Nausea and Vomiting in Palliative Care

Definitions

- **Nausea -** an unpleasant feeling of the need to vomit
- **Vomiting -** the expulsion of gastric contents through the mouth, caused by forceful and sustained contraction of the abdominal muscles and diaphragm

INCIDENCE OF NAUSEA & VOMITING IN TERMINAL CANCER PATIENTS

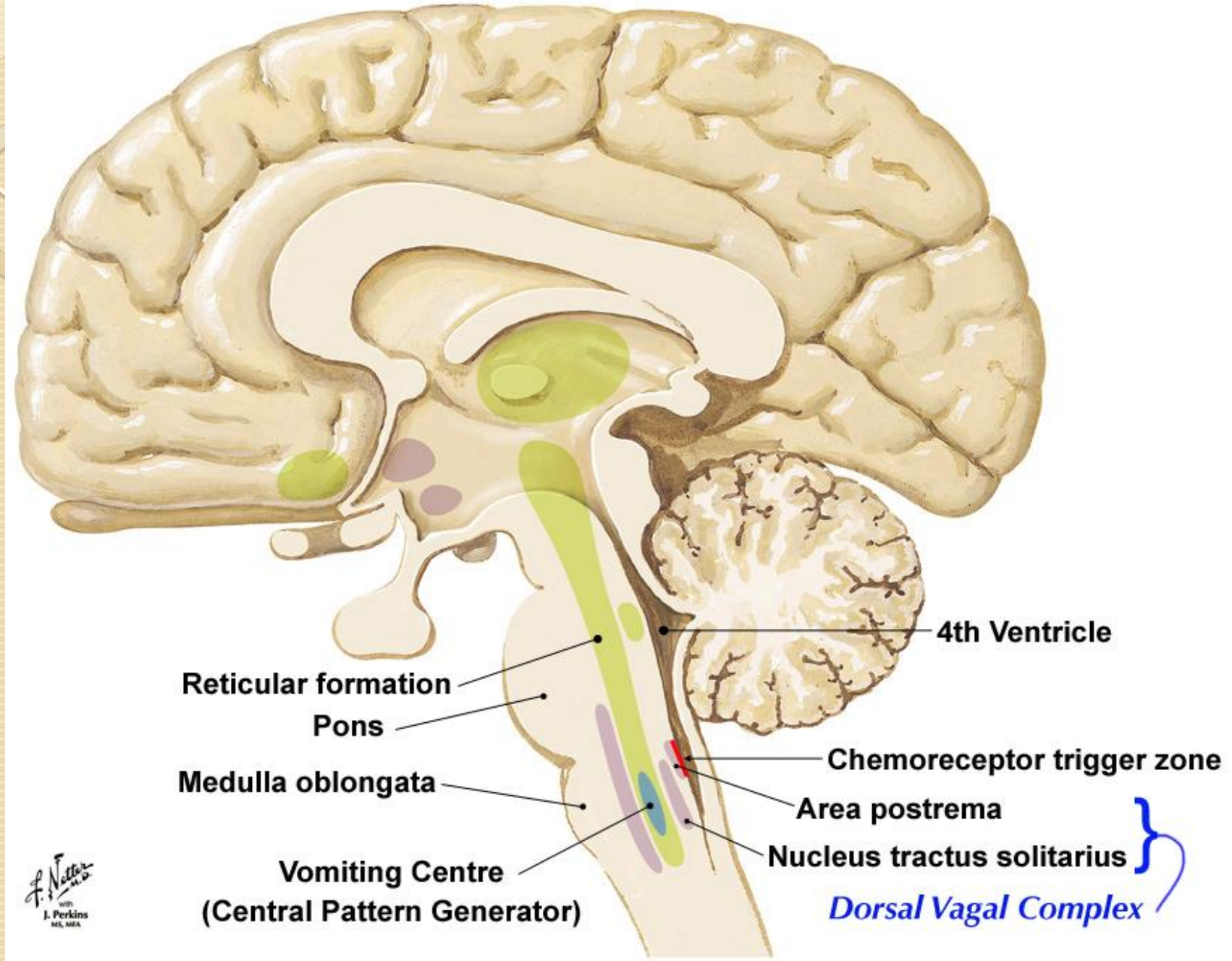
40-70%

Nausea and vomiting

- Complex pathophysiology
- Multiple mechanisms involved
- Various patways and centers
- Critical areas controlling: vomiting centre (VC) and chemoreceptor trigger zone (CTZ)

MECHANISM OF NAUSEA AND VOMITING

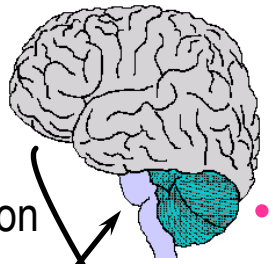
- Vomiting Centre (Central Pattern Generator) in reticular formation of medulla
- activated by stimuli from:
  - Chemoreceptor Trigger Zone (CTZ)
    - in the area postrema, floor of the fourth ventricle, with neural pathways projecting to the nucleus of the tractus solitarius
    - outside blood-brain barrier
  - Upper GI tract & pharynx
  - Vestibular apparatus
  - Higher cortical centres


4th Ventricle
Reticular formation
Pons
Medulla oblongata
Vomiting Centre
(Central Pattern Generator)
Chemoreceptor trigger zone
Area postrema
Nucleus tractus solitarius
Dorsal Vagal Complex
F. Netter M.D.
with
J. Perkins
MS, MFA

- drugs, metabolic,
- chemiotherapy, opioids, uremia, calcium, toxins

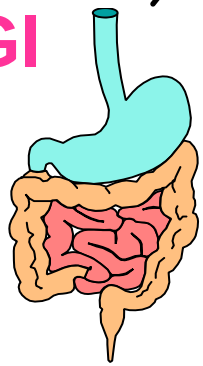
Cortex

- Sensory input
- Anxiety, memory
- Meningeal irritation
- Increased ICP



- **CTZ**
- **dorsal vagal complex**

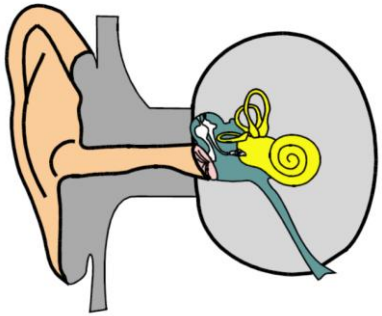
GI



- serotonin release from mucosal enterochromaffin cells
- obstruction
- stasis
- Inflammation
- chemiotherapy

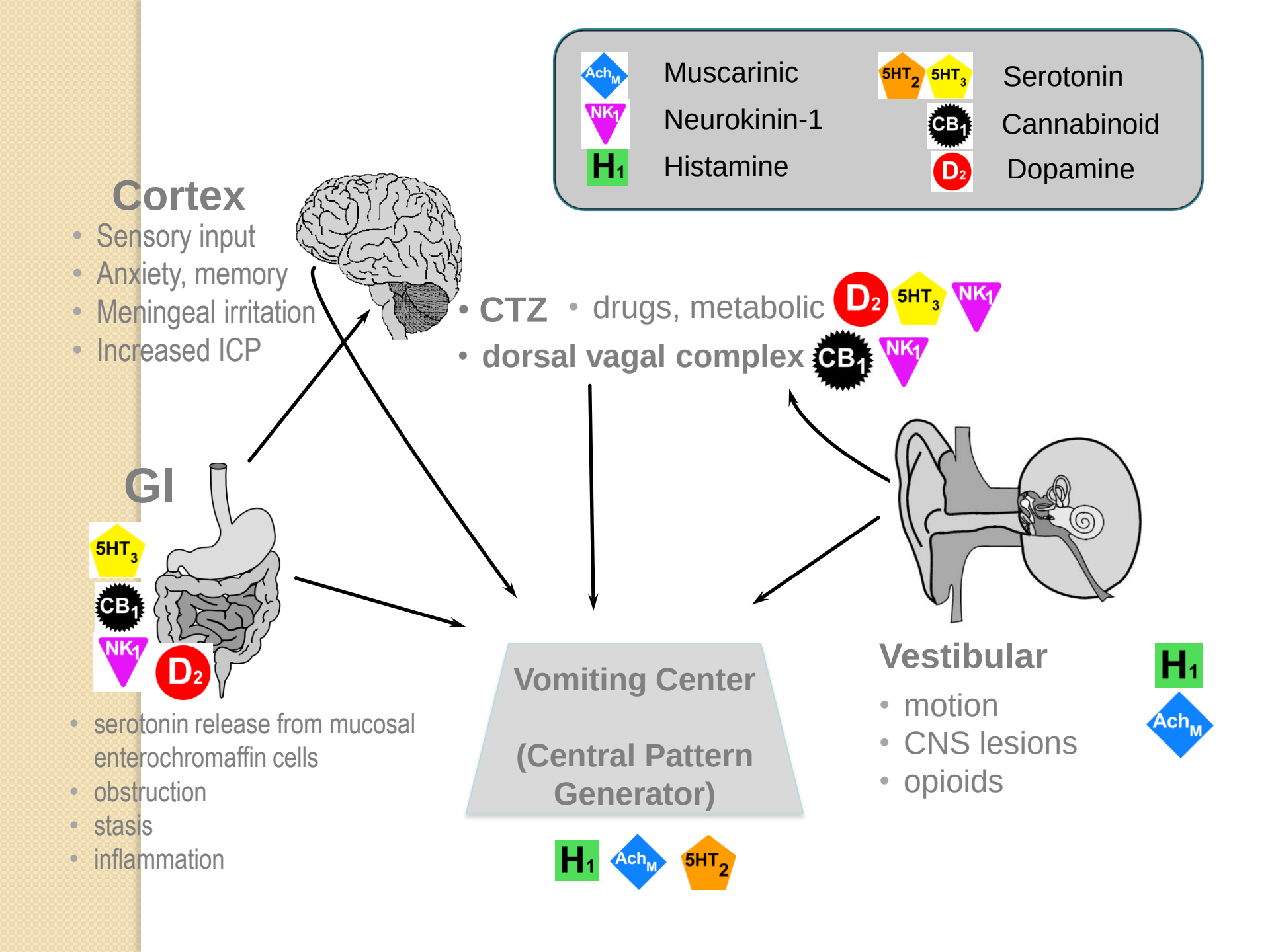
Vomiting Center

(Central Pattern Generator)



Vestibular

- motion
- CNS lesions
- opioids


Muscarinic
Neurokinin-1
Histamine
Serotonin
Cannabinoid
Dopamine
Cortex
• Sensory input
• Anxiety, memory
• Meningeal irritation
• Increased ICP
• CTZ • drugs, metabolic
• dorsal vagal complex
GI
• serotonin release from mucosal enterochromaffin cells
• obstruction
• stasis
• inflammation
Vomiting Center
(Central Pattern Generator)
Vestibular
• motion
• CNS lesions
• opioids

Nausea and vomiting

- Once the vomiting centre receives signals from the various afferent sources the information is processed and vomiting center puts out an appropriate vasomotor efferent response (respiratory, salivatory, gut, diaphragm, abdominal muscles) inducing nausea or vomiting

Nausea and vomiting etiology

- Bowel obstruction
- Constipation
- Opioids
- Other drugs
- Chemiotherapy
- Radiation therapy
- Peptic ulcer
- Metabolic abnormalities
- Increased cranial pressure
- Anxiety
- Autonomic dysfunction

Nausea and vomiting- assesment

- Visual analog scales, numerical scales, verbal description
- There is no gold standard
- Multifactorial causes- multidimentional assesment
- Asses other symptoms (pain, fatigue, depression, anxiety)
- Edmonton Symptom Assesment

Nausea and vomiting

- Detailed history
- Physical examination
- Intensity
- Frequency
- Exacerbating and relieving factors
- Onset and duration
- Investigation to exclude renal impairment, hypercalemia, hyponatremia
- CT of the brain
- X-ray

Nausea and vomiting- management

- Appropriate management depends on assesment
- Good oral hygiene
- Confortable enviroment
- Preventing unpleasant odours
- Small volumes
- Regular intervals

Table 10.1 Clues from history and physical examination to the etiology of chronic nausea and vomiting

Findings on history and physical examination	Possible etiology
Pattern of infrequent large-volume vomitus that relieves nausea	Bowel obstruction—partial or complete Gastric outlet obstruction
Symptoms of nausea or vomiting related to movements	Vestibular dysfunction; mesenteric traction
History of polyuria and polydipsia	Hyperglycemia Hypercalcemia
Associated changes in mental status	Brain metastasis, metabolic abnormalities (examples: hyperglycemia, hypercalcemia, hyponatremia, renal failure, liver failure [elevated ammonia levels])
Papilledema	Raised intracranial pressure as with brain metastasis
Orthostatic blood pressures, absence of heart rate variability with valsalva, syncopal episodes	Autonomic insufficiency
Decreased frequency of bowel movements	Constipation
History of a mood disorder or anxiety	Anxiety
Medication/treatment history Chemotherapy or radiation Antibiotics; HIV medications	Treatment-specific syndromes (delayed chemotherapy-induced nausea and vomiting [CINV])
Epigastric pain, anemia; melena Use of NSAIDs	Peptic ulcer disease (use of NSAIDs or corticosteroids)
Distended abdomen, shifting dullness, fluid wave	Ascites
Distended abdomen, absent bowel sounds	Bowel obstruction

Nausea and vomiting-

specific interventions

Nausea and vomiting- specific interventions

Table 10.2 Examples of specific interventions when the etiology of nausea and vomiting is known or suspected

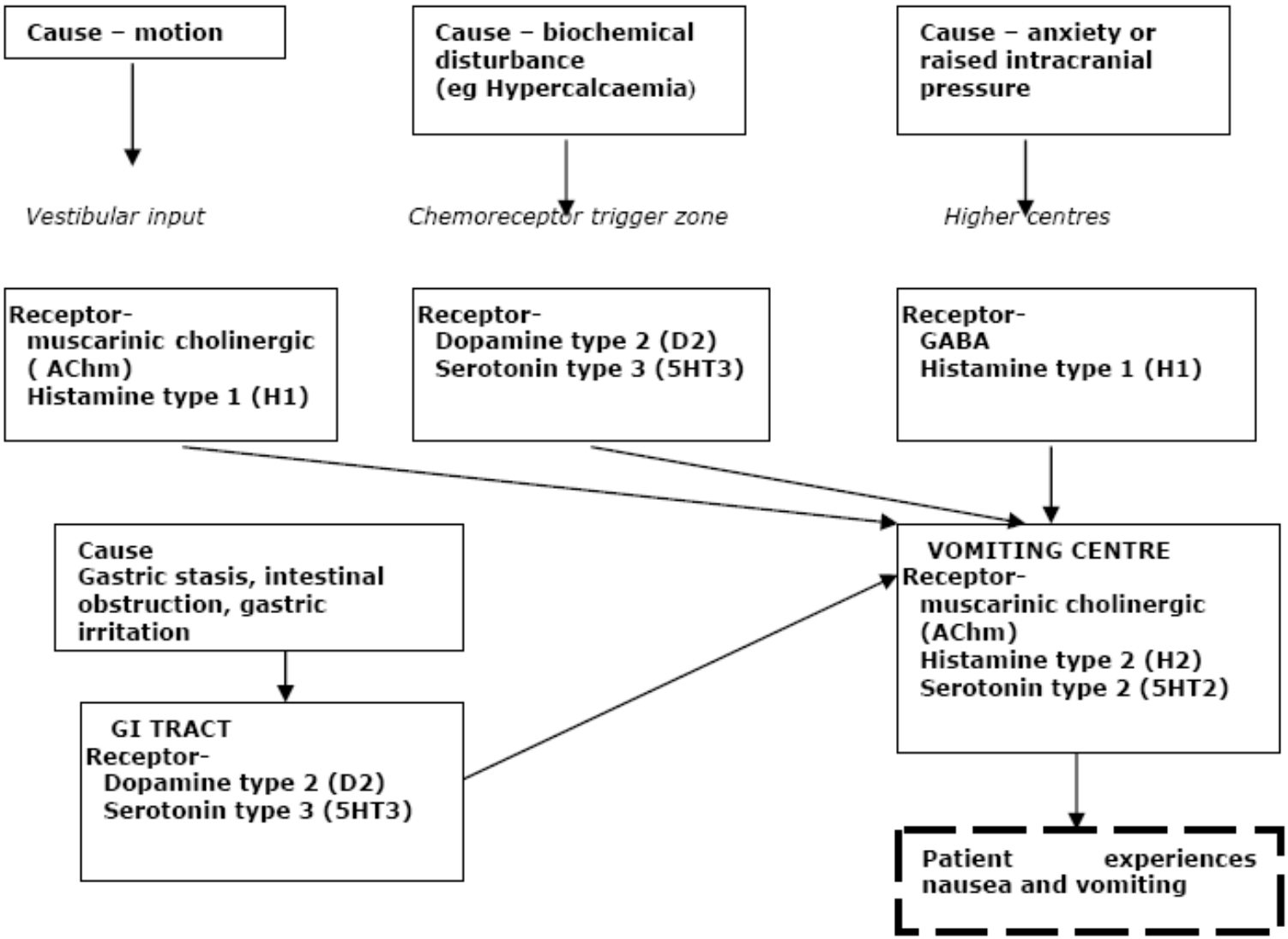
Etiology	Intervention
Hypercalcemia	Hydration, bisphosphonates
Opioid toxicity	Opioid rotation or decrease dose
Constipation	Aggressive bowel regimen. Consider X-rays
Gastric ulceration	Proton pump inhibitors (PPIs), H2-antagonists
Infection	Antibiotics
Tense ascites	Paracentesis, consider intraperitoneal (IP) catheter
Anxiety	Counseling, anxiolytics
Brain metastases	Radiation therapy, steroids
Bowel obstruction	Conservative vs. surgical procedures (e.g., resection, bypassing, or stenting, venting gastrostomy)

Antiemetic agents

Table 10.3 Antiemetic agents

Class	Examples
Dopamine antagonists	MetoclopramideHaloperidol, prochlorperazine, chlorpromazine
Prokinetic agent	Metoclopramide
Antihistaminics	Diphenhydramine, meclizine, hydroxyzine, promethazine
Anticholinergics	Scopolamine (transdermal), hyoscyamine, glycopyrrolate
Serotonin antagonists	Ondansetron, granisetron, dolasetron
Cannabinoids	Dronabinol, nabilone
Corticosteroids	Dexamethasone, methylprednisolone
Other useful agents	Lorazepam, octreotide

Chemo-receptors



Dopamine antagonists

- Central effects predominantly in CTZ
- Antagonize dopamin receptors
- Do not increase GI motility- useful in bowel obstruction

Dopamine antagonists

- Haloperidol: narrow-spectrum agent
- Mainly D2 antagonistic activity
- Negligible anticholinergic or antihistaminic effects
- Oral bioavailabity 65%
- Not cleared by kidneys
- Initial doses: 0,5-2mg p.o., 2,5-5mg s.c., 3 times a day
- Max. up to 60mg, but in nausea/vomiting treatment usually up to 10mg/day

Dopamine antagonists

- Broader spectrum: chlorpromazine, prochlorpromazine, promethazine (dopaminergic, cholinergic, histamine receptor antagosists)
- Side effects- extrapyramidal reactions, urinary retention, hypotension, constipation, dry mouth

Prokinetic agents

- Metoclopramide- dual mechanism of action
- Predominantly a dopaminergic antagonist but also has prokinetic effects via cholinergic system in the myenteric plexus
- Reversing gastroparesis and bringing normal peristalsis in the upper GI tract
- Dose: 10mg 3 times a day ½ hour before meals p.o. or s.c. (i.v.) max. 30mg daily for 5days
- Side effect- extrapyramidal reactions

Antihistaminics

- Cyclizine, promethasine, dimenhydrate
- Useful fo vestibular component of the nausea
- Major side effect- drowsiness
- Dimenhydrate- start with 3x50mg, up to 400mg daily

Antimuscarinic/anticholinergic agents

- Scopolamine or atropine
- Lipophilic
- Cross the the blood-brain barrier
- May cause sedation and confusion
- Used to reduce nausea and abdominal colic when they are associated with mechanical bowel obstruction

Serotonin antagonist

- Effective in management of chemio- and radiotherapy-induced nausea and vomiting
- Ondansetron, graninsetron

Corticosteroids

- Nonspecific, antiemetic effects- not well understood
- may modulate prostaglandin release
- May decrease peritumoral edema, thus reducing ICP
- Useful in combination with 5-HT3 antagonists or metoclopramine in chemiotherapy-induced emesis

	RECEPTOR ANTAGONISM								*Notes*
	D_2	H_1	Ach_M	$5HT_2$	$5HT_3$	$5HT_4$	CB_{1+2}	NK_1	
Metoclopramide	+++				+	++			
Domperidone	++++					+			
Haloperidol	++++	+							
Methotrimeprazine	++++	+++	++	+++					
Chlorpromazine	++++	++	+						
Olanzapine	++	+	+	+++	++				
Prochlorperazine	++	+							
Dimenhydrinate	+	++++	++						
Ondansetron					++++				
Granisetron					++++				
Scopolamine	+	+	++++						
Dronabinol							(++)*		*Agonist

Nonpharmacologic interventions

- Behavioral and complementary therapies (accupuncture, TENS, psychologicical)
- Surgical interventions (percutaneus gastrostomy, colostomy, intestinal bypass

Antiemetic ladder

- 1 step: metoclopramide, haloperidol, dimenhydrinate/cyclolizyne
- 2 step: if it doesn’t work- add or replace metoclopramide ⇔halopoeridol, metoclopramide +halopoeridol
- 3 step: add or replace with other drug: dexamethasone, hyoscine
- 4 step: if the nausea/vomiting continues try other drugs- levomepromasine, ondansetron

Clinical Scenario	Mechanism	Typical Initial Treatment Approach
Chemotherapy Sepsis; metabolic; renal or hepatic failure	• $5HT_3$ released in gut • stimulation of CTZ	$5HT_3$ antagonists; metoclopramide; haloperidol; methotrimeprazine
Opioid-Induced	• constipation; decreased gut motility • stimulation of CTZ • vestibular	laxatives (lactulose, PEG); metoclopramide; haloperidol; methotrimeprazine
Bowel obstruction	• mechanical impasse • stimulation of CTZ • stimulation of gut stretch receptors, peripheral pathways	dexamethasone; octreotide; metoclopramide if incomplete obst; haloperidol
Radiation	• stimulation of peripheral pathways via $5HT_3$ released from enterochromaffin cells in gut	$5HT_3$ antagonists
Brain tumor	• raised ICP • aggravated by movement	dexamethasone; dimenhydrinate
Motion-related	• vestibular pathway	dimenhydrinate; scopolamine