

Drugs Used In The Treatment Of Irritable Bowel Syndrome & Inflammatory Bowel Disease

← التهاب القولون العصبي

* في رابط وتواصل بين ال (Autonomic nerve) والقناة الهضمية ، أي خلل مع يصير عندو ← IBS system

* سواء بال CNS

أو بال gut ← ماني (Connection)

Irritable Bowel Syndrome

MRI/PET studies:

↑ central pain processing with colorectal distension in IBS vs normal

Treatments

Counseling / Stress Management / Diet

Physical activity (increased exercise)

Laxatives (IBS-C)

- osmotic laxatives (PEG)
- Cl-channel activator (lubiprostone)
- guanylate cyclase agonist (linaclotide)

Antidiarrheals (IBS-D)

- loperamide
- bile acid sequestrants (e.g. cholestyramine)
- 5-HT antagonists (alosetron)

Antibiotics (IBS-D)

- rifaximin

Abdominal Pain

- antispasmodics
- tricyclic antidepressants (low dose)
- SSRIs?

Peripheral mechanisms

Brain – Gut Dysregulation

↑ HPA axis
ANS
Enteric Nervous System

gut-based

(5-HT₃) signaling
Serotonine
local reflexes

altered microflora

intestinal irritants (food products)

inflammation

altered mucosal permeability

Risk Factors

Psychosocial stressors:

anxiety
stress
depression

Subtypes

- 1) IBS w/ Constipation (IBS-C)
- 2) IBS w/ Diarrhea (IBS-D)
- 3) Unsubtyped IBS

Pathophysiology

visceral hypersensitivity (common)

- exaggerated response to cholecystokinin
- altered response to meal ingestion

Δ altered bowel motility (diarrhea or constipation)

low grade inflammation (in some IBS-D patients)

Visceral hypersensitivity



cholecystokinin

* هرمون يشارك في الهضم

* يزيد من إفراز العصارة



اضطراب في الحوض

زيادة إفراز

تشكل عصب

Altered bowel Motility

ما يعزى لزيادة إفراز الماء

diarrhea ← انقباض العضلات بشكل أسرع

conception ← أدا بطيء

امتصاص كمية من الماء

بعد ذلك ممكن زيادة (inflammation)

Drugs Used In The Treatment Of Irritable Bowel Syndrome (IBS)

مو معروف نبيات

بنتكس

- IBS is an idiopathic chronic relapsing disorder characterized by abdominal discomfort (**pain, bloating, distention, or cramps**) in association with alterations in bowel habits (**diarrhea, constipation, or both**).

حسب حرية القولون
← برقية ← diarrhea
← بطنية ← constipation
or both

- With episodes of abdominal pain or discomfort, patients note a change in the frequency or consistency of their bowel movements.
- Pharmacologic therapies for IBS are directed at relieving abdominal pain and discomfort and improving bowel function.

العلاج هدفه
← أقل وأحرق الألم
← أنظم حرية القولون (bowel)

Drugs Used In The Treatment Of Irritable Bowel Syndrome (IBS) – D

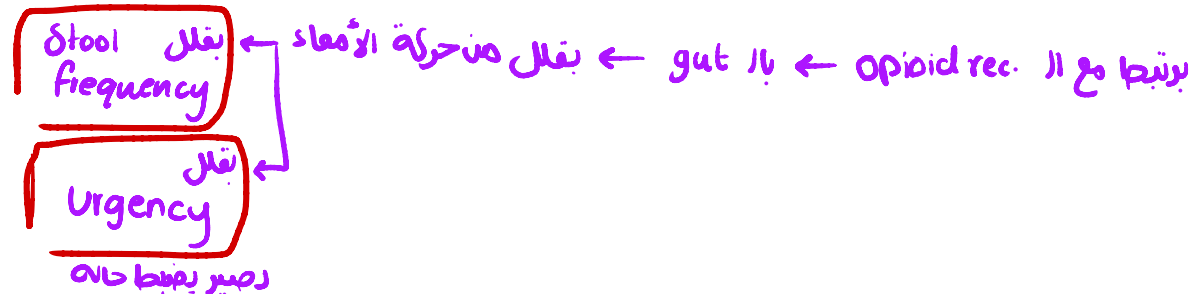
- For patients with predominant diarrhea:

1. Antidiarrheal agents, especially **loperamide**, are helpful in reducing stool frequency and fecal urgency

2. Other agents: **alosetron** (5-HT₃ antagonist). → block Serotinine rec. in gut
5-HT₃ receptors in the gastrointestinal tract activate visceral afferent pain sensation.

Inhibition of gastrointestinal 5-HT₃ receptors may reduce unpleasant sensations including nausea, bloating, and pain.

تقلل من
الألم
والأعراض



Drugs Used In The Treatment Of Irritable Bowel Syndrome (IBS)

مُليّنات

- For patients with predominant constipation:
 1. **fiber supplements** may lead to softening of stools and reduced straining; however, increased gas production may exacerbate bloating and abdominal discomfort.
 2. Consequently, **osmotic laxatives**, especially milk of magnesia, are commonly used to soften stools and promote increased stool frequency
 3. Other agents: **chloride-channel activators**, lubiprostone and linaclotide.

إذا ما شرب ماء معه
رج يصير الموضوع نكسي

← الكثير يتعذّب على الألياف ← يؤدّي إنتاج الغازات

← لسحب الماء من جدران الأمعاء

Lubiprostone acts by stimulating the type 2 chloride channel (ClC-2) in the small intestine. This increases chloride-rich fluid secretion into the intestine, which stimulates intestinal motility and shortens intestinal transit time.

← الـ Na^+ رج يصنع
والـ H_2O رج يصنع معه ← Softing stool

Drugs Used In The Treatment Of Irritable Bowel Syndrome (IBS)

- For chronic abdominal pain, **low doses of tricyclic antidepressants** (eg, amitriptyline or desipramine, 10–50 mg/d) appear to be helpful. At these doses, these agents have no effect on mood.
- For small or large bowel spasm, antispasmodics (anticholinergics) such as **dicyclomine** and **hyoscyamine** are used (However, small or large bowel spasm has not been found to be an important cause of symptoms in patients with IBS.)

← لا تؤثر الجراثيم فليحة

block Muscarinic ←
rec in smooth
Muscle in GI

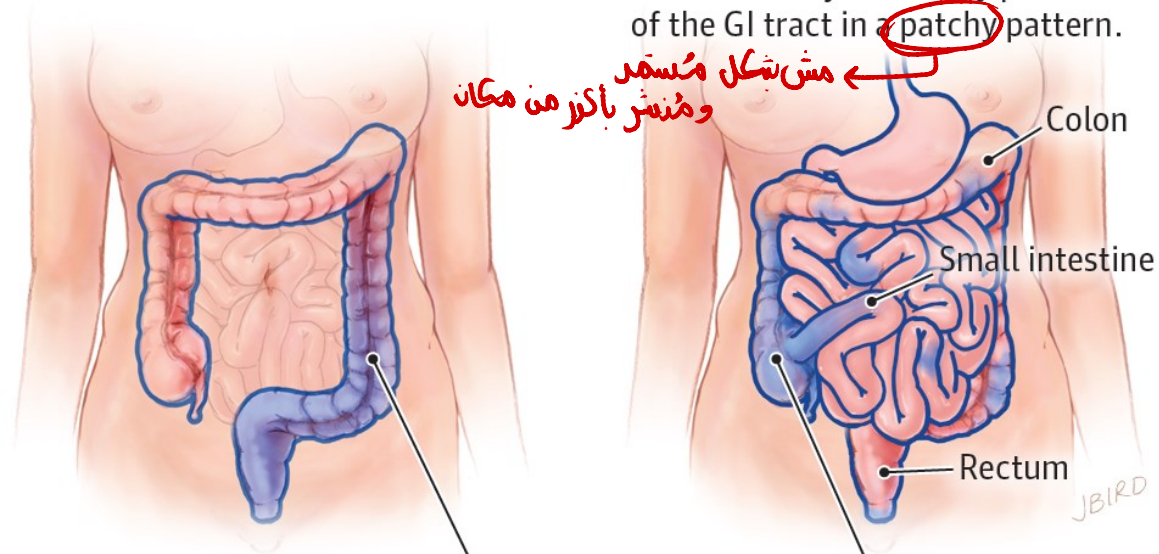
Inflammatory Bowel Disease

- **Inflammatory** bowel disease (IBD) comprises two distinct disorders:

- Ulcerative colitis
- Crohn's disease.

✓ Ulcerative colitis typically begins in the rectum and may extend continuously to involve the entire colon.

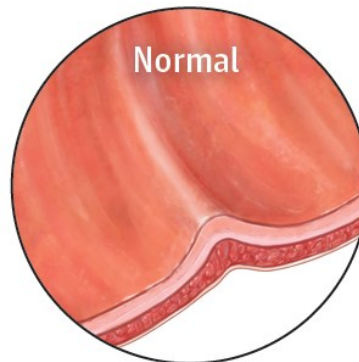
✓ Crohn disease most commonly involves the end of the small intestine and beginning of the colon and may affect any part of the GI tract in a patchy pattern.



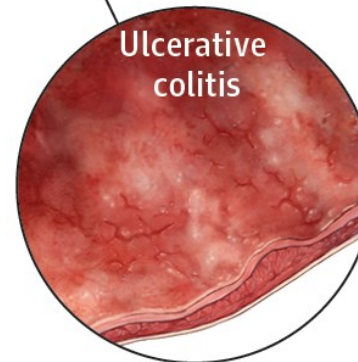
inflammation
بال rectum يصبع ليوصل
القولون

ببداش من زهارة
الأعضاء لبراية القولون

Colon wall



Normal



Ulcerative
colitis

Ulcerative colitis usually affects only the inner layer of the bowel wall.



Crohn
disease

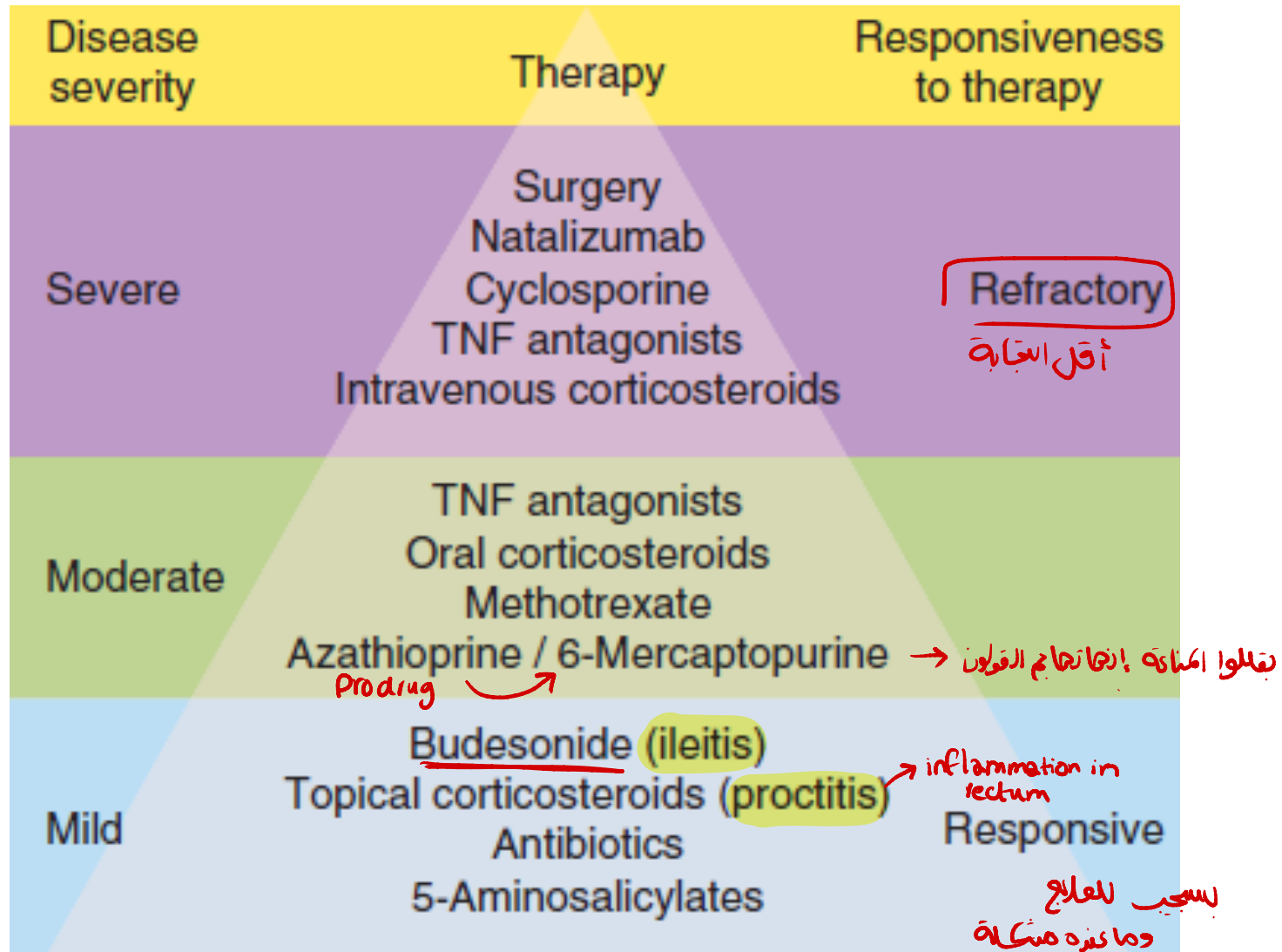
Crohn disease may affect all layers of the bowel wall.

Drugs Used To Treat Inflammatory Bowel Disease

- The etiology and pathogenesis of these disorders remain unknown.
- For this reason, pharmacologic treatment of inflammatory bowel disorders often involves drugs that belong to different therapeutic classes and have different mechanisms of anti-inflammatory action.
- Drugs used in inflammatory bowel disease are chosen on the basis of:
 1. Disease severity
 2. Responsiveness
 3. Drug toxicity.

لأن السبب هو معروف

Drugs Used To Treat Inflammatory Bowel Disease



Antiemetics



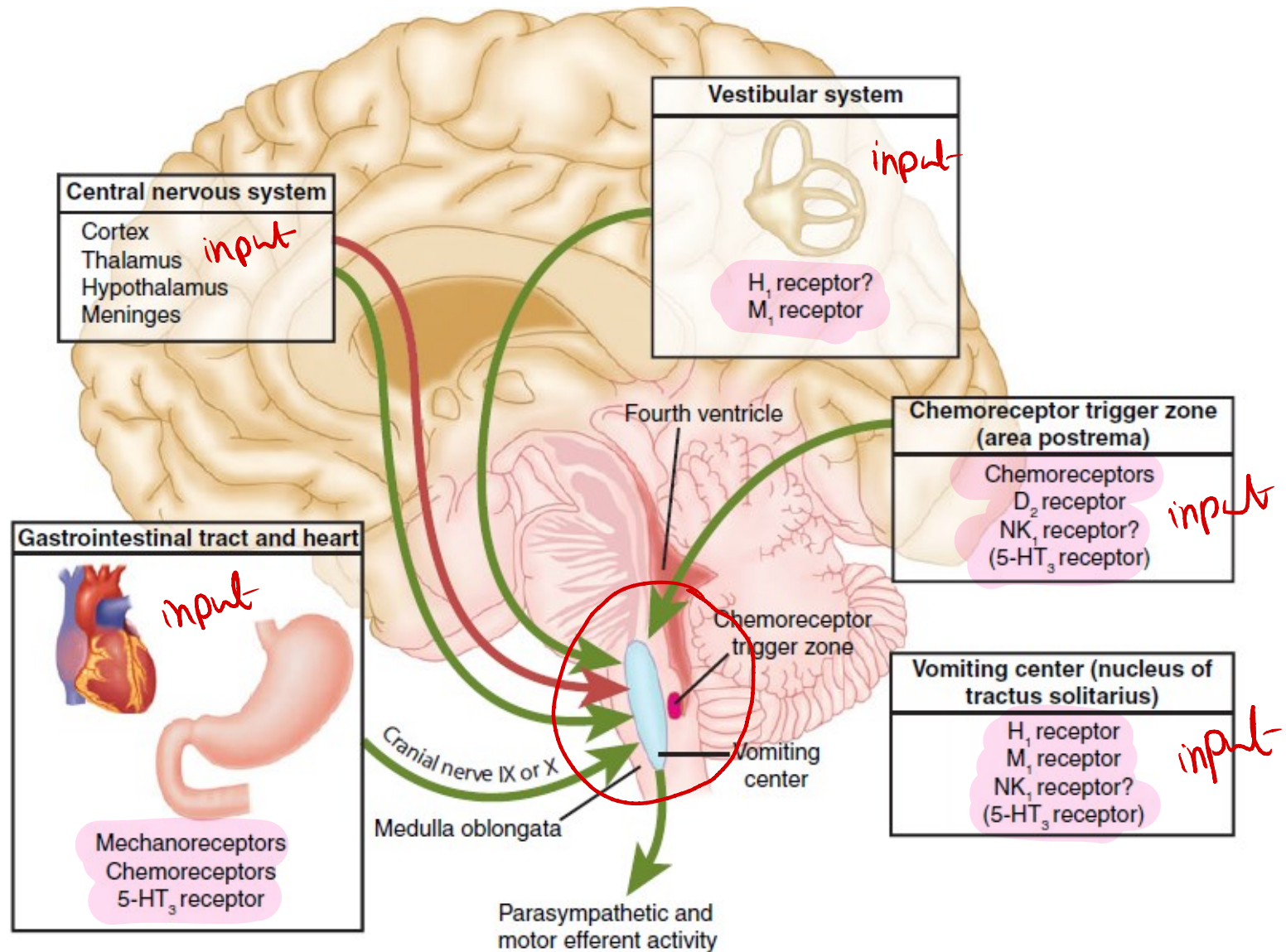
Antiemetics

- Nausea and vomiting may be manifestations of a wide variety of conditions, including:
 1. Adverse effects from medications
 2. Systemic disorders or infections
 3. Pregnancy ← نتيجة تغير الهرمونات
 4. Vestibular dysfunction → (بالأذن الداخلية)
 5. Central nervous system infection or increased pressure
 6. Peritonitis ← التهاب الغشاء الذي يغطي الأعضاء الداخلية بالبطن
 7. Hepatobiliary disorders
 8. Radiation or chemotherapy
 9. Gastrointestinal obstruction
 10. Dysmotility

Mechanism that trigger vomiting

- Two brainstem sites have key roles in the vomiting reflex pathway.
- 1. **The chemoreceptor trigger zone (CTZ)** is located in the **area postrema**. It is outside the blood–brain barrier. Thus, it can respond directly to chemical stimuli in the blood or cerebrospinal fluid.
- 2. **Vomiting center**, which is located **in the medulla**, coordinates the motor mechanisms of vomiting. ← جفزعلى التقيؤ
- The vomiting center responds to afferent input from the vestibular system, the periphery (pharynx and GI tract), and higher brainstem and cortical structures.
- The vestibular system functions mainly in motion sickness.
- High concentrations of muscarinic M 1 , histamine H 1 , neurokinin 1 (NK 1), and serotonin 5-HT 3 receptors have been identified in the vomiting center.

input → Vomiting Center → Vomiting



- Identification of the different neurotransmitters involved with emesis has allowed development of a diverse group of antiemetic agents that have affinity for various receptors.

Antiemetics

1. Serotonin 5-HT₃ antagonists
 - **Ondansetron, granisetron**, dolasetron, and palonosetron.
2. Dopamine receptor antagonists
 - Substituted benzamide: **metoclopramide** and trimethobenzamide
 - Phenothiazines: **Prochlorperazine**, promethazine, and thiethylperazine.
 - Butyrophenone: **Droperidol**
3. Corticosteroids
 - **Dexamethasone** and **methylprednisolone** have antiemetic properties, but the basis for these effects is unknown.
4. Neurokinin receptor antagonists
 - **Aprepitant**, fosaprepitant

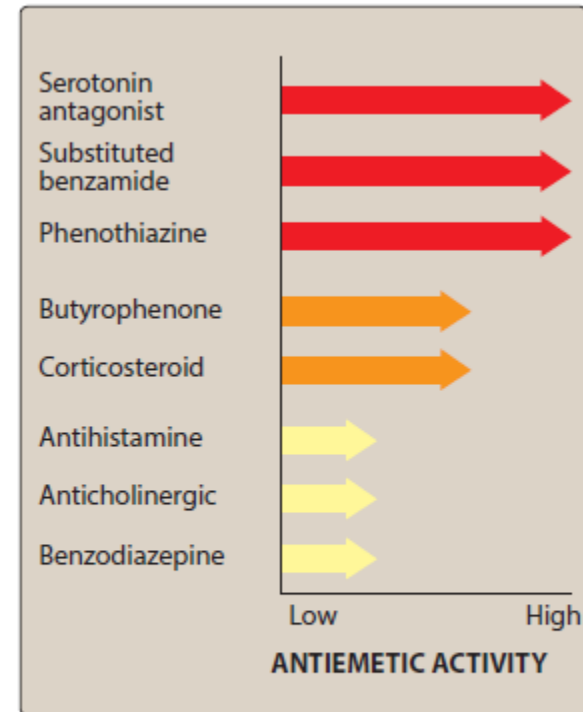


Figure 31.10
Efficacy of antiemetic drugs.

Antiemetics

5. H₁ antihistamines & anticholinergic drugs

- **Diphenhydramine** and one of its salts, **dimenhydrinate** **meclizine** → both
- **Hyoscine (scopolamine)** → block Muscarinic

6. Benzodiazepines

- **Lorazepam** or **diazepam** are used before the initiation of chemotherapy to reduce anticipatory vomiting or vomiting caused by anxiety.

- Combinations of antiemetic agents with different mechanisms of action are often used, especially in patients with vomiting due to chemotherapeutic agents.

إذا السبب العلاج الكيميائي ←
 Combination
 عشان أزيد الفعالية
 أو أقل toxicity

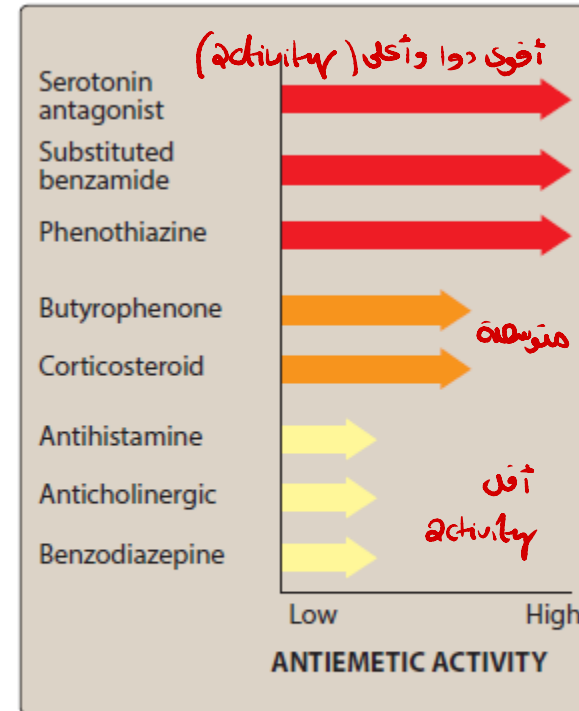


Figure 31.10
Efficacy of antiemetic drugs.

Chemotherapy-induced nausea and vomiting (CINV)

- Several factors influence the incidence and severity of CINV, including:

1. the specific chemotherapeutic drug
2. the dose, route, and schedule of administration
3. patient variables. For example, young patients and women are more susceptible than older patients and men, and 10% to 40% of patients experience nausea and/or vomiting in anticipation of chemotherapy (anticipatory vomiting).

أعلى عرضة له
يصير vomiting
السهل والأصغر نوال من الخوف أو من
العلاج الكيميائي

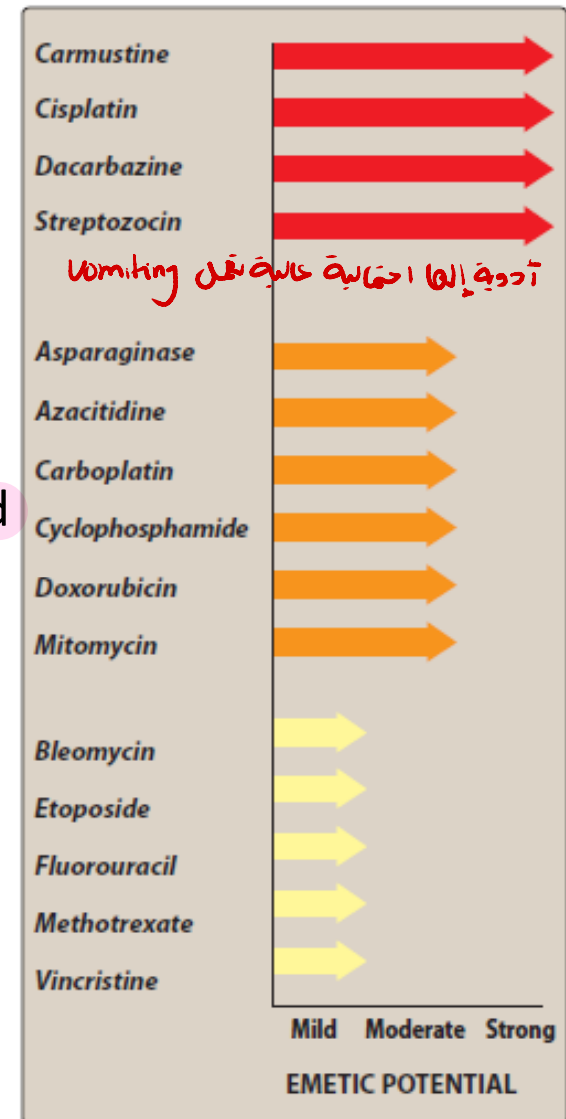


Figure 31.8

Comparison of emetic potential of anticancer drugs.

Chemotherapy-induced nausea and vomiting (CINV)

- Antiemetic drugs are often combined to increase antiemetic activity or decrease toxicity.
 - **Ondansetron** and **granisetron** prevent emesis in 50% to 60% of cisplatin-treated patients.
 - Corticosteroids, most commonly **dexamethasone**, increase antiemetic activity when given with the 5-HT₃ antagonist.
 - Antihistamines, such as **diphenhydramine**, are often administered in combination with high-dose metoclopramide to reduce extrapyramidal reactions.
 - **Aprepitant** is approved for use in combination with other antiemetics for prevention of the nausea and vomiting associated with highly emetogenic chemotherapeutic regimens.

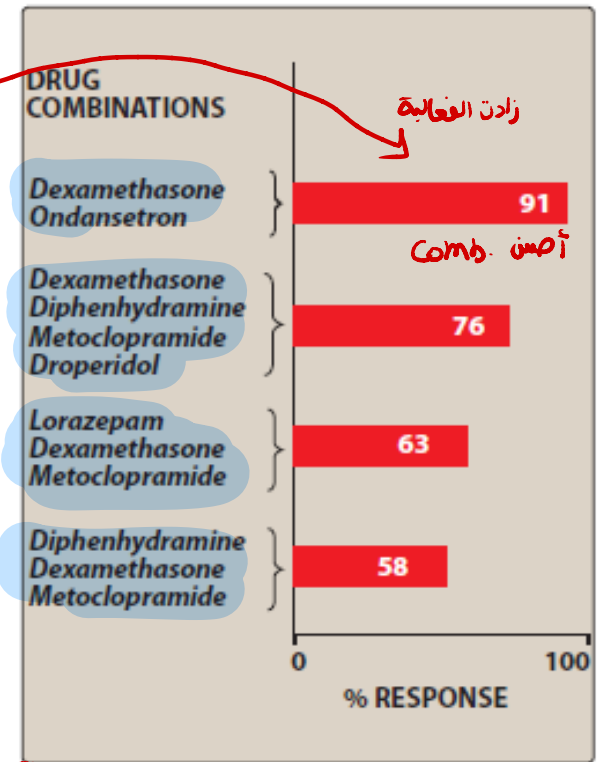


Figure 31.11

Effectiveness of antiemetic activity of some drug combinations against emetic episodes in the first 24 hours after cisplatin chemotherapy.

لے بتلے N_D ۷
تکلیس

Dopamine = Acetylcholine

block
Muscarinic
rec.

لے بعبور (CNS) لے پائوعلی حركة الانسان عصبیة غی إرادیة

+