Management of nausea & vomiting

By/ Shaimaa Yahia Ragab

Agenda

- Aim of management.
- Non-pharmachological therapy.
- Pharmachological therapy.
- Treatment of the cause

- Migraine – associated nausea and vomiting.
- Pregnancy-induced nausea.
- Management of postoperative nausea and vomiting.
- Motion sickness.
- Chemotherapy-induced nausea and vomiting.
- Gastroenteritis
- Gastroparesis.

Management

- Assess the severity of dehydration & rehydration.
- Correct electrolytes imbalance.
- Encourage oral intake.
- Treat underlying cause

Non-pharmacological

- Diet
- Life style
- Complementary and alternative therapies

Pharmacological

Maintain oral hygiene.

Eat small frequent meals.

Dietary fiber can increase symptoms in gastroparesis

Because liquids are emptied from the stomach more efficiently than solids, **a liquid diet is preferred**

Low-fat nutrients are given as lipids delay gastric emptying in symptomatic patients.

If can't tolerate oral feeding

IV hydration to replace lost fluids and electrolytes. Enteral or parenteral nutrition (TPN) may be indicated for some patients

Life style

- Avoid alcohol and tobacco.
- Avoid lying down after eating-sit upright 30-60 minute

Complementary and alternative therapies

- Acupuncture/acupressure
- Use of herbal remedies

Applying pressure at various parts of the body

Difference between Acupressure and Acupuncture

Needle is inserted at specific points in the body

They can be useful in preventing N/V in a variety of conditions, such as pregnancy or motion sickness*

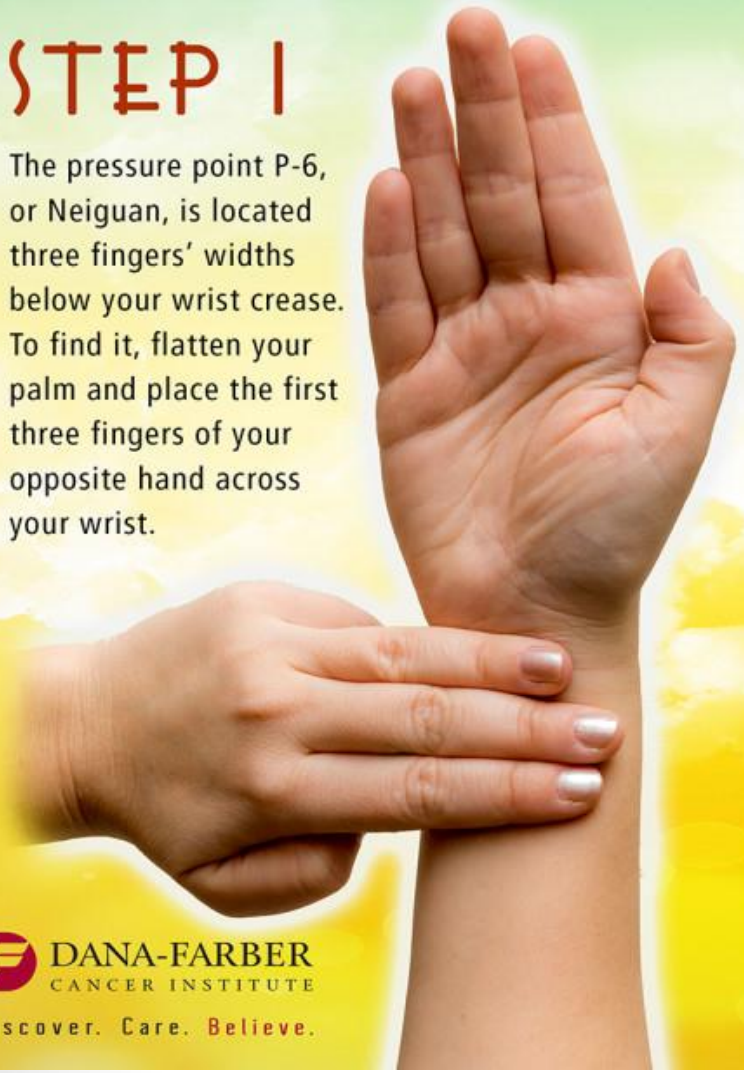
*Berardi RR, Ferrari SP, Hume AL, et al. Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care. 16th ed. Washington, DC: American Pharmacists Association; 2009.

HOW TO PERFORM ACUPRESSURE FOR VOMITING AND NAUSEA

Acupressure is an ancient Chinese therapy that combines acupuncture and pressure. Research shows that it can relieve side effects of chemotherapy, including nausea and vomiting.

STEP 1

The pressure point P-6, or Neiguan, is located three fingers' widths below your wrist crease. To find it, flatten your palm and place the first three fingers of your opposite hand across your wrist.



STEP 2

Place your thumb on the point below your index fingers between two large tendons. Apply firm pressure and massage the point for two to three minutes. The massage should be firm, but not painful.

DANA-FARBER
CANCER INSTITUTE

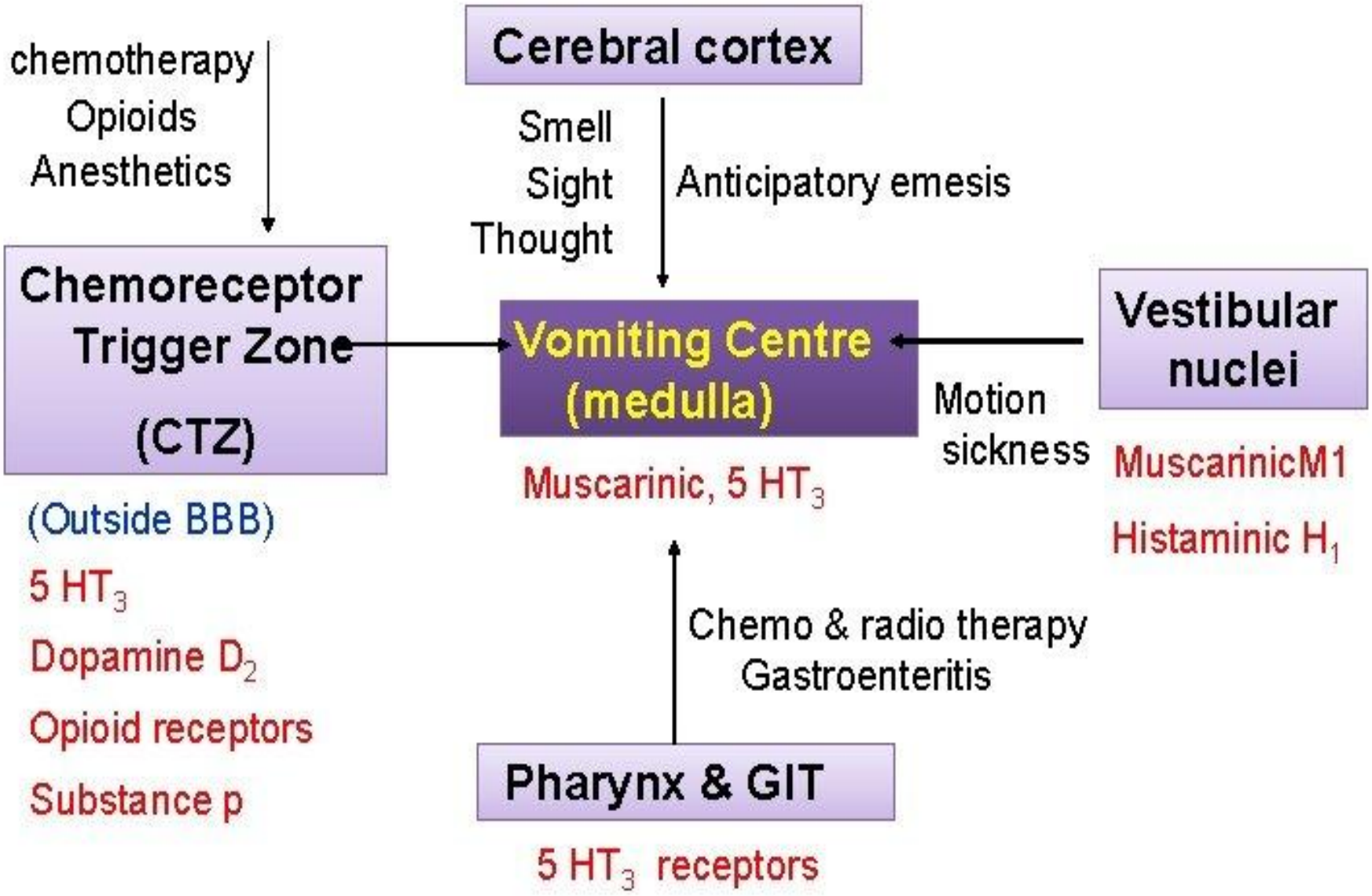
Discover. Care. Believe.

Use of herbal remedies

- **Ginger has been used as an antiemetic.**
- **Its mechanism of action is not completely understood, ginger is thought to antagonize the 5-HT3 and cholinergic receptors, and may have direct activity on the gastrointestinal tract.**
- **Ginger can cause reflux and heartburn, and may potentiate bleeding because of its anticoagulant effects**
- **Its dose is up to 2 g per day in divided doses of 250 mg are considered safe, even in pregnant women.**

** Thomson M, et al. Effects of ginger for nausea and vomiting in early pregnancy: a meta-analysis. J Am Board Fam Med. 2014; 27(1): 115-122.*

Pathophysiology of Emesis



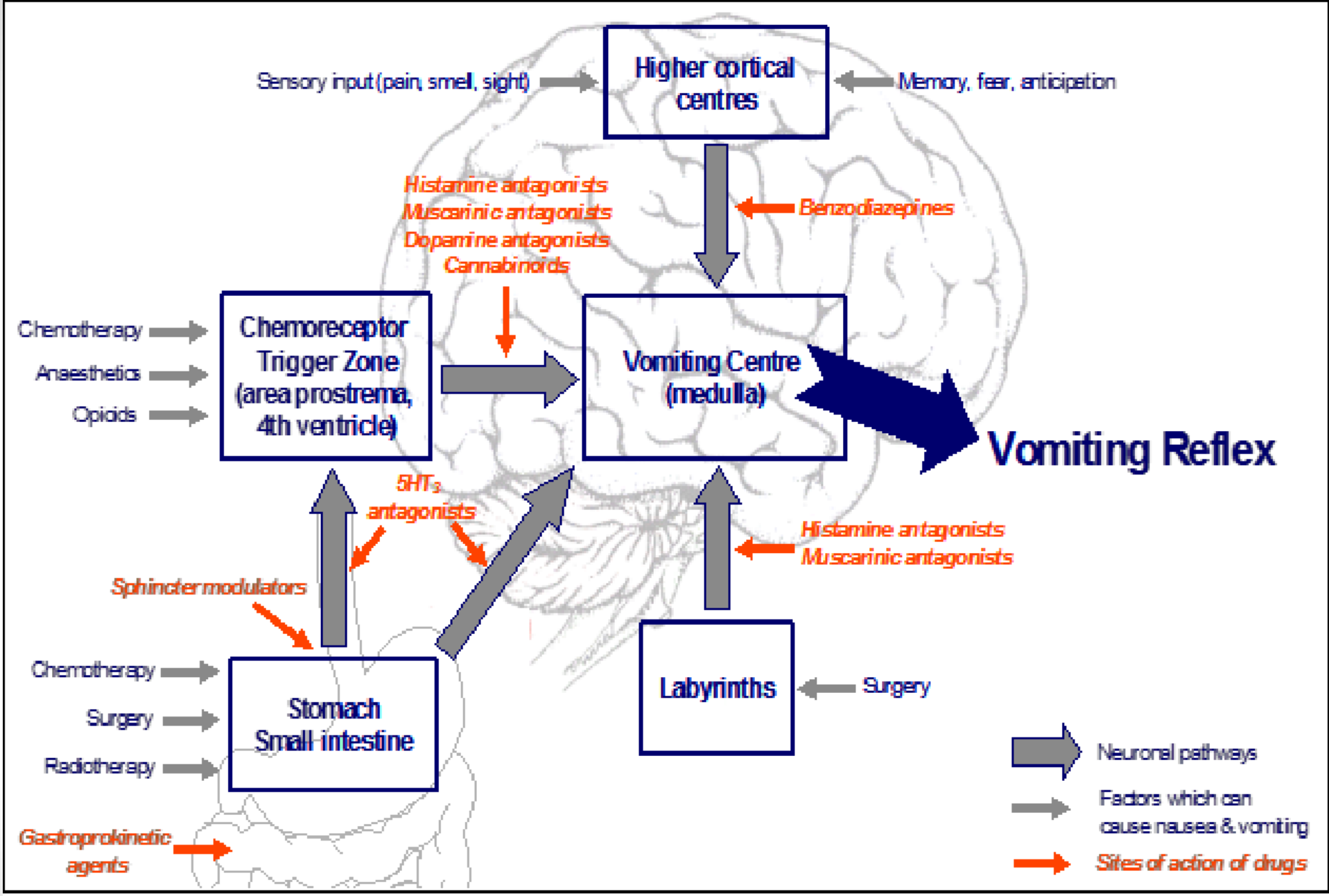


FIGURE 2: ACTION OF ANTIEMETIC DRUGS AT VARIOUS ZONES OR RECEPTORS OF THE BODY

Kumar A and Kumar A (2013). ANTIEMETICS : A REVIEW.

Drug class/name	Receptor antagonist	Indication
Antihistamine	Histamine	Motion sickness, chemotherapy
Cyclizine		
Dimenhydrinate		
Diphenhydramine		
Hydroxyzine		
Anticholinergic	Acetylcholine	Motion sickness prophylaxis, used with opioids to treat post-operative nausea and vomiting
Hyoscyamine		
Benzodiazepine	GABA	Chemotherapy, cyclic vomiting
Lorazepam		
Diazepam		
Midazolam		
Phenothiazine	Dopamine D2 receptor at the chemoreceptor trigger zone (CTZ)	Vomiting
Prochlorperazine		
Chlorpromazine		
Perphenazine		
Promethazine		

Category A in pregnancy

Aprepitant: is a Substance P or Neurokinin1 receptor antagonist that has similar efficacy as the 5-HT3 antagonists in the treatment of chemotherapy-induced nausea & vomiting (Harris, 2010)

Butyrophenones	Dopamine D2 receptor at the chemoreceptor trigger zone (CTZ)	Intractable emesis from gastritis
Droperidol		
Benzamide	Dopamine D2 receptor at the chemoreceptor trigger zone (CTZ)	Gastroesophageal reflux, motility disorders
Metoclopramide		
Anti-serotonin	Serotonin (5HT3)	Chemotherapy, post-op vomiting
Odansetron	Dolasetron Ramosetron	
Granisetron		
Macrolide	Motilin agonist	Gastroparesis and other motility disorders
Erythromycin		

Dexamethasone (Corticosteroids): are used as adjunct agents in the management of nausea & vomiting. It has been shown to improve the effects of other anti-emetics including metoclopramide, 5-HT3 and NK1 antagonists (Harris, 2010).

Dronabinol (Cannabinoid Agonists): have been found to be effective anti-emetics, but there use can be limited by patient acceptance of side effects including sedation, euphoria, hallucinations (e.g. change in time perception), "the munchies" (Harris, 2010).

MIGRAINE-ASSOCIATED NAUSEA

- Approximately 60% of patients with migraines develop nausea and vomiting.

- Nausea and vomiting associated with migraines are caused by a central process, with dopamine being a primary mediator; thus, dopamine antagonists such as metoclopramide, prochlorperazine, and chlorpromazine are logical choices for treatment of vomiting during an acute attack.

- It was found that in patients with acute migraine, a combination of metoclopramide and aspirin improved nausea and vomiting with fewer adverse events compared with sumatriptan (Imitrex).

Kirthi V, et al. Aspirin with or without an antiemetic for acute migraine headaches in adults. Cochrane Database Syst Rev. 2013; (4): CD008041.

PREGNANCY-INDUCED NAUSEA

- Nausea and vomiting occur in more than one half of pregnancies.
- Although the pathogenesis of nausea and vomiting in pregnancy is not completely understood, it is thought to be multifactorial, with hormonal changes having a key role.
- Several antiemetic drug classes have been used for treatment, but there is limited evidence on fetal outcomes.
- The American College of Obstetricians and Gynecologists recommends the use of pyridoxine with or without doxylamine as first-line pharmacotherapy for nausea and vomiting in pregnant women.

- In more severe cases in which dehydration or hyperemesis gravidarum occurs, intravenous rehydration may be necessary, and may be used in combination with antiemetics.
- Ondansetron has comparable effectiveness to older antiemetics, such as promethazine, and causes less sedation.
- Corticosteroids may be used in severe, persistent cases, but are not recommended before 10 weeks' gestation because of the increased risk of oral clefts*.
- Complementary and alternative medicine is often used by pregnant women who wish to avoid pharmacologic therapies. Ginger improves nausea and vomiting if taken for at least four days**.

- ***ACOG practice bulletin: nausea and vomiting of pregnancy. Obstet Gynecol. 2004; 103(4): 803-814.***
- ****Matthews A, et al. Interventions for nausea and vomiting in early pregnancy. Cochrane Database Syst Rev. 2014;(3):CD007575.***

Management of Postoperative Nausea and Vomiting

Guideline 1. Identify Patients' Risk for PONV

Patient

- Female sex (B1)
- History of PONV or motion sickness (B1)
- Non-smoking (B1)
- Younger age (B1)

Surgery

- Type of surgery (cholecystectomy, laparoscopic, gynecological) (B1)
- Duration of surgery >30 min

Anesthesia

Type:

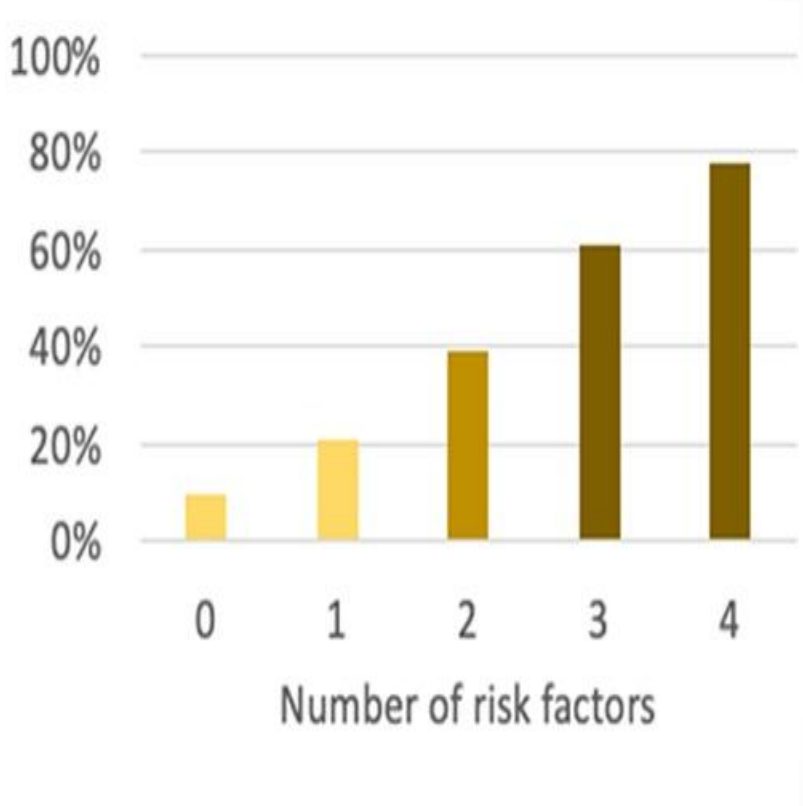
- Volatile anesthetics
- Nitrous oxide,
- Postoperative opioids (evidence A1)

Duration

Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg. 2020 Aug;131(2):411-448.

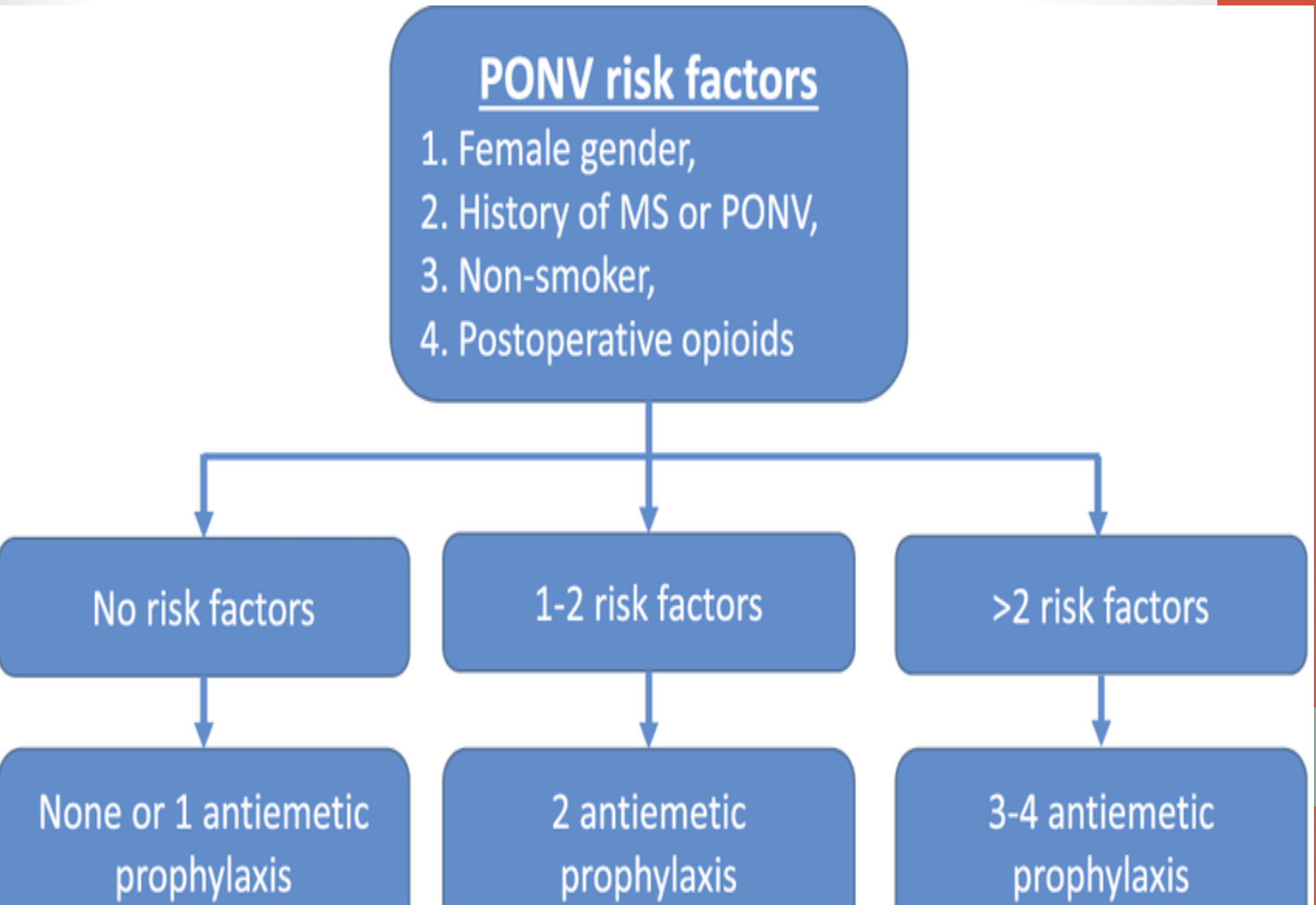
Risk score

Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV and/or Motion Sickness	1
Postoperative Opioids	1
Sum of points	0-4



The Apfel simplified risk score

Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg. 2020 Aug;131(2):411-448.


PONV risk factors
1. Female gender,
2. History of MS or PONV,
3. Non-smoker,
4. Postoperative opioids
No risk factors
1-2 risk factors
>2 risk factors
None or 1 antiemetic prophylaxis
2 antiemetic prophylaxis
3-4 antiemetic prophylaxis

Guideline 2. Reduce Baseline Risk for PONV

Strategies to Reduce Baseline Risk

- Avoidance of GA by the use of regional anesthesia (A1)
- Use of propofol for induction and maintenance of anesthesia (A1)
- Avoidance of nitrous oxide in surgeries lasting over 1 h (A1)
- Avoidance of volatile anesthetics (A2)
- Minimization of intraoperative (A2) and postoperative opioids (A1)
- Adequate hydration (A1)

Guideline 3. Administer PONV Prophylaxis Using 2 Interventions in Adults at Risk for PONV

• 5-HT_3 receptor antagonists + dexamethasone
• 5-HT_3 receptor antagonists + aprepitant (NK1 receptor antagonist)
• 5-HT_3 + droperidol
• Haloperidol + dexamethasone + ondansetron

Ondansetron is the most commonly used and studied 5-HT_3 receptor antagonist and is considered the “gold standard” in PONV management (evidence A1).

Guideline 4. Provide Antiemetic Treatment to Patients With PONV Who Did Not Receive Prophylaxis or When Prophylaxis Failed

- In patients who did not receive PONV prophylaxis, 5-HT_3 receptor antagonists such as ondansetron and ramosetron remain the first-line pharmacotherapy for treating established PONV.
- Recommended treatment rescue antiemetic regimens include ondansetron at 4 mg dose administered orally or IV, ramosetron at 0.3 mg IV, granisetron 0.1 mg and tropisetron 0.5 mg, as well as promethazine 6.25 mg IV.

- When PONV prophylaxis has failed, patients should receive antiemetic treatment from a different pharmacological class to the PONV prophylaxis.
- Administering repeated dose of antiemetics from the same class within 6 hours does not confer additional therapeutic benefit when compared to placebo (evidence A2).
- If more than 6 hours has elapsed, administration of a second dose of 5-HT_3 receptor antagonist or butyrophenone may be considered if no other alternatives are available.

Adult PONV Rx Management

1 RISK FACTORS

Female sex
Younger age
Non-smoker
Surgery type

History of PONV/motion sickness

Opioid analgesia

2 RISK MITIGATION

Minimize use of nitrous oxide, volatile anesthetics, high-dose neostigmine

Consider regional anesthesia

Opioid sparing/ multimodal analgesia (enhanced recovery pathways)

3 RISK STRATIFICATION

Quantify the # of risk factors to determine risk and guide anti-emetic therapy

1-2 Risk Factors

Give 2 agents

> 2 Risk Factors

Give 3-4 agents

4 PROPHYLAXIS

5HT3 receptor antagonists

Antihistamines

Propofol anesthesia

Acupuncture

Corticosteroids

Dopamine antagonists

NK-1 receptor antagonists

Anticholinergics

5 RESCUE TREATMENT

Use anti-emetic from different class than prophylactic drug

Motion Sickness

- Scopolamine, an anticholinergic, is used for the prevention of motion sickness and for acute treatment. Scopolamine's effectiveness is likely due to its central anticholinergic properties.
- Scopolamine is most commonly used as a transdermal patch that is applied behind the ear for up to 72 hours
- Dimenhydrinate , Meclizine and Cyclizine are long-acting piperazine antihistamines and generally cause less sedation than other antihistamines.
- Promethazine (Phenergan) is prescribed for treating nausea or vomiting, motion sickness, and allergic reactions, but causes more sedation than other antihistamines.

- Caffeine has been shown to be of benefit in treating motion sickness only when combined with other pharmacological treatments such as promethazine.
- Benzodiazepines such as diazepam have been shown to prevent motion sickness but not as well as other options.

Chemotherapy-Induced Nausea and Vomiting

- Treatment recommendations are based on four types of chemotherapy-induced nausea and vomiting (CINV), as follows:
- **Acute:** Onset of emesis within a few minutes to several hours after chemotherapy is administered and usually peaking in the first 4-6 hours
- **Delayed:** Onset of emesis more than 24 hours after chemotherapy is administered
- **Anticipatory:** Onset of emesis prior to chemotherapy administration as a conditioned response in patients who have experienced emesis during a previous cycle of chemotherapy
- **Breakthrough/refractory:** Emesis despite prophylactic/breakthrough medications

❖All the guidelines use the following system to classify chemotherapy agents into the following risk groups:

High emetic risk:
- ≥90% or more of patients experience emesis

Moderate emetic risk:
- 30% to 90% of patients experience emesis

Low emetic risk:
- 10% to 30% of patients experience emesis

Minimal emetic risk:
- < 10% of patients experience emesis

- The National Comprehensive Cancer Network (NCCN) recommends basing the choice of antiemetic(s) used on the emetic risk of the therapy, prior experience with antiemetics, and patient factors.
- Patient risk factors for anticancer agent–induced nausea/vomiting include the following:

- Younger age
- Female sex
- Previous history of CINV
- Prone to motion sickness
- History of morning sickness during pregnancy
- Anxiety/high pretreatment expectation of nausea

NCCN Clinical Practice Guidelines in Oncology. Antiemesis. National Comprehensive Cancer Network. 2020

- NCCN guidelines state that the best management of acute or delayed CINV is ***prevention.***
- Patients should be protected before receiving chemotherapy and for the full period of risk (up to 4 days) afterward. General recommendations for prevention are as follows:

- Prevention of acute emesis should start before chemotherapy and continue for the first 24 hours
- Prevention of delayed emesis is a continuation of prophylactic treatment for 2 to 4 days following completion of chemotherapy
- Prevention is also key to the management of anticipatory emesis

NCCN Clinical Practice Guidelines in Oncology. Antiemesis. National Comprehensive Cancer Network. 2020

- Consider using lorazepam as an adjuvant to the antiemetic regimen to decrease anxiety in patients at risk for anticipatory emesis
- Consider using an H2 blocker or a proton pump inhibitor to prevent dyspepsia
- Consider other potential causes of emesis in cancer patients (eg, bowel obstruction)

NCCN Clinical Practice Guidelines in Oncology. Antiemesis. National Comprehensive Cancer Network. 2020

American Society of Clinical Oncology (ASCO) guidelines also include the following recommendations:

- Adult patients treated with high-dose chemotherapy and stem cell or bone marrow transplantation should be offered a three-drug combination of an NK1 RA, a 5-HT3 RA, and dexamethasone, or a four-drug combination of an NK1 receptor antagonist, a 5-HT3 receptor antagonist, dexamethasone, and olanzapine (antipsychotic medication).

Hesketh PJ, Kris MG, Basch E, Bohlke K, Barbour SY, Clark-Snow RA, et al. Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2017 Jul 31. 34 (4):JCO2017744789.

Level	National Comprehensive Cancer Network Recommendations	American Society of Clinical Oncology Recommendations
High	➢ **Day 1 (before chemotherapy):** NK1 RA + 5-HT3 RA + DEX *or* • Olanzapine + palonosetron +DEX *or* • NK1 RA + 5-HT3 RA + DEX + olanzapine ➢ **Days 2-4:** Varies according to day 1 regimen	• **Day 1** (before chemotherapy): NK1 RA + 5-HT3 RA + DEX + olanzapine • **Days 2-4:** continue olanzapine on days 2-4 • Add DEX on days 2-4 for high-emetic risk (non-AC)
Moderate	• **Day 1** (before chemotherapy): 5-HT3 RA + DEX *or* Olanzapine + palonosetron +DEX *or*NK1 RA + 5-HT3 RA + DEX • **Days 2-3:** Varies according to day 1 regimen	• Treated with carboplatin area under the curve (AUC) ≥ 4 mg/mL/min: NK1 RA + 5-HT3 RA + DEX • Other moderate-risk regimens: 5-HT3 RA + DEX on day 1 • Delayed: DEX on days 2-3
Low	• Start before chemotherapy: DEX *or* MCP PO/IV *or* prochlorperazine *or* oral 5-HT3 RA	• Acute: 5-HT3 RA *or* DEX
Minimal	• No routine prophylaxis	• No routine prophylaxis

GASTROENTERITIS

- Oral rehydration solution is strongly recommended as first-line treatment of acute gastroenteritis with mild to moderate dehydration.

- Because nausea in gastroenteritis is a result of visceral stimulation mediated primarily by serotonin, 5-HT3 antagonists are an effective treatment.

- A Cochrane review of several randomized, placebo-controlled trials concluded that a single oral dose of ondansetron (Zofran) controls vomiting and reduces hospitalizations and the need for intravenous fluid administration in children and adolescents.

Gastroparesis

CLASS OF MEDICATION	COMMON USES	COMMON SIDE EFFECTS
• **Anticholinergic** (scopolamine [Maldemar]	• Possible adjunct for cytotoxic chemotherapy, prophylaxis and treatment of motion sickness	• Drowsiness, dry mouth, vision disturbances
• **Antihistamines** (cyclizine [Marezine], diphenhydramine [Benadryl], dimenhydrinate [Dramamine], meclizine [Antivert])	• Migraine, motion sickness, vertigo (due to anti-muscarinic properties.)	• Drowsiness • Worsening urinary retention in BPH(**Anticholinergic)**
• **Corticosteroids** (dexamethasone)	• Adjunct for chemotherapy-related symptoms	• Increased energy, insomnia, mood changes
• **Serotonin 5-hydroxytryptamine antagonists** (dolasetron [Anzemet], odansetron [Zofran], granisetron [Kytril], palonosetron [Aloxi])	• Post-chemotherapy nausea and vomiting, severe nausea and vomiting	• Asthenia, constipation, dizziness, mild headache
• **Substituted benzamides** (metoclopramide [Reglan], trimethobenzamide [Tigan])	• Diabetic gastroenteropathy, gastroparesis	• Extrapyramidal side effects (e.g., akathisia, dyskinesia, dystonia, oculogyric crises,

CLASS OF MEDICATION	*COMMON USES*	*COMMON SIDE EFFECTS*
• **Benzodiazepines** (alprazolam [Xanax], diazepam [Valium], lorazepam [Ativan])	• Adjunct for chemotherapy-related symptoms	• Sedation
• **Butyrophenones** (droperidol [Inapsine†], haloperidol [Haldol])	• Anticipatory and acute chemotherapeutic nausea and vomiting, postoperative nausea and vomiting	• Agitation, restlessness, sedation
• **Cannabinoids** (dronabinol [Marinol])	• Refractory chemotherapy-related nausea and vomiting	• Ataxia, dizziness, euphoria, hypotension, sedation
• **Phenothiazines** (chlorpromazine [Thorazine†], prochlorperazine, promethazine [Phenergan]) **(Dopamine antagonist)**	• Migraine, motion sickness, post-chemotherapy nausea and vomiting, PONV, severe episodes of nausea and vomiting, vertigo	• Extrapyramidal symptoms (e.g., dystonia, tardive dyskinesia), orthostatic hypotension, sedation


Thank
You