Self-Study Module 3p:
Symptoms; Nausea/Vomiting
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Abstract

Many symptoms and syndromes are commonly encountered in patients with cancer. This module first presents general approaches to symptom management, followed by management of the specific symptoms and syndromes, including: anorexia/cachexia, anxiety, constipation, depression, diarrhea, fatigue, insomnia, menopausal symptoms and sexual health, mucositis, nausea and vomiting, and skin problems.

Any symptom can be debilitating and prevent the patient and family from achieving goals that are important to them. As with other aspects of medicine, tailored management is based on the underlying etiology and pathophysiology. When several symptoms occur together, they can be interrelated and management can be complex.

Introduction

Nausea is an unpleasant subjective sensation of being about to vomit. (Ref. 1) (Ref. 2) Vomiting is the reflex expulsion of gastric contents through the mouth. Nausea may be present without vomiting or vice versa. The awareness of nausea, the inability to keep food or fluids down, the associated acid and bitter tastes, and the unpleasant smells associated with vomitus can be very distressing for patients, families, and caregivers.

There are many potential causes for both nausea and vomiting in a patient with cancer. Chemotherapy-associated nausea is only one of them. In this section, the management of all nausea is discussed. For a more extensive discussion of chemotherapy-associated nausea and vomiting, refer to the ASCO Symptom Control Curriculum. (Ref. 3)

Incidence/prevalence

The incidence of chemotherapy-induced acute nausea is related to the specific drug. Most writers have divided chemotherapeutic agents into five emetogenic categories based on the incidence of acute nausea (Table 1).
### Table 1: Emetogenic Classes

<table>
<thead>
<tr>
<th>Emetogenic Class</th>
<th>Medications</th>
<th>Incidence of Acute Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Capecitabine, Rituximab</td>
<td>Minimal (&lt;10 %)</td>
</tr>
<tr>
<td>II</td>
<td>Gemcitabine, Paclitaxel</td>
<td>Low (10-30%)</td>
</tr>
<tr>
<td>III</td>
<td>Doxorubicin, Carboplatin</td>
<td>Mild (30-60%)</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td>Moderate (80-90%)</td>
</tr>
<tr>
<td>V</td>
<td>Cisplatin, high-dose cyclophosphamide</td>
<td>High (&gt;90%)</td>
</tr>
</tbody>
</table>

The incidence of radiation-associated nausea is related to the irradiated region. While there is minimal nausea associated with peripheral sites, if a substantial portion of the GI tract is in the radiation field, nausea occurs in nearly all patients.

The prevalence of nausea in patients with advanced cancer not associated with chemotherapy or radiotherapy ranges from 40 to 70%. (Ref. 1)

Opioids have been associated with acute nausea in up to 30% of patients, particularly young women.

**Prognosis**

If acute, treatment-related nausea/vomiting is not prevented and controlled, treatment is delayed or stopped prematurely. If chronic nausea is not controlled, nutritional status, emotional coping, and ability to function are impaired.

Overall, uncontrolled symptoms are associated with a worse prognosis. When symptom severity is combined with measures of functional status, the resulting measure is more accurate than functional status alone.
Case

Review the case below, and keep it in mind as you progress through the module. How would you approach the assessment of this patient? What interventions might be appropriate?

P.T. is a 92-year-old farmer with colon cancer metastatic to the liver. Right upper quadrant pain is well controlled with extended-release morphine, 60 mg PO bid, and dexamethasone, 4 mg PO q AM. However, he complains of constant nausea that limits his ability to eat.

Pathophysiology

Two organ systems are particularly important in nausea and vomiting: the brain and the GI tract. These are shown schematically in Figure 1.

![Figure 1: Pathophysiology of Nausea/Vomiting](image)

The motor function of the gut is controlled at three levels: the parasympathetic and sympathetic nervous systems, enteric brain neurons, and smooth muscle cells. The GI tract, the chemoreceptor trigger zone (CTZ), the vestibular apparatus, and the cortex are all involved in the intricate physiology of nausea. The neuromuscular reflex that constitutes the final common pathway after stimulation from one or more of these areas emanates from the vomiting center. (Ref. 4)
Stimulation is mediated through the neurotransmitters serotonin, dopamine, acetylcholine, and histamine. All four neurotransmitters can be demonstrated in the chemoreceptor trigger zone. Although all are present in the lining of the gastrointestinal tract, serotonin is particularly important. Acetylcholine and histamine are important in the vestibular apparatus.

Nausea/vomiting that is mediated by the cortex is more complex and is not associated with specific neurotransmitters. Cortical responses seem to be learned responses (e.g., the anticipatory nausea associated with chemotherapy, nausea related to anxiety, etc.).

Table 2 relates pathophysiology to the underlying etiology.

**Assessment**

A thorough assessment of nausea and vomiting is crucial to understanding which of the potential etiologies is present, what the likely pathophysiology is, and which medications are most appropriate to prescribe. Different causes will require different interventions if the symptoms are to be controlled effectively.

Ask the patient to describe the nausea:

- When does it occur?
- Is it acute or chronic?
- Is it intermittent or constant?
- Is it associated with sights or smells or events?
- What happens after eating?
- Does the patient vomit right after the food is swallowed (a cortical learned response or anxiety-related) or after about 45 minutes (associated with delayed gastric emptying or a “squashed stomach” syndrome from an enlarged liver) or hours after eating (suggesting intestinal or bowel involvement)?
- Does vomiting make it better?
- Does the patient only get nauseated for a moment immediately before vomiting? This suggests hyperperistalsis trying to overcome a mechanical obstruction in the intestine.
- What are the patient's bowel patterns? Constipation is a frequently missed cause of chronic nausea.
- What medications have been tried? With what frequency?
The physical examination and selected studies help confirm impressions from the history. For example, changing posture or head position may reproduce or worsen nausea, implicating the vestibular apparatus. Funduscopic examination may confirm increased intracranial pressure. Abdominal examination that shows the absence of bowel sounds suggests obstruction. An enlarged liver crossing the midline or presence of ascites or stool in the rectal vault increase the likelihood that diminished peristalsis plays a role.

There are a range of diagnostic studies that can be judiciously deployed. A plain radiograph of the abdomen looking for presence and quantity of stool, and evidence of ileus is frequently useful. Abdominal ultrasound (for enlarged liver or ascites assessment), computed tomography scans of the head or abdomen, and motility studies may be useful in selected cases.

Management

This module focuses on the general symptomatic management of nausea/vomiting. It does not provide in detail all possible causes or specific treatments to reverse each of these etiologies.

In the management of nausea/vomiting, it is frequently not possible to identify or specifically correct the underlying etiology. Time-limited therapeutic trials may provide both relief and clues to underlying causes. When causes are known, the burden of the disease-modifying intervention may also outweigh its potential benefit.

Table 2 relates major causes of nausea/vomiting to their principal site of action and lists the “11 Ms” of emesis. This clarification is intended to set the stage for the rational use of antiemetics, which can be classified by their principal site of action.

Correction of dehydration, hypokalemia, and metabolic alkalosis will sometimes resolve the symptom.

Few high-quality therapeutic trials have compared the efficacy of different drugs in specified types of nausea/vomiting outside of chemotherapy. There are five classes of antiemetic drugs: antidopaminergic drugs, antiserotinergic drugs, antihistamines, anticholinergics, and neurokinins. In addition, there are a group of adjunctive drugs that, while not directly antiemetics, treat specific causes of nausea such as hyperacidity or gut dysmotility or causes whose mechanism of action is poorly understood.

Empiric therapy with antiemetics usually begins with a single medication targeting the presumed mechanism of nausea/vomiting. The dose should be optimized before a second medication with a different mechanism of action is added. If the first medication is rationally chosen, addition rather than substitution of a second may be wise. Sequential combination therapy may be required in some patients.
### Table 2: Management of Nausea/Vomiting Based on Etiology
(the 11 Ms of emesis)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Pathophysiology</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metastases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral (increased ICP)</td>
<td>Increased ICP, direct CTZ effect</td>
<td>Steroids, mannitol, anti-DA/Hist</td>
</tr>
<tr>
<td>Liver</td>
<td>Toxin buildup</td>
<td>anti-DA/Hist</td>
</tr>
<tr>
<td><strong>Meningeal irritation</strong></td>
<td>Increased ICP</td>
<td>Steroids</td>
</tr>
<tr>
<td><strong>Movement</strong></td>
<td>Vestibular stimulation (may be worse with morphine)</td>
<td>Anti-Ach</td>
</tr>
<tr>
<td><strong>Mentation</strong> (e.g., anxiety)</td>
<td>Cortical</td>
<td>Anxiolytics (e.g., benzodiazepines, THC)</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>CTZ, vestibular effect, GUT</td>
<td>Anti-DA/Hist, anti-Ach, prokinetic agents, stimulant cathartics</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>CTZ, GUT</td>
<td>Anti-5HT/DA, steroids</td>
</tr>
<tr>
<td>Others (NSAIDs, see Mucosal Irritation)</td>
<td>CTZ</td>
<td>Anti-DA/Hist</td>
</tr>
<tr>
<td><strong>Mucosal irritation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>GUT, gastritis</td>
<td>Cytoprotective agents</td>
</tr>
<tr>
<td>Hyperacidity, gastroesophageal reflux</td>
<td>GUT, gastritis, duodenitis</td>
<td>Antacids</td>
</tr>
<tr>
<td>Etiology</td>
<td>Pathophysiology</td>
<td>Therapy</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td><strong>Mechanical obstruction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraluminal</td>
<td>Constipation, obstipation</td>
<td>Manage constipation</td>
</tr>
<tr>
<td>Extraluminal</td>
<td>Tumor, fibrotic stricture</td>
<td>Reversible — surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Irreversible — manage fluids, steroids, inhibit secretions with octreotide, scopolamine</td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids, ileus, other medications</td>
<td>GUT, CNS</td>
<td>Prokinetic agents, stimulant laxatives</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercalcemia, hyponatremia, hepatic/renal failure</td>
<td>CTZ</td>
<td>Anti-DA/ Hist, rehydration, steroids</td>
</tr>
<tr>
<td><strong>Microbes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local irritation (e.g., esophagitis, gastritis from Candida, H pylori, herpes, CMV)</td>
<td>GUT</td>
<td>Antibacterials, antivirals, antifungals, antacids</td>
</tr>
<tr>
<td>Systemic sepsis</td>
<td>CTZ</td>
<td>Anti-DA/ Hist, antibacterials, antivirals, antifungals</td>
</tr>
<tr>
<td><strong>Myocardial</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemia, congestive heart failure</td>
<td>Vagal stimulation, cortical, CTZ</td>
<td>Oxygen, opioids, anti-DA/ Hist, anxiolytics</td>
</tr>
</tbody>
</table>

**Legend:**
- anti-Ach = Acetylcholine antagonists
- anti-DA = Dopamine antagonists
- anti-Hist = Histamine antagonists
- anti-5HT = Serotonin antagonists
- CTZ = Chemoreceptor trigger zone
- GUT = Gastrointestinal tract
- ICP = Intracranial pressure
- THC = Tetrahydrocannabinol
Chemotherapy-associated nausea/vomiting

Three distinct types of chemotherapy-associated nausea/vomiting have been defined: acute, delayed, and anticipatory. (Ref. 4)

**Acute nausea/vomiting** occurs within the first 24 hours after chemotherapy. It usually starts within 1-2 hours and peaks at 4-6 hours. Several groups have classified the emetogenic potential of chemotherapy agents into five categories and have identified effective oral antiemetic therapies (Table 3). (Ref. 4) (Ref. 5)

**Delayed nausea/vomiting** occurs more than 24 hours after chemotherapy. With cisplatin, this peaks 48-72 hours after therapy, then gradually subsides for 2-3 days. It is also seen with carboplatin, cyclophosphamide, and the anthracyclines. The antiserotonergic and antidopaminergic medications have minimal effect on delayed nausea. The antineurokinin class is the first to show definitive, albeit small, effects on this syndrome.

**Anticipatory nausea/vomiting** is a conditioned response to previous experiences. If acute and delayed nausea are prevented, anticipatory nausea does not occur. Once it occurs, it is a learned response—it is not mediated by the usual emetic neurotransmitters.

Management is challenging. It is better prevented. Once established, benzodiazepines for their anxiolytic and amnestic properties are most useful. Psychotherapy with a focus on cognitive/behavioral interventions may be adjunctive.
Table 3: Antiemetic Regimens Based on Emetogenic Potential of Chemotherapy

<table>
<thead>
<tr>
<th>Emetogenic Class</th>
<th>Medications</th>
<th>Incidence of Acute Nausea</th>
<th>Regimen to Prevent Acute Chemotherapy-Associated Nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Capecitabine, Rituximab</td>
<td>Minimal (&lt;10%)</td>
<td>PRN antidopaminergic</td>
</tr>
<tr>
<td>II</td>
<td>Gemcitabine, Paclitaxel</td>
<td>Low (10-30%)</td>
<td>Dexamethasone 20 mg orally once</td>
</tr>
<tr>
<td>III</td>
<td>Doxorubicin, Carboplatin</td>
<td>Mild (30-60%)</td>
<td>5 FT-3 inhibitor + Dexamethasone 20 mg orally once</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td>Moderate (80-90%)</td>
<td>5 HT-3 inhibitor + Dexamethasone 20 mg orally once</td>
</tr>
<tr>
<td>V</td>
<td>Cisplatin, high-dose cyclophosphamide</td>
<td>High (&gt;90%)</td>
<td>5 HT-3 inhibitor + Dexamethasone 20 mg orally once + Aprepitant (NK1 inhibitor)</td>
</tr>
</tbody>
</table>

**Opioid-induced nausea/vomiting**

Opioids have been associated with acute nausea in up to 30% of patients, particularly young women. This is thought to be due to direct effects on the chemoreceptor trigger zone and the vestibular apparatus. Antidopaminergics (e.g., prochlorperazine) can be given as a premedication in patients at high risk. Antihistamines and anticholinergic and antiserotoninergic drugs have all been observed to be effective. (Ref. 6) Fortunately, patients generally develop pharmacological tolerance to this side effect within 5-7 days of initiating therapy, and the antiemetics can be discontinued. For some patients, changing to a different opioid is also effective.

Nausea that emerges after chronic use is most likely mediated through diminished gut motility and/or constipation causing pseudo-obstruction. Management is best directed at increasing gut motility and relieving constipation.
**Dopamine antagonists**

Dopamine-mediated nausea is probably the most common form of nausea, and the most frequently targeted for initial symptom management outside of the chemotherapy setting, even when the precise mechanism of nausea is not known. These medications are phenothiazines or butyrophenone neuroleptics and have the potential to cause drowsiness and extrapyramidal symptoms, particularly in young women. Haloperidol is less sedating. Medication dosing options include:

- **Droperidol**, 2.5-5 mg IV q 6 h
- **Haloperidol**, 0.5-2.0 mg PO, IV, SC q 6 h, then titrate
- **Metoclopramide**, 10-20 mg PO q 6 h
- **Olanzapine**, 5-10 mg PO daily
- **Perphenazine**, 2-8 mg PO, IV q 6 h
- **Prochlorperazine**, 10-20 mg PO q 6 h or 25 mg pr q 12 h or 5-10 mg IV q 6 h
- **Promethazine**, 12.5-25 mg IV, 25 mg PO/pr q 4-6 h
- **Thiethylperazine**, 10-20 mg PO q 6 h
- **Trimethobenzamide**, 250 mg PO q 6-8 h, 200 mg pr q 6-8 h

**Histamine antagonists (antihistamines)**

All antihistamines typically used to control nausea may also cause sedation. (Ref. 7) In some patients, this adverse effect may be an added benefit. Because antihistamines also have anticholinergic properties, they may do double duty as a single agent and cover both mechanisms. Consider using:

- **Diphenhydramine**, 25-50 mg PO q 6 h.
- **Hydroxyzine**, 25-50 mg PO q 6 h.
- **Meclizine**, 25-50 mg PO q 6 h.

**Acetylcholine antagonists (anticholinergics)**

If a motion-related component is elicited, the vestibular apparatus is implicated. In addition, opioids and anesthetics can trigger acetylcholine-mediated nausea in the vestibular apparatus. (Ref. 8) A medication from this class may be added to other antiemetics in empiric therapy. Consider using: (Ref. 9)

- **Scopolamine**, 0.1-0.4 mg SC, IV q 4 h or 1-3 transdermal patches q 72 h or 10-80 µg/h by continuous IV or SC infusion.
Serotonin antagonists

Serotonin (hydroxytryptophan) subtype 3 (commonly abbreviated HT-3) has been particularly implicated in chemotherapy-associated nausea. Serotonin antagonists can be exceedingly effective if serotonin is a mediator, but they are very expensive. For each drug, there is a plateau in therapeutic efficacy; titration beyond this dose gives no improvement in outcome. Outside the setting of prophylaxis before chemotherapy and before radiotherapy to the abdomen (which stimulates serotonin release from the gut lining) and postoperative nausea, they can be useful for refractory nausea of diverse types, but are typically tried only when other medications have failed. (Ref. 10) They should be promptly stopped if they are not effective after a short trial. Medication and dosing options include:

- **Dolasetron**, 200 mg PO or 50 mg IV
- **Granisetron**, 1 mg PO daily or bid
- **Ondansetron**, 8 mg PO tid
- **Palonosetron**, 0.25 mg IV

Neurokinin antagonists

The newest class of antiemetics, neurokinin-1 receptor antagonists, is used in combination with a serotonin inhibitor and dexamethasone for highly emetogenic chemotherapy with significant potential for delayed nausea and vomiting. A dosing option is:

- **Aprepitant**, 125 mg PO day 1 followed by 80 mg days 2 and 3.

Prokinetic agents

A sluggish or dyskinetic gut due to carcinomatosis, opioid therapy, other medications, etc., may be a profound source of nausea/vomiting in patients with advanced disease. (Ref. 11) (Ref. 12) A large liver may cause a “squashed stomach.” Ascites or peritoneal disease may cause pseudo-obstruction. Constipation can be an exacerbating factor. Medication and dosing options include:

- **Domperidone**, 10-20 mg PO q 6 h (AC & HS)
- **Erythromycin**, 250 mg PO q 6 h (AC & HS); remember that erythromycin itself can be emetogenic
- **Metoclopramide**, 10-20 mg PO or IV q 6 h (AC & HS)
Antacids

Hyperacidity, with or without gastroesophageal reflux and/or gastric or duodenal erosions, may produce considerable nausea, heartburn, acidity, or bitter taste. It may also be associated with vomiting. Possible therapies include:

- **Antacids**, 1-2 tablespoons PO q 2 h PRN
- H₂ receptor antagonists (e.g., *cimetidine* 800 mg PO q HS, *famotidine* 40 mg PO q HS, *ranitidine* 150 mg PO q HS)
- Proton pump inhibitors (e.g., *omeprazole* 20 mg PO daily, *lansoprazole* 30 mg PO daily, *pantoprazole* 40 mg PO daily)

Other medications

This heterogeneous class of medications has unclear mechanisms of action, but uncontested benefits in some patients. (Ref. 13) (Ref. 14) (Ref. 15) Consider using:

- **Dexamethasone**, 6-20 mg PO daily.
- **Lorazepam**, 0.5-2 mg PO, buccal, SC q 4-6 h.
- **Tetrahydrocannabinol**, 2.5-5 mg PO tid.

Bowel obstruction

The nausea associated with bowel obstruction is associated with reverse peristalsis in response to accumulated fluid behind the obstruction. This is discussed in detail in EPEC™-O Module 3e: Symptoms - Bowel Obstruction.

Summary

Acute and chronic nausea is associated with misery and poor quality of life, and can impair comprehensive cancer care. Management requires a solid knowledge of the pathophysiology, including neurotransmitters; a careful evaluation to target likely etiologies; and skillful administration of medications, frequently in combination and titrated to effect.
Key Take-Home Points

1. Nausea is better prevented than treated once it emerges.
2. Untreated nausea may become “learned” and refractory to neurotransmitter-based antiemetic therapy.
3. Control of chemotherapy- and radiotherapy-associated nausea is as important to cancer therapy as the antineoplastic strategies.
4. Control of chronic nausea that is not associated with antineoplastic strategies is associated both with improved quality of life as well as longevity.

Pearls

1. Use antiemetic agents for their neurotransmitter blocking functions; combine them strategically.
2. Titrate drugs to effect or side effects before adding additional agents.
3. It is better to prevent than to treat nausea; err on the side of aggressive overtreatment initially, then reduce the intensity of therapy to maintain control. This approach is preferable to one that slowly increases therapy while the patient remains nauseated.
4. When treating nausea empirically without a firm sense of underlying pathophysiology, cover all of the possible mechanisms.
5. Make a partnership with your patient and the family caregiver; draw them into the interdisciplinary team and foster their active participation in the care plan.

Pitfalls

1. Changing drugs within a single class. This is a mistake. Add drugs with different mechanisms of action.
2. Using small doses of many drugs because you are unsure. Check your reference source and rationalize your treatment.
3. Treating serially with single agents. Use a rational, additive approach resulting in a patient-tailored regimen.
### Appendix: Nausea Medication Table

#### Nausea Medication Table

<table>
<thead>
<tr>
<th>Nausea (antacids, antinauseants)</th>
<th>Generic Name</th>
<th>Trade Name(s)</th>
<th>Dosage Forms/Time $C_{\text{max}}$</th>
<th>Elimination $t_{1/2}$</th>
<th>Route of Elimination</th>
<th>Adult Doses</th>
<th>Pediatric Doses</th>
<th>Adverse Effects</th>
<th>Common Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>H$_2$ receptor antagonist, antacid</td>
<td>Various; Tagamet® is an example: tabs: 200, 300, 400, 800 mg; liquid: 300 mg/5 ml; inj: 300 mg/2 ml</td>
<td>PO: 45-90 minutes IM:15 minutes</td>
<td>Liver metabolism: extensive Renal excretion: 48%-75% Feces: 2-3% Bile: less than 2%</td>
<td>2 hr Metabolites: 2.2 hr</td>
<td>300 mg PO qid ac + hs, or 400-600 mg PO q 12 h, or 800 mg PO nightly, or 300 mg IV q 6 h (max 2,400 mg/24h; reduce dose for renal failure)</td>
<td>1-12 y: 20-25 mg/kg/24h PO: IV + q 4-6 h &lt;1 y: 20 mg/kg/24h PO: IV + q 4-6 h (reduce dose for renal failure)</td>
<td>• cognitive abnormalities, especially if hepatic or renal function is impaired • leukopenia, thrombocytopenia</td>
<td>• ketoconazole • hypoglycemics • theophylline • food, antacids, sucralfate • propantheline</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>Synthetic cannabinoid antiemetic and appetite stimulant</td>
<td>Marinol®: caps: 2.5, 5, 10 mg</td>
<td>PO: 1 hr</td>
<td>Liver metabolism: extensive Renal excretion: 10%-15% Feces: 35%-50%</td>
<td>19-36 hr Metabolites: 49-53 hr</td>
<td>2.5 mg PO q 8-12 h and titrate</td>
<td>• ataxia, blurred vision • depression • dizziness, vertigo • drowsiness • dry mouth • headache • hallucinations • a cannabis &quot;high&quot; • hypersensitivity to marijuana</td>
<td></td>
<td>• alcohol • barbiturates • benzodiazepines • opioids</td>
</tr>
</tbody>
</table>
# Nausea (antacids, antinauseants)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name(s)</th>
<th>Dosage Forms/Time C&lt;sub&gt;max&lt;/sub&gt;</th>
<th>Elimination t&lt;sub&gt;1/2&lt;/sub&gt;</th>
<th>Route of Elimination</th>
<th>Adult Doses</th>
<th>Pediatric Doses</th>
<th>Adverse Effects</th>
<th>Common Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Droperidol</td>
<td>Inapsine&lt;sup&gt;®&lt;/sup&gt;</td>
<td>IM: 2-4 hr IV: 2-4 hr</td>
<td>2 hr Metabolite: 8-12 hr</td>
<td>Liver metabolism: extensive Renal excretion: 75% Feces: 22% (11-50%)</td>
<td>2.5-5 mg q 3-4 h</td>
<td>2-12 years of age: 0.05-0.06 mg/kg/dose IV/IM q 4-6 h</td>
<td>• diarrhea • sedation • hypotension • hypersensitivity</td>
<td>• alcohol • anticholinergics • barbiturates, β-blockers • cimetidine, clonidine • disulfiram • levodopa, lithium • metoclopramide • meperidine • phenytoin • pyrimethamine • SSRIs, TCAs • trazodone, valproate • vitamin C</td>
</tr>
<tr>
<td>Famotidine</td>
<td>Various; Pepcid&lt;sup&gt;®&lt;/sup&gt; is an example: tabs: 10, 20, 40 mg inj: 10 mg/ml</td>
<td>PO: 1-3.5 hr</td>
<td>2.6-4 hr</td>
<td>Liver metabolism: 30%-35% Renal excretion: 25%-70% Feces: 50%</td>
<td>20-40 mg PO daily, or 10-20 mg IV q 12 h</td>
<td></td>
<td>• headache • malaise • dizziness, vertigo • somnolence • insomnia</td>
<td>• warfarin anticoagulants • benzodiazepines • β-blockers • TCAs • corticosteroids • digoxin • ketoconazole • sucralfate</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Prevacid&lt;sup&gt;®&lt;/sup&gt;: PO caps: 15, 30 mg Granule packets: 15, 30 mg ODT: 15, 30 mg IV: 30 mg/vial</td>
<td>PO enteric-coated granules: 1.5-3 hr ODT: 1.8-2.0 hr</td>
<td>0.9-1.5 hr Metabolites: 3 hr</td>
<td>Liver metabolism: extensive Renal excretion: 14%-25% Bile: 67%</td>
<td>15-30 mg PO daily</td>
<td></td>
<td>• generally well tolerated</td>
<td>• phenytoin • warfarin anticoagulants • benzodiazepines • corticosteroids • digoxin • ketoconazole • sucralfate</td>
</tr>
<tr>
<td>Generic Name</td>
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<td>Dosage Forms/ Time $C_{max}$</td>
<td>Elimination $t_{1/2}$</td>
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<td>Metoclopramide</td>
<td>Various; Reglan® is an example: tabs: 5, 10 mg liquid: 1 mg/ml inj: 5 mg/ml</td>
<td>IV: 15 minutes PO: 60-160 minutes PR: 1-3 hr SC: 30 minutes</td>
<td>5-6 hr</td>
<td>Liver metabolism: Renal excretion: 70%-85% Feces: 2%</td>
<td>5-10 mg PO IM, SC, IV tid-qid, ½ h ac and hs (reported as continuous SC, IV infusion)</td>
<td>0.5 mg/kg/24h PO tid-qid, ½ h ac + hs</td>
<td>• dizziness • gynecomastia, galactorrhea, amenorrhea • abdominal cramps • ↑ risk of perforation if bowel obstructed • hypersensitivity</td>
<td>• alcohol, anticholinergics • barbiturates, β-blockers • cimetidine, clonidine • disulfiram, levodopa, lithium • metoclopramide • meperidine • phenytoin, pyrimethamine • SSRIs, TCAs • trazodone, valproate • vitamin C</td>
</tr>
<tr>
<td>Misoprostol</td>
<td>Cytotec®: tabs: 100, 200 μg</td>
<td>PO: 9-15 minutes</td>
<td>20-40 minutes</td>
<td>Liver metabolism: extensive Renal excretion: 80% Feces: 15%</td>
<td>100-200 μg PO q 6 h, after food 200 μg PO bid may be sufficient for NSAID prophylaxis (reduce in renal failure)</td>
<td></td>
<td>• diarrhea, abdominal pain, flatulence • nausea/vomiting • headache</td>
<td>• salicylic acid</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Prilosec®: tab: 10, 20, 40 mg</td>
<td>PO: 0.5-3.5 hr</td>
<td>0.5-1 hr</td>
<td>Liver metabolism: extensive (inactive metabolites) Renal excretion: 77% Bile: excretion of metabolites (16-19%)</td>
<td>20-40 mg PO daily (do not exceed 20 mg/24h with liver failure)</td>
<td></td>
<td>• generally well tolerated</td>
<td>• phenytoin • warfarin anticoagulants • benzodiazepines • corticosteroids • digoxin • disulfiram • phenytoin</td>
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### Nausea (antacids, antinauseants)

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<tr>
<th>Generic Name</th>
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<tr>
<td>Ondansetron</td>
<td>Zofran®: tab: 4, 8 mg inj: 2 mg/ml soin: 4 mg/5 ml ODT: 4, 8 mg</td>
<td>PO: 1-2.2 hr IM: 0.38 hr IV: end of infusion (30 min)</td>
<td>3-5.5 hr</td>
<td>Liver metabolism: extensive Renal excretion: 44%-60% Feces: 25%</td>
<td>4-16 mg PO, IV q 8 h</td>
<td>☺</td>
<td>• headache • constipation • flushing/warmth in head or epigastrium • hypersensitivity</td>
<td>• CNS depressants • anticonvulsants • lithium</td>
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<tr>
<td>Prochlorperazine</td>
<td>Compazine® is an example: tabs: 5, 10 mg liquid: 5 mg/5 ml supp: 2.5, 5, 25 mg inj: 5 mg/ml</td>
<td>1.5-5 hr</td>
<td>6.8-9 hr</td>
<td>Liver metabolism: extensive</td>
<td>5-20 mg PO PR, IM, IV, PR q 4 h PRN or routinely</td>
<td>0.5 mg/kg/24h PO: PR + bid-tid</td>
<td>• drowsiness • dizziness • hypotension • EPS</td>
<td>• alcohol, anticholinergics • barbiturates, β-blockers • cimetidine, clonidine • disulfiram, levodopa, lithium • metoclopramide • meperidine • phenytoin, pyrimethamine • SSRIs, TCAs • trazodone, valproate • vitamin C</td>
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<tr>
<td>Promethazine</td>
<td>Phenergan® tab: 25, 50 mg supp: 12.5, 25, 50 mg syrup 6.25 mg/5 ml</td>
<td>IM: 2-3 hr inj: 25 mg/ml</td>
<td>7-15 hr</td>
<td>Liver metabolism: extensive first-pass metabolism</td>
<td>12.5-25 mg PO/PR q 4–6 h</td>
<td>0.5 mg/lb PO/PR q 4–6 h</td>
<td>• drowsiness • dry mouth • blurred vision</td>
<td>• CNS depressants • anticholinergics</td>
</tr>
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### Nausea (antacids, antinauseants)

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<td>Ranitidine</td>
<td>Various; Zantac® is an example: tabs: 75, 150, 300mg caps:150, 300mg inj: 25 mg/ml syrup: 15 mg/ml</td>
<td>PO: 0.5-2 hr IM: 15 minutes</td>
<td>2-3 hr</td>
<td>Liver metabolism: Renal excretion: 30%-70%</td>
<td>150 mg PO bid or 300 mg PO daily (300 mg PO bid may be used for up to 4 wk to promote healing) 50 mg IV, IM q 6-8 h</td>
<td>2.5-3.8 mg/kg/24h PO + bid</td>
<td>• nausea/vomiting • constipation • diarrhea • abdominal discomfort • drug-induced hepatitis • impotence • gynecomastia • hypersensitivity</td>
<td>• phenytoin • probenecid • procainamide • quinidine • acetaminophen</td>
</tr>
<tr>
<td>Sucralfate</td>
<td>Various; Carafate® is an example: tab: 1 g suspension: 1 g/10 ml</td>
<td>Initial response: 1 hr</td>
<td>Duration PO: 6 hr</td>
<td>Sucralfate is not metabolized; any amount of sucrose octasulfate and aluminum absorbed is excreted unchanged in urine Renal excretion: 0.5-2.2% Feces: 90%</td>
<td>1 g PO qid ac + HS 2 g PO q 12 h (may add antacids, but don’t use within ½ h of sucralfate dose as acid is required to activate sucralfate)</td>
<td>☺</td>
<td>• constipation, diarrhea • nausea, gastric discomfort • dry mouth • pruritus • sleepiness, vertigo • AI buildup may occur with renal failure</td>
<td>• no antacids within ½ h of dose, no H₂ blockers • tetracycline • phenytoin • digoxin • ketoconazole • theophylline • ciprofloxacin • norfloxacin</td>
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<td>Trimethobenzamide</td>
<td>Tigan(^\text{®}): caps:100, 250mg supp: 100, 200mg inj: 100 mg/ml</td>
<td>PO: 45 minutes IM: 30 minutes</td>
<td>7-9 hr</td>
<td>Liver metabolism: unknown Renal excretion: 50%-70%</td>
<td>250 mg PO q8h 200 mg PR q8h</td>
<td>30-90 lb child 100-200 mg PO q 6-8 h &lt;30 lb child 100 mg supp PR tid</td>
<td>• drowsiness • dizziness • hypotension • EPS</td>
<td>• alcohol, anticholinergics • barbiturates, β-blockers • cimetidine, clonidine • disulfiram, levodopa, lithium • metoclopramide • meperidine • phenytoin, pyrimethamine • SSRIs, TCAs • trazodone, valproate • vitamin C</td>
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References

Module 3p: Symptoms - Nausea / Vomiting


   A review is presented of the mechanism by which morphine induces nausea in the vestibular apparatus. An initial trial of the use of scopolamine to control morphine-induced nausea and vomiting is described.


   Several pharmacologic agents provide antihistamine effects by acting at the H1 histamine receptor site. The classic agents are relatively nonselective, resulting in a wide range of effects, both therapeutic and undesirable. The newer agents preferentially block peripheral H1 receptor sites and, consequently, have fewer side effects, including sedation.

8  Ferris FD, Kerr IG, Sone M, Marcuzzi M. Transdermal scopolamine use in the

The authors present a review of the mechanism by which morphine induces nausea in the vestibular apparatus. An initial trial of the use of scopolamine to control morphine-induced nausea and vomiting is described.


Controlled trials have indicated that a single transdermal hyoscine (scopolamine) patch is significantly superior to placebo and oral meclizine in preventing motion sickness. Most commonly cited adverse effects have been dry mouth, drowsiness, and impairment of ocular accommodation, including blurred vision and mydriasis. Adverse central nervous system (CNS) effects, difficulty in urinating, rashes, and erythema have been reported only occasionally.


Self-Assessment

Module 3p: Symptoms; Nausea/Vomiting

9. Nausea/Vomiting

Which of the following antiemetics acts primarily at dopamine receptors?

- a). haloperidol
- b). ondansetron
- c). meclizine
- d). scopolamine
Self-Assessment Answers

The correct answer is: a)

This question is aimed at understanding the pathophysiology of nausea and vomiting. Haloperidol is a potent dopamine antagonist. Ondansetron antagonizes serotonin. Meclizine is an antihistamine. Scopolamine is an anticholinergic.