

Approach to Nausea & Vomiting

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Why nausea and vomiting?

Pain	80-90+ %
Fatigue / asthenia	75-90%
Constipation	70%
Dyspnea	60+ %
Nausea	50-60%
Vomiting	30%
Delirium	30-90%
Depression / suffering	40-60%

Prevalence of symptoms in palliative population,
Daeninck presentation, 2014

Why nausea and vomiting?

Almost everyone experiences nausea



Objectives

1. Review the pathophysiology of nausea & vomiting
 2. Recognize the underlying cause(s) of nausea & vomiting
 3. Know the nonpharmacologic and pharmacologic management of nausea & vomiting
- Concentration on palliative population

Nausea

- Unpleasant sensation of the need to vomit
- Pallor, sweats, tachycardia, retching
- A symptom, not a disease
 - One of the most unpleasant symptoms!

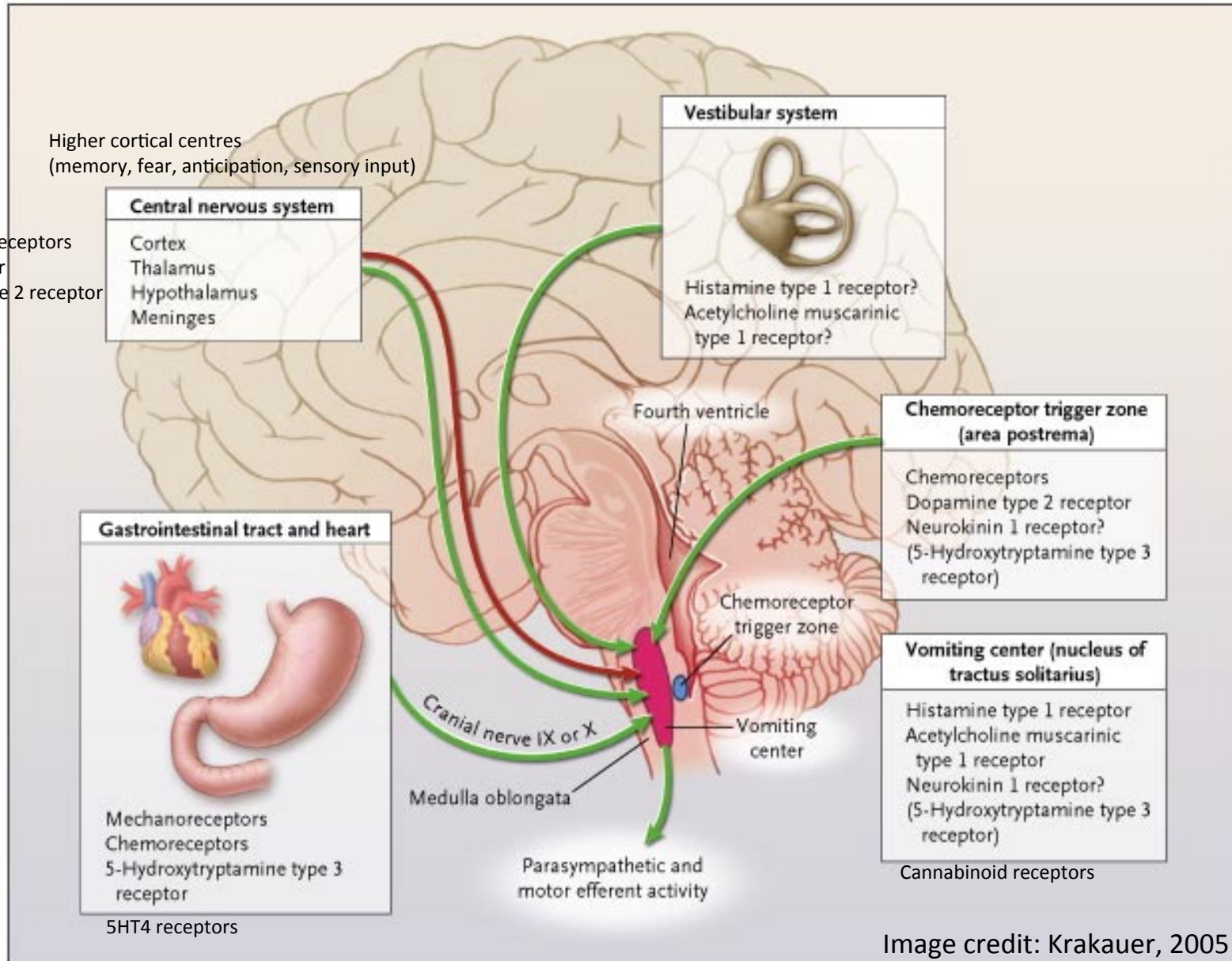


Vomiting

- Cardiac sphincter relaxes
- Abdominal muscles and diaphragm contract
- Larynx closes
- Lower portion of stomach contracts
- Stomach contents expelled through the esophagus and mouth



Pathophysiology of Nausea and Vomiting



Pathophysiology

Centre	Causes	Neurotransmitter involved
GI tract and other viscera	Tumour Bowel obstruction Bowel distension Radiotherapy Ischaemia	Serotonin (5HT3, 5HT4) Dopamine (D2) Mechanoreceptors

Pathophysiology

Centre	Causes	Neurotransmitter involved
Chemoreceptor trigger zone	Medication - opioids, SSRIs, chemotherapy Toxins - uremia, hypercalcemia, infection	Dopamine (D2) Serotonin (5HT3) Substance P / Neurokinin 1

Pathophysiology

Centre	Causes	Neurotransmitter involved
Vestibular apparatus	Motion-induced nausea Vestibular disease	Histamine (H1) Acetylcholine (M)

Pathophysiology

Centre	Causes	Neurotransmitter involved
Brain cortex Other brain causes	Anticipatory nausea prior to chemotherapy Anxiety, fear Increased ICP	GABA receptors Cannabinoid receptors

Pathophysiology

Centre	Causes	Neurotransmitter involved
Vomiting Centre	Receive input from other causes Chemotherapy	Acetylcholine (M) Histamine (H1) Serotonin (5HT3) Substance P / Neurokinin 1

Common Causes of Nausea

- Constipation
- Gastric dysmotility
 - Gastroparesis
 - Autonomic neuropathy
 - Gastric outlet obstruction
 - Ileus
 - Malignant bowel obstruction

Common Causes of Nausea

- Abdominal involvement / visceral traction
 - Omental metastases
 - Peritoneal carcinomatosis
 - Masses
 - Extensive liver involvement

Common Causes of Nausea

- Medications
 - Opioids
 - SSRIs
 - NSAIDs
 - Digoxin

Common Causes of Nausea

- Severe pain
- Intracranial disease
- Radiation, chemotherapy
- Poor mouth care
- Vestibular apparatus stimulation

- Often multi-factorial

Mechanism-based Approach

1. Thorough evaluation
 2. Determine the underlying cause(s) and neuroreceptors involved
 3. Target treatment to the underlying cause(s) and neuroreceptors
- remember to align with the patient's goals

The case of Mr. L

- 58M – pancreatic cancer, diagnosed 15 months ago, neoadjuvant chemotherapy followed by partial resection
- 8 months ago – palliative chemotherapy
- 6 months ago – chemotherapy stopped
- Daily nausea, has ondansetron left over from chemotherapy treatments

1. Thorough Evaluation

- History

1. Thorough Evaluation

- Physical exam

1. Thorough Evaluation

- Investigations

2. Determine the underlying cause

- The case of Mr. L – scenario 1
 - No recent opioid changes
 - Abdominal pain stable
 - No bowel movement in ~ 7 days
 - Epigastric mass
 - Liver mets

2. Determine the underlying cause

- The case of Mr. L – scenario 2
 - Abdominal pain increased
 - No BM x 7 days
 - No flatus x 2+ days

2. Determine the underlying cause

- The case of Mr. L – scenario 3
 - No recent opioid changes
 - Abdominal pain stable
 - No bowel movement in ~ 7 days
 - Epigastric mass
 - Moments of confusion

Management

- Nonpharmacologic
 - Avoid constipation
 - Small meals and snacks
 - Foods that are tolerable
 - Good mouth care
 - Ginger, herbal products (mild effect)
 - Hypnotherapy for anticipatory nausea

Management

- Pharmacologic – general principles
 - Opioid-induced usually self-limited
 - Dexamethasone for brain involvement
 - Aim to use one anti-emetic at a time. Combine for refractory cases
 - Avoid prokinetic + anticholinergic agents (theoretically cancel each other out)

Management

anti-dopamine & prokinetic

Drug / Class	Receptor	Centre / Mechanism
Metoclopramide	5HT4 agonist (prokinetic) 5HT3 antagonist (at high doses) Dopamine (D2) antagonist	GI tract, except obstruction Chemoreceptor trigger zone Higher cortical centres
Domperidone - crosses BBB to lesser degree	5HT4 agonist (prokinetic) D2 antagonist	GI tract, except obstruction

- Monitor EPS
- Use carefully in patients with parkinsonism

Management anti-dopamine

Drug / Class	Receptor	Centre / Mechanism
Haldol	Dopamine (D2) antagonist (more potent than metoclopramide)	GI tract, good choice for obstruction Chemoreceptor Trigger Zone Higher cortical centres
Methotrimeprazine Olanzapine	Multiple (D2, 5HT2, H1, Ach antagonism)	GI tract Chemoreceptor Trigger Zone Higher cortical centres Vomiting centre Vestibular system

- Monitor EPS
- Sedating
- Use carefully in patients with parkinsonism

Management

anti-5HT3

Drug / Class	Receptor	Centre / Mechanism
Ondansetron	5HT3 antagonist	Chemoreceptor trigger zone GI tract Vomiting centre

- Expensive, constipating, QT-prolonging

Management

anti-histamine

Drug / Class	Receptor	Centre / Mechanism
Dimenhydrinate	H1 antagonist	Vestibular system Chemoreceptor trigger zone Vomiting centre

- Increased risk of falls in the elderly

Management

anti-cholinergic

Drug / Class	Receptor	Centre / Mechanism
Scopolamine (Hyoscine hydrobromide)	Ach muscarinic antagonist	Vestibular system Vomiting centre GI tract – dries secretions
Buscopan (Hyoscine butylbromide)	Ach muscarinic antagonist	Vestibular system GI tract- dries secretions

- Scopolamine: sedating, available in patch
- Buscopan: no central effect, doesn't cross BBB

Management

corticosteroid

Drug / Class	Receptor	Centre / Mechanism
Dexamethasone	Unclear	Brain involvement (good choice for brain mets, increased ICP) Reduces secretions (good choice for bowel obstruction)

- High side-effect profile with long-term use

Management cannabinoid

Drug / Class	Receptor	Centre / Mechanism
Cannabinoids Nabilone (THC) Sativex (THC & CBD) Herbals	Cannabinoid receptors	Higher cortical centres Chemoreceptor trigger zone Vomiting centre

- High side effect profile
- For chemotherapy-induced nausea and vomiting or refractory cases

Management

benzodiazepine

Drug / Class	Receptor	Centre / Mechanism
Benzodiazepines	GABA receptors	Higher cortical centres
Lorazepam		

- Sedating

Mechanism-based Approach

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3. Targeted treatment

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 - No recent opioid changes
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 - Liver mets

3. Targeted treatment

- The case of Mr. L – scenario 2
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3. Targeted treatment

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Medication Summary

Suspected Cause	Best choices
Opioid-induced nausea	Metoclopramide, domperidone, haloperidol
Malignant bowel obstruction	Haloperidol, dimenhydrinate, ondansetron, dexamethasone
Chemotherapy and radiotherapy-induced nausea	Ondansetron, cannabinoids, corticosteroids, metoclopramide
Anticipatory nausea or anxiety-related nausea	Benzodiazepine, hypnotherapy
Motion sickness / vestibular	Dimenhydrinate, scopolamine
GI / visceral cause	Metoclopramide
Increased ICP	Dexamethasone