 1-smell :stimulate the smell center in the cerebral cortex which sends signals to the vomiting center 2-vision 3-emotions(anticipations in general):pain /headache/fear

**3-signals from GIT(visceral stimulation):**

any irritation in the GIT produce signal sends them to the vomiting center

**e.g: gastroenteritis** (may due to microbe produce toxin and make irritation in the mucosa >>signals may go to the vomiting center )

**##things cause irritation**

**1-bacteria 2-bacterial toxin 3-drugs such as cytotoxic drugs**

**##note : any drug may cause vomiting by 2 ways :**

**1-itself cause stimulation to the CTZ**

**2-by its irritation of GIT cause vomiting**

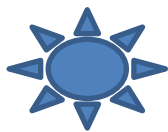
**4-from the internal ear(vestibular stimulation)**

>>due to motion >>sends signals from the vestibular part of the internal ear to the vomiting center

**#remember : internal ear has 2 parts :**

**1-cocular part >> السمع**

**2-vestibular part >> الاتزان**



**#the receptors مهم**

#receptors are very important >because it gives you clue about the kind of antiemetic that is effective> and if you give other antiemetic it may not be effective

**NEUROTRANSMITTERS Involved in Emesis:**

Acetylcholine

Histamine 1

Dopamine 2

Serotonin 3



**1#GIT>>SEROTONIN>>**it is responsible of stimulation and sending signals from GIT to the vomiting center

**>>so. What is more effective treatment for vomiting caused by gastroenteritis**

**>antiserotonin >especially receptor called 5HT3 (5 hydroxytreptamine3)**

>>also ,drugs for chemotherapy induced vomiting >antiserotonin will be effective

 **2#CTZ**>>the receptor responsible of sending signals from CTZ to vomiting center?by

**1- dopamine receptor D2**

**2-also by serotonin 5HT3** Cancer drugs irritate mucosa of GIT & Centrally (CINV)

**3- also by nurokinin receptor NK**

##substance p:substace in the CNS also called nurokinin located in the CTZ and send signals to the vomiting signals

##when the CTZ send signals ?when chemical stimulate it and as we say these signals send by 1-D2 2-5HT3 3-NK

#why digoxin cause vomiting? >because it stimulate the CTZ >then send signals by D2/5HT3/NK to vomiting centers >so any antagonist of these will be good antiemetic in cases of digoxin induce vomiting

 **3#vestibular part of inner ear** >>the signals sent by

**1-histamin H1 receptors**

**2-muscarinic receptor M3**

>>when I need antiemetic in cases of motion sickness >we don't use serotonin antagonist (it has no effect )>we use either antihistamine or antimuscarinic

 **4#cerebral cortex** >direct order >without any chemicals or receptors

Visual area safe, taste area small



##the most common causes of vomiting



**1#chemotherapy** :one of the most common causes of vomiting is anticancer drug

>how anticancer drug cause vomiting :

1-by irritation of GIT mucosa and send signals by serotonin receptors

2-these as chemicals will stimulate the CTZ

**#so to treat it we can use**

**1-serotonin antagonist**

**2-dopamine antagonist**

**3-nurokinene antagonist also affective**

◆ **2#motion sickness** :signals from the vestibular part of the inner ear to the vomiting center

**For motion sickness we use:**

**1-antihistamine**

**2-anticholenergic**

◆ **3#gastroenteritis** :inflammation in both stomach and intestine

If the patient mainly present by vomiting more than diarrhea so the inflammation in the stomach

If the patient suffer mainly from diarrhea it will be enteritis more

**#the antiemetic that is strong and useful in cases of gastroenteritis**

**>antiserotonin**

◆ **4#sensory** :various stimuli (fear/smell/anticipation /pain )

◆ **5#toxin**:cause irritation of stomach mucosa

**#Antiemetic medications target these receptors and inhibit/reduce vomiting.**



## #anticholinergic

#we need anticholinergic that have more central effect than peripheral (not like atropine that close all receptors) because we want to prevent signals from the vestibular part of inner ear

**#scopolamine :mainly central depressant** (it has no stimulant effect on CNS) unlike atropine (atropine cause stimulation followed by depressant when act centrally )

So atropine not work as antiemetic

We have scopolamine butylbromide (trans dermal patches)

**1-use in motion sickness**

**2- Also use in the emesis that occur in the first trimester of pregnancy and this vomiting mainly morning sickness**

**3- Post operative**

#what cause vomiting post operation ?

1- either the morfine that is used as anesthetic ,and the morfine cause vomiting by stimulate the CTZ

2- due to the motion after the operation >>in this case we give anticholinergic



## #antihistamine

1-diphenhydramine

2-dimenhydrinate

3-cyclizine

**#note:**

**Anti H1:antiemesis ,Anti H2:antiulcer**



#according to FDA the most important anti histamine for pregnancy is  
>doxylamine and pyridoxine(vitamin B6)(the drug of choice of morning sickness during pregnancy)

#note :antihistamine has anticholinergic effect so they cause  
:constipation/urinary retention/dry mouth

## #serotonin antagonist (Central & Peripheral)

1-dolasetron

2-palonosetron

3-ondansetron (Zofran) CINV

4-granisetron

### ##effective in

1-gastroenteritis

2-chemotherapy induced vomiting

### ##note::chemotherapy induced vomiting

1-antiserotonine :because the serotonin stimulate the CTZ

2-anti dopamine

3-antinurokinin

4-also steroids have antiemetic effect in chemotherapy induced vomiting

## #dopamine antagonist

>1-useful in cases of digoxin induced vomiting

2-in anticancer drug induced vomiting

>effective when there is CTZ stimulation

>>>1-domperidone(motilium)

2-metocolpramide(primprane) → cross BBB --> close dopamin receptor --> Parkinson like

مهم جدا

**###metoclopramide** :close dopamine receptor in CTZ

#But it can go to the substantia nigra and close dopamine and cause manifestation similar to Parkinson disease this called extrapyramidal manifestation

#parkinsonism : occur due to decrease dopamine in the substantia nigra

#note : dopamine has balance with ACH >>>استيلكولين (يمنع) يلجم>>>if ACH control the body motor activity alone will cause rigidity >>>but due to dopamine effect our movement is flexible

#the symptoms occur due to antagonize the dopamine in the substantia nigra called extrapyramidal symptoms (EPS)

#so when we give a child metoclopramide (under long term use)>>>will cause spasm because metoclopramide go and close dopamine in the substantia nigra  
بالااصل اعطينا الدواء لحتى يضاد الدوبامين بال CTZ...>>>so ACH will increase the motor activity and cause rigidity of muscles (flexures)

#if extrapyramidal symptoms occur >>>we give anticholinergic >>>to antagonize the excess ACH >>> diphyll hydramine >>>antihistamine هوهantihistamine لبس ليه significant atropine like action

#DOSE OF metoclopramide(3مل) شرط 3 بنعطيه 6 كغ بنعطيه 3 شرط 3مل) نص الوزن بالشرط,,يعني اذا طفل وزنه 6 كغ بنعطيه 3 شرط 3مل)

**###dompridone**

\*not cause extrapyramidal syndrome>>>because it doesn't close the dopamine in substantia nigra (not cross the BBB )it only close dopamine in the CTZ

\*BUT :it cause ventricular fibrillation in child's (but not in adult)>>>domperidone is contraindicated in child's



#nurokinin antagonist (substance p antagonist ):

\*NK1 receptor send signals from the CTZ to the vomiting center

**1-aprepitant**

**2-fosa apripetant**

**\*uses :**

**1-in chemotherapy induced vomiting >>but not given alone >give with dexamethasone (corticosteroid)>>>taken for three days (125mg/80mg/80mg)**

cisplatin هو ال vomiting اكثر واحد من ادويه السرطان بعمل

**2- Post operative nausea and vomiting (PONV)>>in single dose (40mg)**

#fossa aprepitant given only parenteral but aprepitant can given orally

# نتيجة استخدام ال morphin بالتخزين وممكن يسبب الحركة الفجائية بعد العملية

## **## Over The Counter Options**

- Emetrol: (Fructose, Dextrose, and Phosphoric Acid)
- Pepto-Bismol: (Bismuth-Subsalicylate)

**##Bismuth :the hero of GIT**

## **Natural Antiemetic Options**

- Ginger: Tea or Ale
- Peppermint
- Chamomile Tea
- Lemon --> counter irritant
- Cinnamon
- Baking Soda

**“Let food be thy medicine and medicine be thy food.”**



- Antiemetics are drugs used to inhibit dopamine, serotonin, histamine, and acetylcholine receptors in signaling the chemoreceptor trigger zone and vomiting center.
- Vomiting center is activated by visceral, vestibular, or chemoreceptor trigger zone stimulation.
- Antihistamines and anticholinergics aim to treat motion sickness related nausea.
- Dopamine and Serotonin antagonists aim to treat cytotoxic drug and post-operative nausea.

***Study hard until you can say trust me I am your DOCTOR***