Chapter 53: Nausea and Vomiting

Leigh Anne Hylton Gravatt; Krista L. Donohoe; Mandy L. Gatesman

CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 27, Nausea and Vomiting.

KEY CONCEPTS

KEY CONCEPTS

1. Nausea and/or vomiting is often a part of the symptom complex for a variety of gastrointestinal (GI), cardiovascular, infectious, neurologic, metabolic, or psychogenic processes.
2. Nausea or vomiting is caused by a variety of medications or other noxious agents.
3. The overall goal of treatment should be to prevent or eliminate nausea and vomiting regardless of etiology.
4. Treatment options for nausea and vomiting include drug and nondrug modalities such as relaxation, biofeedback, and hypnosis.
5. The primary goal with chemotherapy-induced nausea and vomiting (CINV) is to prevent nausea and vomiting throughout the entire risk period; the emetic risk of the chemotherapeutic regimen is a major factor to consider when selecting a prophylactic regimen.
6. Patients at high risk of vomiting should receive prophylactic antiemetics for postoperative nausea and vomiting (PONV).
7. Antihistaminic–anticholinergic agents are the most effective therapy for balance disorders.

BEYOND THE BOOK

BEYOND THE BOOK

Drug Information Question: Can you use medical marijuana for nausea and vomiting in your state? Research your state laws and the evidence-based literature for using medical marijuana for nausea and vomiting.

INTRODUCTION

Nausea and vomiting are common complaints from individuals of all ages. Management can be simple or detailed and complex, depending on the etiology. This chapter provides an overview of nausea and vomiting, two multifaceted problems. Nausea is defined as the inclination to vomit or as a feeling in the throat or epigastric region alerting an individual that vomiting is imminent. Vomiting is the ejection or expulsion of gastric contents through the mouth and is often a forceful event. Either condition may occur transiently with no other associated signs or symptoms; however, these conditions may be part of a more complex clinical presentation.

ETIOLOGY

Nausea and vomiting may be associated with a variety of conditions, including gastrointestinal (GI), cardiovascular, infectious, neurologic, or metabolic disease processes. Nausea and vomiting may be a feature of conditions such as pregnancy, or may follow operative procedures or administration of certain medications such as those used in treating cancer. Psychogenic etiologies of these symptoms may be present. Anticipatory etiologies may be involved, such as in patients who have experienced poor nausea and/or vomiting control with previous antineoplastic agents. Table 53-1 lists specific etiologies associated with nausea and vomiting.[1]

TABLE 53-1

Etiologies of Nausea and Vomiting

Intraperitoneal

- Mechanical obstruction
  - Gastric outlet obstruction
  - Bowel obstruction
- Altered sensorimotor function
  - Gastroparesis
  - Gastroesophageal reflux
  - Intestinal pseudo-obstruction
- Irritable bowel syndrome
- Chronic idiopathic nausea
- Functional vomiting
- Cyclic vomiting syndrome
- Cannabinoid hyperemesis syndrome
- Rumination syndrome
- Inflammatory diseases
- Pancreatitis
- Pyelonephritis
- Cholecystitis
- Appendicitis
- Hepatitis
- Acute gastroenteritis
  - Viral
  - Bacterial
  - Biliary colic
  - Liver failure

Cardiovascular diseases

- Acute myocardial infarction
- Cardiomyopathy

Neurologic processes

- Increased intracranial pressure
- Migraine headache
- Vestibular disorders
- Intracerebral hemorrhage
- Intracerebral malignancy

Metabolic disorders
- Diabetes mellitus (diabetic ketoacidosis)
- Addison's disease
- Renal disease (uremia)

Psychiatric causes
- Depression
- Anxiety disorders
- Anorexia and bulimia nervosa

Therapy-induced causes
- Antineoplastic agents
- Radiation therapy
- Anticonvulsant preparations
- Digoxin, Cardiac antiarrhythmics
- Opiates
- Oral hypoglycemics
- Oral contraceptives
- Antibiotics
- Volatile general anesthetics
- Lubiprostone

Drug withdrawal
- Opiates
- Benzodiazepines

Miscellaneous causes
- Pregnancy
- Noxious odors
- Postoperative vomiting

Data from Reference 1.

The etiology of nausea and vomiting may vary with the age of the patient. For example, vomiting in the newborn during the first day of life suggests upper digestive tract obstruction or an increase in intracranial pressure.

2 Nausea or vomiting is caused by a variety of medications or other noxious agents. Drug-induced nausea and vomiting is of particular concern, especially with the increasing number of patients receiving antineoplastic agents. A four-level classification system defines the risk for emesis with agents used in oncology (Table 53-2).[2] Although some agents may have greater emetic risk than others, combinations of agents, higher doses, clinical settings, psychological conditions, prior treatment experiences, and unusual stimulus of sight, smell, or taste may alter a patient's response to antiemetic treatment. In this setting, nausea and vomiting may be unavoidable and some patients experience these problems so intensely that chemotherapy is postponed or discontinued.

TABLE 53-2

Emetic Risk of Agents Used in Oncology and Treatment Options

Antiemetic Agent	Antiemetic Dose on Day 1 of Chemotherapy	Antiemetic Dose on Subsequent Days
High Risk (>90%): Anthracycline/Cyclophosphamide combination, Carmustine, Cisplatin, Cyclophosphamide >1,500 mg/m^2, Dacarbazine, Mechlorethamine, Streptozocin		
NK-1 Antagonist		
Aprepitant	125 mg oral or 130 mg IV	80 mg oral on days 2-3
Fosaprepitant	150 mg IV	
Netupitant-palonosetron	300 mg/0.5 mg oral	
Fosnetupitant-palonosetron	235 mg fosnetupitant/0.25 mg palonosetron IV	
Rolapitant	180 mg oral	
5-HT$_3$ Antagonist[a]		
Granisetron	2 mg oral or 1 mg IV or 10 mcg/kg IV or 1 patch or 10 mg SQ	
Ondansetron	24 mg oral or 8 mg IV or 0.15 mg/kg IV	
Palonosetron	0.5 mg oral	
Ramosetron	0.3 mg IV	
Tropisetron	5 mg oral OR 5 mg IV	
Dexamethasone[b]	12 mg or 20 mg oral/IV	8 mg oral/IV daily or twice daily on days 2-4
Olanzapine	5 mg or 10 mg oral	5 mg or 10 mg oral on days 2-4
Moderate Risk (30%-90%): Aldesleukin, Alemtuzumab, Arsenic trioxide, Azacitidine, Bendamustine, Busulfan, Carboplatin, Clofarabine, Cyclophosphamide <1,500 mg/m^2, Cytarabine >1,000 mg/m^2, Daunorubicin, Daunorubicin and cytarabine liposomal, Doxorubicin, Epirubicin, Fam-trastuzumab deruxtecan-nxki, Idarubicin, Ifosfamide, Irinotecan, Irinetecan liposomal injection, Oxaliplatin, Romidepsin, Temozolomide, Thiotepa, Trabectidin		
5-HT$_3$ Antagonist		
Granisetron	2 mg oral or 1 mg IV or 10 mcg/kg IV or 1 patch or 10 mg SQ	
Ondansetron	8 mg oral twice daily or 8 mg IV or 0.15 mg/kg IV	
Palonosetron	0.5 mg oral or 0.25 mg IV	
Ramosetron	0.3 mg IV	
Tropisetron	5 mg oral or 5 mg IV	

Dexamethasone	8 mg oral/IV	8 mg oral/IV on days 2-3[c]
Low Risk (10%-30%): Aflibercept, Axicabtogene ciloleucel, Belinostat, Blinatumomab, Bortezomib, Brentuximab, Cabazitaxel, Carfilzomib, Cetuximab, Copanlisib, Cytarabine <1,000 mg/m^2, Decitabine, Docetaxel, Elotuzumab, Enfortumab vedotin-ejfv, Eribulin, Etoposide, Fluorouracil, Gemcitabine, Gemcitabine ozogamicin, Inotuzumab ozogamicin, Ixabepilone, Methotrexate, Mitomycin, Mitoxantrone, Moxetumomab pasudotox, Nab-paclitaxel, Necitumumab, Nelarabine, Paclitaxel (conventional and albumin-bound), Panitumumab, Pegylated liposomal doxorubicin, Prmetrexed, Pertuzumab, Tagraxofusp-erzs, Topotecan, Trastuzumab emtansine, Vinflunine		
Choose One:		
5-HT$_3$ Antagonist		
Granisetron	2 mg oral or 1 mg IV or 10 mcg/kg IV or 1 patch or 10 mg SQ	
Ondansetron	8 mg oral or IV	
Palonosetron	0.5 mg oral or 0.25 mg IV	
Ramosetron	0.3 mg IV	
Tropisetron	5 mg oral or IV	
OR		
Dexamethasone	8 mg oral or IV	
Minimal Risk (<10%): Avelumab, Atezolizumab, Bevacizumab, Bleomycin, Cemiplimab, 2-Chlorodeoxyadenosine, Cladribine, Daratumumab, Durvalumab, Emapalumab, Fludarabine, Ipilimumab, Nivolumab, Obinutuzumab, Ofatumumab, Pembrolizumab, Pralatrexate, Ramucirumab, Rituximab (IV and SQ), Trastuzumab, Vinblastine, Vincristine (conventional and liposomal), Vinorelbine		
No routine prophylactic antiemetics are needed		

[a]No additional 5-HT$_3$-RA is needed if netupitant/palonosetron is used.

[b]Dexamethasone dose on day 1 should be reduced to 12 mg when given with aprepitant, fosaprepitant, and netupitant/palonosetron due to drug interactions. Dexamethasone dose on days 2-4 should be omitted when used as antiemetic with anthracycline/cyclophosphamide combination regimen or carboplatin AUC ≥4.

[c]Only if regimen is known to cause delayed nausea/vomiting (eg, cyclophosphamide, doxorubicin, oxaliplatin).

Data from Reference 2.

PATHOPHYSIOLOGY

The three consecutive phases of emesis include nausea, retching, and vomiting. Nausea, the subjective feeling of the need to vomit, may be considered a separate and singular symptom. Retching is the labored movement of abdominal and thoracic muscles before vomiting. The final phase of emesis is vomiting, the forceful expulsion of gastric contents caused by GI retroperistalsis. The act of vomiting is coordinated by the brainstem, but requires the contractions of the abdominal muscles, pylorus, and antrum, a raised gastric cardia, diminished lower esophageal sphincter pressure, and esophageal dilation.[1] Vomiting should not be confused with regurgitation, an act in which the gastric or esophageal contents rise to the pharynx but is not usually associated with forceful ejection seen with vomiting. Accompanying autonomic symptoms of pallor, tachycardia, and diaphoresis account for many of

the distressing feelings associated with emesis.

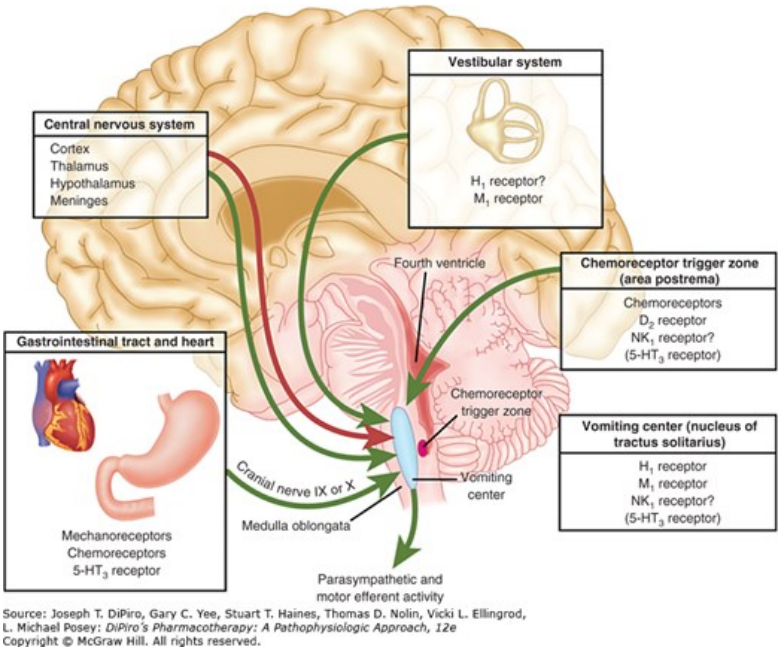
Vomiting is triggered by afferent impulses to the vomiting center (VC), a nucleus of cells in the medulla. Impulses are received from sensory centers, which include the chemoreceptor trigger zone (CTZ), cerebral cortex, and visceral afferents from the pharynx and GI tract. The VC integrates the afferent impulses, resulting in efferent impulses to the salivation center, respiratory center, and the pharyngeal, GI, and abdominal muscles, leading to vomiting.

The CTZ, located in the area postrema of the fourth ventricle of the brain, is a major chemosensory organ for emesis and is usually associated with chemically induced vomiting. Because of its location, blood-borne and cerebrospinal fluid toxins have easy access to the CTZ. Antineoplastic agents primarily stimulate this area rather than the cerebral cortex and visceral afferents. Pregnancy-associated vomiting probably occurs through stimulation of the CTZ.

Numerous neurotransmitter receptors are located in the VC, CTZ, and GI tract, including cholinergic, histaminic, dopaminergic, opiate, serotonergic, neurokinin (NK), and benzodiazepine receptors. Antineoplastic agents, their metabolites, or other emetic compounds theoretically trigger the process of emesis through stimulation of one or more of these receptors. Antiemetics have been developed to antagonize or block these emetogenic receptors.[3] See Fig. 53-1.

Figure 53-1

Pathogenesis of nausea and vomiting: neurologic pathways involved in pathogenesis of nausea and vomiting (see text).



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

(*Reprinted, with permission, from Krakauer EL, et al. Case records of the Massachusetts General Hospital.* Weekly clinicopathological exercises. Case 6-2005. A 58-year-old man with esophageal cancer and nausea, vomiting, and intractable hiccups. *N Engl J Med. 2005;352:817. © Massachusetts Medical Society.*)

CLINICAL PRESENTATION

Nausea and vomiting is commonly seen in many clinical situations. Patients may present in varying degrees of distress summarized in the Patient Care Process (PCP).

Clinical Presentation of Nausea and Vomiting

General

Depending on severity of symptoms, patients may present in mild to severe distress

Symptoms

Simple: Self-limiting, resolves spontaneously, and requires only symptomatic therapy

Complex: Not relieved after administration of antiemetics; progressive deterioration of patient secondary to fluid-electrolyte imbalances; usually associated with noxious agents or psychogenic events

Signs

Simple: Patient complaint of queasiness or discomfort

Complex: Weight loss; fever; abdominal pain

Laboratory tests

Simple: None

Complex: Serum electrolyte concentrations; upper/lower GI evaluation

Other information

Fluid input and output

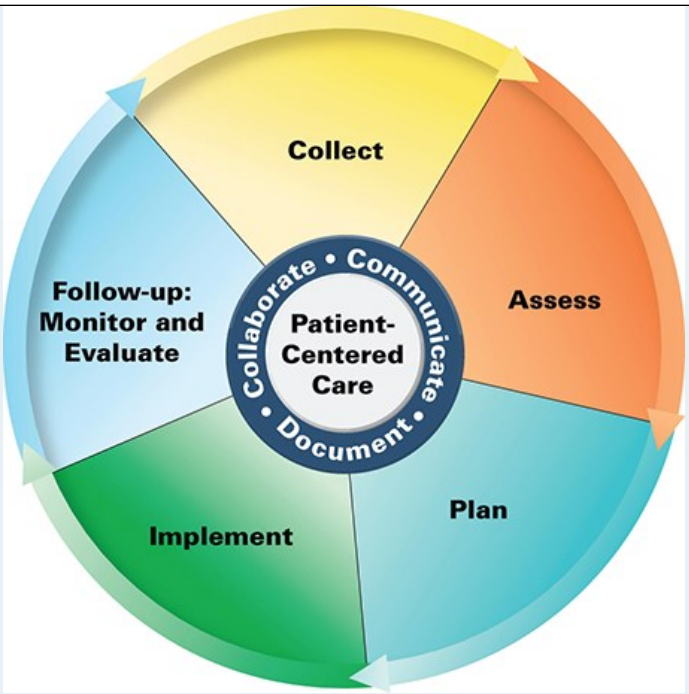
Medication history

Recent history of behavioral or visual changes, headache, pain, or stress

Family history positive for psychogenic vomiting

PATIENT CARE PROCESS

Patient Care Process for Nausea and Vomiting



Collect

- Patient characteristics (eg, age, sex, pregnancy status, triggers)
- Patient medical history (personal and family), history of NV
- Social history (eg, tobacco/ethanol/cannabis use) and dietary habits
- Current medications including prescription and nonprescription medications, herbal products, dietary supplements
- Objective data (eg, QTc prolongation, BP/pulse, complete metabolic panel, CBC, liver function, weight, skin turgor, urine output)

Assess

- Duration, frequency, severity of nausea and vomiting
- Ability/willingness to pay for treatment options
- Emotional status (eg, presence of anxiety, depression)
- Assess ability of the patient to use oral, rectal, injectable, or transdermal medications
- Success of previous antiemetic regimens
- For CINV: Assess emetic risk of chemotherapy (see Table 53-6)
- For PONV: Assess risk factors for developing PONV (see Table 53-5)

Plan*

- Drug therapy regimen including specific antiemetic(s), dose, route, frequency, and duration (see Tables 53-4 and 53-6)
- Monitoring parameters including efficacy (eg, reduction in symptoms, resolution of lab abnormalities, resumption of normal oral intake) and safety (eg, QTc prolongation, drug-drug interactions); frequency and timing of follow-up

- Patient education (eg, purpose of treatment, dietary and lifestyle modification, invasive procedures, drug-specific information, medication administration technique)
- Self-monitoring for resolution of symptoms, when to seek emergency medical attention
- Referrals to other providers when appropriate (eg, gastroenterologist, dietitian, OBGYN, oncologist, anesthesiologist)

Implement*

- Provide patient education regarding all elements of treatment plan
- Use motivational interviewing and coaching strategies to maximize adherence
- Schedule follow-up, adherence assessment

Follow-up: Monitor and Evaluate

- Resolution of nausea and vomiting symptoms
- Need for rescue antiemetics
- Presence of adverse effects
- Patient adherence to treatment plan

****Collaborate with patient, caregivers, and other healthcare professionals.***

TREATMENT

Desired Outcomes

The overall goal of antiemetic therapy is to prevent or eliminate nausea and vomiting. This should be accomplished without adverse effects or with clinically acceptable adverse effects. In addition to these clinical goals, appropriate cost issues should be considered, particularly in the management of chemotherapy-induced nausea and vomiting (CINV) and postoperative nausea and vomiting (PONV).

General Approach to Treatment

Treatment options include drug and nondrug modalities such as relaxation, biofeedback, and hypnosis. Initially patients may choose to not treat or to self-medicate with nonprescription drugs. As symptoms become worse or are associated with more serious medical problems, patients are more likely to utilize prescription antiemetic drugs. When prescribed and used appropriately, these agents can provide relief; however, some patients will never be totally free of symptoms. This lack of relief is most disabling when it is associated with an unresolved medical problem or when the necessary therapy for this condition is the cause of the nausea or vomiting, as in the case of patients who are receiving antineoplastic agents of moderate or high emetic risk.

Nonpharmacologic Management

Nonpharmacologic management of nausea and vomiting involves dietary, physical, or psychological strategies that are consistent with the etiology of nausea and vomiting. For patients who are suffering due to excessive or disagreeable food or beverage consumption, avoidance or moderation in dietary intake may lead to symptom resolution. Patients suffering from symptoms of systemic illness may quickly improve as their underlying condition resolves. Patients in whom these symptoms result from labyrinthine changes produced by motion may benefit quickly by assuming a stable physical position.

Nonpharmacologic interventions include relaxation, biofeedback, hypnosis, cognitive distraction, optimism, guided imagery, acupuncture, yoga,

transcutaneous electrical stimulation, chewing gum, and systematic desensitization.[4-8] Chewing gum after certain surgical procedures improves bowel function and decreases time to first flatus as well as decreases the incidence of postoperative ileus.[6,7] Some of these modalities, such as acupuncture, are effective at preventing nausea and vomiting in the surgical population.[8] Other therapies, such as ginger and pyridoxine, may be beneficial in specific situations as with pregnancy associated nausea and vomiting.

Changes in diet such as restricting oral intake, eating smaller meals, avoiding spicy or fried foods, and instead eating bland foods such as with the BRAT diet (**B**ananas, **R**ice, **A**pplesauce, and **T**oast) can help alleviate symptoms.

Pharmacologic Therapy

Although many approaches to the treatment of nausea and vomiting have been suggested, antiemetic drugs (nonprescription and prescription) are most often recommended. These agents work in various ways and may be used singularly or in conjunction with each other, and have a number of delivery methods.

Factors that enable the clinician to choose the appropriate regimen include: (a) the suspected etiology of the symptoms; (b) the frequency, duration, and severity of the episodes; (c) the ability of the patient to use oral, rectal, injectable, or transdermal medications; and (d) the success of previous antiemetic medications. See Table 53-3 for dosing information of commonly available antiemetic preparations.

TABLE 53-3

Common Antiemetic Preparations and Adult Dosage Regimens[a]

Drug	Adult Dosage Regimen	Dosage Form/Route	Availability
Antacids: Useful with simple nausea/vomiting *Adverse drug reactions: Magnesium products—diarrhea; Aluminum or calcium products—constipation*			
Antacids (various)	15-30 mL every 2-4 hr prn	Liquid/oral	Nonprescription
Antihistaminic–Anticholinergic Agents: Especially problematic in the elderly; increased risk of complications in patients with benign prostatic hyperplasia (BPH), narrow angle glaucoma, or asthma *Adverse drug reactions: Drowsiness, confusion, blurred vision, dry mouth, urinary retention*			
Dimenhydrinate (Dramamine)	50-100 mg every 4-6 hr prn	Tab, chew tab, cap	Nonprescription
Diphenhydramine (Benadryl)	25-50 mg every 4-6 hr prn 10-50 mg every 2-4 hr prn	Tab, cap, liquid IM, IV	Prescription/Nonprescription
Hydroxyzine (Vistaril, Atarax)	25-100 mg every 4-6 hr prn	Tab (unlabeled use)	Prescription
Meclizine (Bonine, Antivert)	12.5-25 mg 1 hr before travel; repeat every 12-24 hr prn	Tab, chew tab	Prescription/Nonprescription
Scopolamine (Transderm Scop)	1.5 mg every 72 hr	Transdermal patch	Prescription
Trimethobenzamide (Tigan)	300 mg three to four times daily 200 mg three to four times daily	Cap IM	Prescription
Benzodiazepine: Used for ANV but is contraindicated with olanzapine			

Adverse drug reactions: Dizziness, sedation, appetite changes, memory impairment; observe for additive sedation especially if used with narcotic analgesics			
Lorazepam (Ativan)	0.5-2 mg on night before and morning of chemotherapy	Tab, IV	Prescription (C-IV)
Butyrophenones: Used for breakthrough CINV; Droperidol has limited use *Adverse drug reactions: Haloperidol—sedation, constipation, hypotension, extrapyramidal symptoms (EPS); Droperidol—QTc prolongation and/or torsade de pointes, 12-lead electrocardiogram prior to administration, followed by cardiac monitoring for 2-3 hr after administration*			
Haloperidol (Haldol)	0.5-2 mg every 4-6 hr prn	Tab, liquid, IM, IV	Prescription
Droperidol (Inapsine)[b]	2.5 mg; additional 1.25 mg may be given	IM, IV	Prescription
Cannabinoids: Used for breakthrough CINV *Adverse drug reactions: Eurphoria, somnolence, xerostomia*			
Dronabinol (Marinol, Syndros)	5-15 mg/m^2 every 2-4 hr prn 4.2-12.6 mg/m^2 every 2-4 hr prn	Cap Oral solution	Prescription (C-III)
Nabilone (Cesamet)	1-2 mg twice daily	Cap	Prescription (C-II)
Corticosteroids: Useful as a single agent or combination therapy for prophylaxis of CINV or PONV *Adverse drug reactions: Insomnia, GI symptoms, agitation, appetite stimulation, hypertension, and hyperglycemia*			
Dexamethasone	See Table 53-6 for CINV dosing and Table 53-5 for PONV dosing	Tab, IV	Prescription
Histamine (H2) Antagonists: Useful with nausea secondary to heartburn or GERD *Adverse drug reactions: Headache, constipation, or diarrhea*			
Cimetidine (Tagamet HB)	200 mg twice daily prn	Tab	Nonprescription
Famotidine (Pepcid AC)	10 mg twice daily prn	Tab	Nonprescription
Nizatidine (Axid AR)	75 mg twice daily prn	Tab	Nonprescription
5-Hydroxytryptamine-3 Receptor Antagonists: Useful as a single-agent or combination therapy for prophylaxis of CINV or PONV *Adverse drug reactions: Asthenia, constipation, headache*			
	See Table 53-6 for CINV dosing and Table 53-5 for PONV dosing	Tab, IV	Prescription
Miscellaneous Agents • **Metoclopramide:** Prokinetic activity useful in diabetic gastroparesis. *Adverse drug reactions: Asthenia, headache, somnolence, EPS* • *Amisulpride: Mainly used in PONV; avoid use in severe renal impairment. Adverse drug reactions: Increased serum prolactin, prolonged QTc interval* • **Olanzapine:** Use with caution in elderly; contraindicated with benzodiazepines. *Adverse drug reactions: Sedation, prolonged QTc interval, EPS* • **Pyridoxine:** Used in NVP. May be used alone or in combination with doxylamine 12.5 mg. Combination product available as prescription. *Adverse drug reactions: Drowsiness, headache*			
Metoclopramide (Reglan)	10-20 mg (0.5-2 mg/kg) four times daily	Tab, IV	Prescription

Olanzapine (Zyprexa)	5-10 mg daily	Tab	Prescription
Pyridoxine (Vitamin B_6)	10-25 mg orally three to four times daily	Tab, cap	Nonprescription
Amisulpride	5-10 mg once either before or after surgery	5-10 mg once either before or after surgery	Prescription
Phenothiazines: Useful in simple nausea/vomiting or breakthrough CINV *Adverse drug reactions: Prolonged QTc interval, constipation, dizziness, tachycardia, tardive dyskinesia, drowsiness*			
Chlorpromazine (Thorazine)	10-25 mg every 4-6 hr prn	Tab, liquid	Prescription
	25-50 mg every 4-6 hr prn	IM, IV	
Prochlorperazine (Compazine)	5-10 mg every 4-6 hr prn	Tab, liquid	Prescription
	5-10 mg every 3-4 hr prn	IM	
	2.5-10 mg every 3-4 hr prn	IV	Prescription
	25 mg twice daily prn	Supp	Prescription
Promethazine (Phenergan)	12.5-25 mg every 4-6 hr prn	Tab, liquid, IM, IV, supp	Prescription
Substance P/Neurokinin-1 Receptor Antagonist: Useful in combination therapy for prophylaxis of CINV and PONV *Adverse drug reactions: Constipation, diarrhea, headache, hiccups, dyspepsia, and fatigue*			
Aprepitant	See Table 53-6 for CINV dosing and Table 53-5 for PONV dosing	Cap, IV	Prescription
Fosaprepitant		IV	Prescription
Fosnetupitant-palonosetron		IV	Prescription
Netupitant/palonosetron		Cap	Prescription
Rolapitant		Cap	Prescription

[a]All regimens should be monitored for resolution or occurrence of nausea and vomiting as well as maintaining an adequate hydration status.

[b]See text for warnings.

ANV, anticipatory nausea and vomiting; C-II, C-III, and C-IV, controlled substance schedule 2, 3, and 4, respectively; cap, capsule; chew tab, chewable tablet; CINV, chemotherapy-induced nausea and vomiting; GI, gastrointestinal; GERD, gastroesophageal reflux disease; liquid, oral syrup, concentrate, or suspension; NVP, nausea and vomiting of pregnancy; PONV, postoperative nausea and vomiting; supp, rectal suppository; tab, tablet.

The treatment of simple nausea and vomiting often involves self-care from a list of nonprescription products. Both nonprescription and prescription

drugs are useful in the treatment of simple nausea and vomiting in small, infrequently administered doses and are associated with minimal side effects. As the symptoms persist or become worse, prescription medications may be chosen, either as single-agent therapy or in combination.

The management of complex nausea and vomiting, such as in patients who are receiving antineoplastic agents, may require initial combination therapy. In combination regimens, the goal is to achieve symptomatic control through administration of agents with different pharmacologic mechanisms of action.

Antacids

Patients who are experiencing simple nausea and vomiting may initially use antacids, as many of these products are readily available without a prescription. Single or combination products, especially those containing magnesium hydroxide, aluminum hydroxide, and/or calcium carbonate, may provide rapid relief, primarily through gastric acid neutralization. These agents are most effective for those with symptoms related to acid reflux or heartburn and must be used with caution in those who experience acute or chronic kidney disease due to the risk of accumulation. These agents may exacerbate other GI complaints that accompany nausea and vomiting, such as diarrhea or constipation, so attention must be paid to which of these agents may worsen these other conditions.

Antihistamine–Anticholinergic Drugs

Antiemetic drugs from the antihistaminic–anticholinergic category work on muscarinic and histamine receptors in the VC and the vestibular system that stimulate nausea and vomiting. These agents are frequently initiated as self-care to prevent nausea and vomiting associated with motion disturbances such as vertigo and motion sickness.

Benzodiazepines

Benzodiazepines are relatively weak antiemetics and are primarily used for their anxiolytic activity to prevent anxiety or anticipatory nausea and vomiting (ANV) that may occur in patients experiencing suboptimal CINV control. Lorazepam may be used as an adjunct to other antiemetics in patients experiencing ANV.

Butyrophenones

Haloperidol and droperidol work by blocking dopaminergic stimulation of the CTZ, which in turn decreases the incidence of nausea and vomiting. The use of these agents may be complicated by their propensity to cause extrapyramidal symptoms and QTc prolongation. For these reasons, haloperidol is not considered first-line therapy for uncomplicated nausea and vomiting but has been used in breakthrough CINV and palliative care situations.[9] Droperidol use is limited to rescue antiemetic for PONV. The current labeling of droperidol recommends that all patients should undergo a 12-lead electrocardiogram prior to administration, followed by cardiac monitoring for 2 to 3 hours after administration because of the possibility of the development of potentially fatal QT prolongation and/or torsade de pointes.[10]

Cannabinoids

Cannabinoids have complex effects on the CNS and their effects at cannabinoid receptor 1 (CB1) in neural tissues may explain efficacy in CINV. Medicinal cannabis can be in the use of cannabis or cannabinoids in order to treat various conditions, including nausea and vomiting. Cannabinoids can be administered in a variety of methods including orally, topically, or sublingually. Oral dronabinol and nabilone, FDA-approved synthetic analogs of delta-9-tetrahydrocannabinol (THC), may be therapeutic options when CINV is refractory to other antiemetics. Medicinal marijuana has been approved for use in over half of states in the United States; however, its use remains debatable.[11] There is limited data to support the use of smoked or ingested cannabis for CINV. FDA-approved cannabinoids and medicinal cannabis improved symptoms in comparison to placebo or active comparators in some trials.[12] The combination of dronabinol and prochlorperazine was significantly more effective when used in combination for the treatment of CINV versus either agent alone.[11] Cannabinoids have the advantage of being effective for other cancer-related side effects such as pain or use as an appetite stimulant.[11-13] Despite these advantages, cannabinoids are not indicated as first-line agents. There is also concern that chronic cannabis use can lead to cyclic nausea and vomiting, which is called cannabinoid hyperemesis syndrome. This syndrome is primarily treated by supportive care, frequent hot showers, and cannabis cessation.[14]

Corticosteroids

Corticosteroids have demonstrated antiemetic efficacy since the initial recognition that patients who received prednisone as part of their Hodgkin's disease protocol appeared to develop less nausea and vomiting than did those patients who were treated with protocols that excluded this agent. The site and mechanism of action of corticosteroids for CINV and PONV are unknown.

Dexamethasone is the most commonly studied and used corticosteroid in the management of CINV and PONV, either as a single agent or in combination with 5-hydroxytryptamine-3 receptor antagonists (5-HT_3-RAs). Dexamethasone is effective in the prevention of both CINV acute emesis and delayed nausea and vomiting when used alone or in combination.[15,16] Given the risk of corticosteroids such as hyperglycemia, fluid retention, and even psychosis, steroids are not indicated for the treatment of simple nausea and vomiting.

H2-Receptor Antagonists

Histamine-2 receptor antagonists (H2RA) work by decreasing gastric acid production and are used to manage simple nausea and vomiting associated with heartburn or gastroesophageal reflux. Except for potential drug interactions with a variety of oral chemotherapy agents, these agents cause few side effects when used for episodic relief.

5-Hydroxytryptamine-3 Receptor Antagonists

5-Hydroxytryptamine-3 receptor antagonists (5-HT_3-RAs) block serotonin receptors on sensory vagal fibers in the gut wall; thus, blocking the acute phase of CINV. These agents do not completely block the acute phase of CINV and are less efficacious in preventing the delayed phase, but they are considered the standard of care in the management of CINV, PONV, and radiation-induced nausea and vomiting (RINV).[2,16]

The 5-HT_3-RAs are considered equivalent when used in equipotent doses/schedules so any agent may be used for CINV. Intravenous doses of ondansetron should not exceed 16 mg due to QTc prolongation.[17] Palonosetron has less effect on QTc and a significantly longer half-life compared to other 5-HT_3-RAs. Granisetron is available in two nonoral formulations: a transdermal patch and an extended-release subcutaneous injection. The granisetron patch should be applied 24 to 48 hours prior to chemotherapy and may be worn for up to 7 days. The choice of 5-HT_3-RAs for CINV should be based on route of administration, potential side effects, and cost concerns.

Metoclopramide

Metoclopramide works by blocking dopaminergic receptors centrally in the CTZ. It also increases lower esophageal sphincter tone, aids gastric emptying, and accelerates transit through the small bowel, possibly through the release of acetylcholine. The prokinetic activity of metoclopramide makes it useful in patients with nausea and vomiting associated with diabetic gastroparesis. Due to the risk of extrapyramidal symptoms, metoclopramide should be used with caution if used in combination with other dopamine antagonists such as olanzapine or haloperidol.

Neurokinin-1 Receptor Antagonists

Substance P is a peptide neurotransmitter in the NK family whose preferred receptor is the NK_1 receptor. The acute phase of CINV is thought to be mediated by both serotonin and substance P, where substance P is believed to be the primary mediator of the delayed phase. An NK_1 receptor antagonist in combination with other antiemetics is now standard of care for prevention of CINV in both adults and children receiving highly emetogenic chemotherapy.[2] Aprepitant, fosaprepitant, and rolapitant are NK_1 receptor antagonists currently in clinical use, along with two combination NK_1 receptor antagonist/5-HT_3-RA co-formulated products, netupitant/palonosetron (NEPA) and fosnetupitant-palonosetron.[18]

Aprepitant has the potential for numerous drug interactions because it is a substrate and moderate inhibitor of cytochrome isoenzyme CYP3A4 as well as a weak inducer of CYP2C9. It can increase serum concentrations of many drugs, including chemotherapeutic agents metabolized by CYP3A4 such as anthracyclines, bosutinib, cabazitaxel, cyclophosphamide, and ifosfamide.[19] Other significant drug interactions include decreased effectiveness of estrogen-containing contraceptives (oral, patches, vaginal rings), and a decrease in the international normalized ratio when used with warfarin.[20] The

dose of oral dexamethasone within the antiemetic regimen should be reduced 50% when coadministered with aprepitant, because of the 2.2-fold increase in observed area under the plasma-concentration-versus-time curve.[21] Conversely, if dexamethasone is used as part of the chemotherapy regimen, the dexamethasone dose should remain the same.

Fosaprepitant is an injectable form of aprepitant approved by the FDA as an IV substitute for oral aprepitant, given on day 1 only of the CINV prevention regimen.[22] Drug interactions are likely reduced with fosaprepitant compared to oral aprepitant.[19]

Rolapitant has a significantly longer half-life in comparison with aprepitant (7 days vs 9 hours) and therefore should only be administered once in a 2-week period.[23] Although rolapitant has no effects on CYP3A4, it does inhibit p-glycoprotein/ABCB1 and CYP2D6, which may lead to drug interactions with certain antineoplastic agents, including doxorubicin, liposomal vincristine, pazopanib, topotecan, and venetoclax. Postmarketing reports of anaphylaxis, anaphylactic shock, and severe hypersensitivity reactions during or shortly after initiation of IV rolapitant resulted in an FDA warning for this product. Patients with known hypersensitivity to components of IV rolapitant, including soybean oil, may be at an increased risk of reactions. All patients should be screened for cross-reactive allergens including soybeans and other legumes prior to administration.[23]

NEPA, when given in one dose combined with dexamethasone, was noninferior to a combination regimen of aprepitant, granisetron, and dexamethasone regimen in individuals receiving moderate or highly emetogenic chemotherapy.[24] Netupitant is also a moderate inhibitor of CYP3A4, and requires a significant decrease in the dexamethasone dose when used together. Drug interactions with other CYP3A4 substrates would also be expected with NEPA.[18]

Olanzapine

Olanzapine is an antipsychotic that blocks several neurotransmitters including dopamine, serotonin, adrenergic, histamine (H_1), and 5-HT_3-RA. Olanzapine in combination with aprepitant/fosaprepitant, 5-HT_3-RA, and dexamethasone significantly improved nausea control after highly emetogenic chemotherapy.[25] The American Society of Clinical Oncology (ASCO) antiemesis practice guidelines include olanzapine as part of the standard four drug combination antiemetic regimen for highly emetogenic chemotherapy.[2] Sedation is the most common side effects with olanzapine; it should be used with caution in older adults and dose reductions may be necessary in this population.[26-28]

Phenothiazines

Phenothiazines have been the most widely prescribed antiemetic agents and appear to block dopamine receptors, most likely in the CTZ. They are marketed in an array of dosage forms, none of which appears to be more efficacious than the other. These agents may be most practical for long-term treatment and are inexpensive in comparison with newer drugs. Rectal administration is a reasonable alternative for patients in whom oral or parenteral administration is not feasible.

Phenothiazines are most useful in adult patients with simple nausea and vomiting. Intravenously administered prochlorperazine provided faster and more complete relief with less drowsiness than IV promethazine in adult patients treated in an emergency department for nausea and vomiting associated with uncomplicated gastritis or gastroenteritis.[28]

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

There are five categories of CINV: acute, delayed, anticipatory, breakthrough, and refractory. Nausea and vomiting that occurs within 24 hours of chemotherapy administration is defined as acute CINV, whereas when it starts more than 24 hours after chemotherapy administration, it is defined as delayed CINV.[29]

Nausea or vomiting that occurs prior to receiving chemotherapy is termed anticipatory nausea and vomiting (ANV). ANV is believed to be a learned, conditioned, or psychological response that occurs in about 14% of patients by the third cycle of chemotherapy.[4,31,32] ANV triggers include tastes, odors, sights, or thoughts associated with chemotherapy. Risk factors associated with ANV include experiencing CINV with prior chemotherapy cycles and anxiety before receiving chemotherapy.[4] In the setting of optimal antiemetic prophylaxis and no prior history of emesis, reported chemotherapy-induced ANV is rare. Use of newer antiemetic regimens appears to have resulted in a decreased rate of ANV.[30]

Breakthrough nausea and vomiting is defined as emesis occurring despite prophylactic administration of antiemetics and requiring the use of rescue antiemetics. Breakthrough emesis occurs in 10% to 40% of patients treated with antiemetics.[29]

Refractory nausea and vomiting is evident when there is a poor response to antiemetic regimens in prior cycles of chemotherapy. It is also important to rule out other potential causes of nausea and vomiting in the cancer population that are listed in Table 53-4.[2]

TABLE 53-4

Nonchemotherapy Etiologies of Nausea and Vomiting in Cancer Patients

- Fluid and electrolyte abnormalities
- Hypercalcemia
- Volume depletion
- Water intoxication
- Adrenocortical insufficiency
- Drug induced
- Opiates
- Anti-infectives
- GI obstruction
- Increased intracranial pressure
- Peritonitis
- Malignancy (primary tumor or metastases)
- Brain
- Meninges
- Hepatic
- Gastrointestinal
- Uremia
- Infections (septicemia, local)
- Radiation therapy

Data from Reference 25.

5 The primary goal with CINV is to prevent nausea and/or vomiting, and the emetic risk of the chemotherapeutic regimen is a major factor to consider when selecting a prophylactic regimen.[2]

Clinical practice guidelines for the use of antiemetics in CINV have been published by the National Comprehensive Cancer Network (NCCN), the Multinational Association of Supportive Care in Cancer/European Society of Medical Oncology (MASCC/ESMO), and ASCO.[28,32] The NCCN guidelines are updated annually, while the ASCO and ESMO guidelines are updated less frequently. Despite the demonstrated improvement in outcomes with the use of these practice guidelines, they are underutilized by a high percentage of practitioners.[32] Product availability and recommended doses are often institution-specific and may vary considerably from the doses listed in Table 53-2.

Principles of Antiemetic Use for CINV

The ASCO, MASCC, and NCCN consensus groups share several of the principles listed below that are important for the effective prevention of CINV in adults.[27,28,31,32]

1. The primary goal of emesis prevention is no nausea and/or vomiting throughout the period of emetic risk.
2. The duration of emetic risk is 2 days for patients receiving moderately emetogenic chemotherapy and 3 days for highly emetogenic chemotherapy.

Emetic prophylaxis should be provided through the entire period of risk.

3. The selection of the antiemetic regimen should be based on the chemotherapy drug with highest emetogenicity (see Table 53-2). Prior emetic experience and patient-specific factors should also be considered.

4. When given in equipotent doses, oral and IV 5-HT_3-RAs are equivalent in efficacy.

5. The toxicities of antiemetics should be considered and managed appropriately.

Prophylaxis of CINV

Each of the practice guidelines states that the most effective classes of drugs for the prevention of acute emesis, anticipatory, breakthrough, and refractory CINV are the 5-HT_3-RAs, NK_1 receptor antagonists, olanzapine, and glucocorticoids (especially dexamethasone). Treatment recommendations for the different categories of emesis are outlined in Table 53-2. For a full treatment algorithm, see Chapter 150, "Supportive Care."

RADIATION-INDUCED NAUSEA AND VOMITING

Nausea and vomiting associated with radiation therapy (RT) is not well understood and often underestimated by radiation oncologists.[34] RINV is neither as predictable nor as severe as CINV, and many patients receiving RT will not experience nausea or vomiting. RINV occurs in approximately one-third of patients, is site dependent, and can have a substantial impact on a patient's quality of life. Risk factors associated with the development of RINV include combination chemoradiotherapy, prior CINV, upper abdomen RT, and field size.[27] For more information on treatment options for the prevention of RINV, see Chapter 150, "Supportive Care."

POSTOPERATIVE NAUSEA AND VOMITING

PONV in adults occurs in 30% of patients and usually within 24 hours of undergoing anesthesia.[35] Patients with multiple risk factors are at highest risk for PONV (Table 53-5). In adults with 0, 1, 2, 3, and 4 of the risk factors in Table 53-5, the incidence of PONV is 10%, 20%, 40%, 60%, and 80%, respectively. Those who are found to have 0 to one risk factors are considered low risk, those with two risk factors are considered medium risk, and those with three or more risk factors are considered high risk. In children, those with no risk factors are considered low risk, those with one to two risk factors are considered as medium risk, and those with three or more risk factors are considered high risk. The use of a risk assessment tool can help identify patients most likely to benefit from prophylaxis.[16,36,37]

TABLE 53-5

Risk Factors for Postoperative Nausea and Vomiting (PONV)

Patient-related factors • Age less than 50 years old • Female sex (two to three times greater incidence of PONV vs male sex) • Nonsmoker • History of PONV or motion sickness (threefold increase in incidence of PONV) • Hydration status
Factors related to anesthesia • Use of general anesthesia • Use of volatile anesthetics • Nitrous oxide use for >1 hr • Use of opioids (intraoperative or postoperative)
Factors related to surgery • Type of surgical procedure (laparoscopic, gynecological, cholecystectomy) • Duration of surgery

Data from References 36 and 37.

In addition to using prophylactic antiemetics in moderate- and high-risk patients, other strategies to prevent PONV include using regional rather than systemic anesthesia, propofol, and hydration, as well as avoiding the use of extended duration nitrous oxide, volatile anesthetics, or opioids.[16]

Prophylaxis of PONV

6 Patients at highest risk of vomiting (>2 risk factors) should receive three or four prophylactic antiemetics from different pharmacologic classes, while those at moderate risk (1-2 risk factors) should receive a two-drug regimen. Adherence to consensus guidelines for prophylaxis and treatment of PONV decrease emetic episodes.[16] Timing the administration of the antiemetic is vital to the efficacy with PONV and may vary dependent upon the agent. Scopolamine patches must be initiated the evening before the surgery or at least 2 hours prior, whereas NK_1 antagonists should be given during the induction of anesthesia; all other agents are recommended to be administered at the end of the surgery. Pharmacological options for the prevention of PONV include 5-HT_3-RAs, an NK_1 antagonist, corticosteroids, droperidol, haloperidol, amisulpride, antihistamines, and anticholinergics.

Ondansetron is considered the “gold standard” 5-HT3-RA and has the most data supporting its use at the end of surgical procedures. It has greater antivomiting activity versus antinausea activity and is as effective as dexamethasone and IV haloperidol. However, it is less effective than longer acting agents such as aprepitant, ramosetron, granisetron, and fosaprepitant in decreasing emesis beyond 24 hours, and less effective than palonosetron for decreasing the incidence of PONV.[16,38-41,42-45]Ondansetron has greater efficacy compared to metoclopramide.[16]

Steroids, such as dexamethasone and methylprednisolone, are useful low-cost agents for preventing PONV. The recommended dose of dexamethasone ranges from 4 to 10 mg; however, there is limited evidence to support the use of doses greater than 8 mg. Dexamethasone should be administered after the induction of anesthesia, and when given in a single dose, has low risk of postoperative infections and only a mild increase in blood glucose values.[16,34,46] Palonosetron is more efficacious than dexamethasone in reducing PONV over a 24-hour interval.[47] One unique advantage dexamethasone has over other agents is that it decreases the need for other analgesic agents.[48] In patients undergoing hip and knee arthroplasty, methylprednisolone in doses from 40 mg to 125 mg decreased both PONV and pain.[16,49-51]

When evaluating antiemetics for PONV, there are several options including agents with antidopaminergic, antihistaminic, or anticholinergic activity. Intravenous amisulpride at 5 mg was more effective when compared to placebo in decreasing nausea severity. While it may lead to small increases in prolactin levels at lower doses, it was not found to be associated with QTc prolongation or a high risk of extrapyramidal symptoms, but may lead to small increases in prolactin levels.[53] Droperidol can be effective for PONV when administered at the end of surgery; however, its use has been limited due to the risk of sudden cardiac death.[16] Haloperidol, while not an FDA-approved agent for PONV, was efficacious and safe at low doses (0.5-2 mg) for prevention of PONV when compared to 5-HT3 antagonist.[42] Diphenhydramine at a dose of 50 mg decreased the incidence of PONV following outpatient laparoscopic gynecologic surgery.[43]

Several other agents have been studied to decrease the incidence of PONV including gabapentin and midazolam. When used 1 to 2 hours before laparoscopic cholecystectomy gabapentin decreased both pain and the incidence of PONV.[54] When administered at induction of anesthesia midazolam reduced the incidence of PONV, and when combined with other antiemetics has increased efficacy.[55]

Guidelines advocate the use of a combination of antiemetics; however, the optimal regimen when using more than two agents is more ambiguous.[16] The choice should be based on the use of different mechanisms of action, adverse effect profiles, and cost. When evaluating two-drug regimens, the combination of a 5-HT3-RA plus dexamethasone 4 to 8 mg is considered the cornerstone of therapy.[44] There is also strong evidence to support the use of aprepitant plus dexamethasone. The addition of low-dose midazolam has increased efficacy, and amisulpride plus either ondansetron or dexamethasone was beneficial when compared to either ondansetron or dexamethasone alone.[16,45] Table 53-6 summarizes the doses for prophylactic antiemetics from the consensus guidelines.[16]

In children, those with no risk factors who are considered low risk can either use no antiemetic or either a 5-HT3- RA or dexamethasone. In those with one to two risk factors and are at a medium risk for PONV, it is recommended to use a combination of a 5-HT_3-RA plus dexamethasone. For those with three or more risk factors and at a high risk for developing PONV, the recommendation is to use a 5-HT_3-RA plus dexamethasone, or consider total intravenous anesthesia.[16]

TABLE 53-6

Recommended Prophylactic Doses of Selected Antiemetics for Postoperative Nausea and Vomiting in Adults and Postoperative Vomiting in Children

Drug	Adult Dose	Pediatric Dose (IV)	Timing of Dose[a]
Amisulpride	5 mg	Not included in consensus guidelines	At induction
Aprepitant	40 mg orally	3 mg/kg up to 125 mg	At induction
Dexamethasone	4-8 mg IV	150 mcg/kg up to 5 mg	At induction
Dimenhydrinate	1 mg/kg IV	0.5 mg/kg up to 25 mg	Not specified
Droperidol[b]	0.625 mg IV	10-15 mcg/kg up to 1.25 mg	At end of surgery
Granisetron	0.35-3 mg IV	40 mcg/kg up to 0.6 mg	At end of surgery
Haloperidol	0.5-2 mg (IM or IV)	Not included in consensus guidelines	Not specified
Methylprednisolone	40 mg IV	Not included in consensus guidelines	Not specified
Metoclopramide	10 mg	Not included in consensus guidelines	Not specified
Ondansetron	4 mg IV, 8 mg orally or orally disintegrating tablet	50-100 mcg/kg up to 4 mg	At end of surgery
Palonosetron	0.075 mg IV	0.5-1.5 mcg/kg	At induction
Promethazine[b]	6.25 mg IV	Not included in consensus guidelines	At induction
Ramosetron	0.3 mg IV	Not included in consensus guidelines	At end of surgery
Rolapitant	70-200 mg orally	Not included in consensus guidelines	At induction
Scopolamine	Transdermal patch	Not included in consensus guidelines	Prior evening or 24 hr before surgery
Tropisetron	2 mg IV	0.1 mg/kg up to 2 mg	At end of surgery

[a]Based on recommendations from consensus guidelines.

[b]See FDA "black box" warning.

Data from Reference 16.

Treatment of PONV

Patients who experience PONV after receiving prophylactic treatment with a combination of a 5-HT_3-RA plus dexamethasone should be given rescue therapy from a different drug class such as a phenothiazine, metoclopramide, or droperidol. Repeating the agent given for PONV prophylaxis within 6 hours of surgery offers no additional benefit. A repeated dose of a 5-HT_3-RA is not effective in treatment of PONV.[58,59] If an emetic episode occurs more

than 6 hours postoperatively, a second dose of a 5-HT_3-RA can be used; however, it is not recommended to repeat doses of either dexamethasone or transdermal scopolamine.[16]

If no prophylaxis was given initially, the recommended treatment is low-dose 5-HT_3-RA such as ondansetron 4 mg orally or IV or ramosetron 0.3 mg IV. Alternative treatments for established PONV include haloperidol 1 mg, vestipitant 4 to 36 mg, amisulpride 5 to 10 mg, droperidol 0.625 mg IV, and promethazine 6.25 mg IV.[50-52]

DISORDERS OF BALANCE

Disorders of balance include vertigo, dizziness, and motion sickness. The etiology of these complaints may include diseases that are infectious, postinfectious, demyelinative, vascular, neoplastic, degenerative, traumatic, toxic, psychogenic, or idiopathic. Symptoms of imbalance perceived by the patient present a particular clinical challenge.

7 Beneficial therapy for patients with balance disorders can most reliably be found among the antihistaminic–anticholinergic agents. However, the precise mechanisms of action of these agents are unknown. Oral regimens of antihistaminic–anticholinergic agents given one to several times each day may be effective, especially when the first dose is administered prior to motion.

Motion sickness may be associated with nausea and vomiting; however, medication is more effective when given prophylactically. Scopolamine is effective for the prevention of motion sickness and is considered first line for this indication.[56] The usefulness of scopolamine in preventing motion sickness was enhanced with the development of the transdermal system (patch) that increased patient satisfaction and decreased untoward side effects. The patch should be placed several hours before the anticipated motion exposure. First-generation sedating antihistamines are also effective. However, second-generation nonsedating antihistamines, ondansetron, and ginger root are not effective in the prevention and treatment of motion sickness.[56]

ANTIEMETIC USE DURING PREGNANCY

As many as 80% of pregnant females experience nausea and 50% will have vomiting or retching.[56] The severity of the symptoms varies considerably, from mild nausea to incapacitating nausea and vomiting. The etiology of nausea and vomiting of pregnancy (NVP) is not well understood, but theories proposed include hormonal stimulus, evolutionary adaptation, and psychological predisposition.[56,57] Symptoms are self-limited for a majority of females, although up to 3% develop hyperemesis gravidarum, a serious condition marked by severe physical symptoms and/or medical complications requiring hospitalization.[58] Hyperemesis gravidarum may result in volume contraction, starvation, and electrolyte abnormalities.

Treatment recommendations for the management of NVP are available from the American College of Obstetricians and Gynecologists (ACOG).[59,60] Prevention of NVP should be the initial treatment approach. A prenatal vitamin should be started 1 month prior to becoming pregnant, which may help reduce the incidence and severity of NVP.[60] Dietary changes and/or lifestyle modifications such as eating smaller, more frequent meals every 1 to 2 hours, and avoiding foods or odors that trigger symptoms are recommended. Ginger is beneficial in reducing nausea but not vomiting.[59] Persistent nausea and/or vomiting leads to the consideration of drug therapy at a time when teratogenic potential of each agent must be considered. Pyridoxine (vitamin B_6), with or without doxylamine, is recommended as first-line therapy.[59] A delayed-release formulation of doxylamine and pyridoxine hydrochloride (Diclegis®) is available as a prescription product.[59] Dimenhydrinate, diphenhydramine, prochlorperazine, or promethazine may also be considered in the treatment of NVP.

Patients with persistent NVP or who show signs of dehydration should receive intravenous hydration with thiamine administered before dextrose to prevent Wernicke encephalopathy. Enteral tube feedings should be considered in females with hyperemesis gravidarum not responsive to medical therapy and who cannot maintain weight.[59] Ondansetron, promethazine, and metoclopramide have similar effectiveness for hyperemesis gravidarum, although ondansetron may be better tolerated due to less adverse effects.[61-64] Glucocorticoids, like methylprednisolone, may be used in patients with severe NVP or hyperemesis gravidarum, but should only be used after 10 weeks of gestation due to the increased risk of cleft lip.[56]

ANTIEMETIC USE IN SPECIAL POPULATIONS

Gastroenteritis in Children

Nausea and vomiting associated with pediatric gastroenteritis is usually self-limited and improves with correction of dehydration. The majority of patients can be successfully treated with oral rehydration therapy. Pediatric practitioners may prescribe antiemetics for intractable vomiting due to gastroenteritis. The use of promethazine is contraindicated in patients less than 2 years old and should be used with caution in older children due to the potential risk of fatal respiratory depression.[65] Administration of ondansetron is associated with decreased vomiting, a reduced need for intravenous rehydration therapy, and preventing hospital admissions.[66,67,69,70]

Antiemetic Use in Older Patients

Many of the commonly used antiemetics are on the Beers Criteria list, which are medications that may be inappropriate in older adults due to the risks outweighing the benefits.[68] These include first-generation antihistamines and scopolamine due to their highly anticholinergic side effects. Metoclopramide is also on the Beers list because it may cause extrapyramidal effects including tardive dyskinesia especially in frail older adults.[69] Ondansetron may be considered a preferred antiemetic in older adults; however, consider drug-drug interactions and potential adverse effects before prescribing.[70]

EVALUATION OF EMETIC OUTCOMES

In assessing emetic outcomes, standardized monitoring criteria should include a subjective assessment and objective parameters. For patients on chemotherapy, evaluation of emetic outcomes should occur after the administration of each chemotherapy cycle. In regards to PONV, the patient should be monitored both immediately post procedure as well as for delayed symptoms.

ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
ANV	anticipatory nausea and vomiting
ASCO	American Society of Clinical Oncology
BRAT	bananas, rice, applesauce, or toast
CINV	chemotherapy-induced nausea and vomiting
CTZ	chemoreceptor trigger zone
GI	gastrointestinal
ESMO	European Society of Medical Oncology
HEC	high emetogenic chemotherapy
5-HT_3-RA	5-hydroxytryptamine-3 receptor antagonist
MASCC	Multinational Association of Supportive Care in Cancer
NCCN	National Comprehensive Cancer Network
NEPA	netupitant/palonosetron
NK_1	neurokinin-1
NVP	nausea and vomiting of pregnancy
PONV	postoperative nausea and vomiting
RINV	radiation-induced nausea and vomiting
RT	radiation therapy
TBI	total-body irradiation
VC	vomiting center

REFERENCES

1. Hasler WL. Nausea, vomiting, and indigestion. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2014. http://accessmedicine.mhmedical.com/content.aspx?bookid=1130§ionid=79726154.

2. Hesketh PJ, Kris MG, et al. Antiemetics: ASCO guideline update. *J Clin Oncol.* 2020 Aug 20;38(24):2782–2797. [PubMed: 32658626]

3. Krakauer EL, Zhu AX, Bounds BC, Sahani D, McDonald KR, Brachtel EF. Case records of the Massachusetts General Hospital. *N Engl J Med.*

2005;352:817. Massachusetts Medical Society. [PubMed: 15728815]

4. Kamen C, Tejani MA, Chandwani K, et al. Anticipatory nausea and vomiting due to chemotherapy. *Eur J Pharmacol.* 2014;722:172–179. [PubMed: 24157982]

5. Morehead A, Salmon G. Acupressure in the prevention and treatment of nausea and vomiting across multiple patient populations: Implications for practice. *Nurs Clin N Am.* 2020;55:571–580.

6. Craciunas L, Sajid MS, Ahmed AS. Chewing gum in preventing postoperative ileus in women undergoing caesarean section: A systematic review and meta-analysis of randomised controlled trials. *BJOG.* 2014;121:793–799. [PubMed: 24628729]

7. Short V, Herbert G, Perry R, et al. Chewing gum for postoperative recovery of gastrointestinal function. *Cochrane Database of Syst Rev.* 2015;(2):CD006506.

8. Acar HV. Acupuncture and related techniques during perioperative period: A literature review. *Complement Ther Med.* 2016 Dec;29:48–55. [PubMed: 27912957]

9. Murray-Brown F, Dorman S. Haloperidol for the treatment of nausea and vomiting in palliative care patients. *Cochrane Database Syst Rev.* 2015;11:CD006271.

10. Droperidol [package insert]. Lake Forest, IL: Hospira, Inc.; 2004.

11. Wilkie G, Sakr B, Rizack T. Medical marijuana use in oncology: A review. *JAMA Oncol.* 2016;2(5):670–675. [PubMed: 26986677]

12. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medicinal use: A systematic review and meta-analysis. *JAMA.* 2015;313:2456–2473. [PubMed: 26103030]

13. Inglet S, Winter B, Yost SE, et al. Clinical data for the use of cannabis-based treatments: A comprehensive review of the literature. *Ann Pharmacother.* 2020;54(11):1109–1143. [PubMed: 32483988]

14. Sorensen CJ, DeSanto K, Borgelt L, Phillips KT, Monte AA. Cannabinoid hyperemesis syndrome—diagnosis, pathophysiology, and treatment: A systematic review. *J Med Toxicol.* 2017;13:71–87. [PubMed: 28000146]

15. Italian Group for Antiemetic Research. Double-blind, dose-finding study of four intravenous doses of dexamethasone in the prevention of cisplatin-induced acute emesis. *J Clin Oncol.* 1998;16:2937–2942. [PubMed: 9738561]

16. Gan T, Kumar G, Bergese S, et al. Fourth Consensus Guidelines for the management of postoperative nausea and vomiting. *Anesth Analg.* 2020;131(2):411–448. [PubMed: 32467512]

17. Ondansetron [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2017.

18. Akynzeo (netupitant and palonosetron) [package insert]. Iselin, NJ: Helsinn Therapeutics, Inc.; 2018.

19. Patel P, Leeder JS, Piquette-Miller M, et al. Aprepitant and fosaprepitant drug interactions: A systematic review. *Br J Clin Pharmacol.* 2017;83(10):2148–2162. [PubMed: 28470980]

20. Emend (aprepitant) [package insert]. Whitehouse Station, NJ: Merck & Co, Inc.; 2017.

21. McCrea JB, Majumdar AK, Goldberg MR, et al. Effects of the neurokinin-1 receptor antagonist aprepitant on the pharmacokinetics of dexamethasone and methylprednisolone. *Clin Pharmacol Ther.* 2003;74:17–24. [PubMed: 12844131]

22. Emend (fosaprepitant) [package insert]. Whitehouse Station, NJ: Merck & Co, Inc.; 2018.

23. Varubi (rolapitant) [package insert]. Waltham, MA: Tesaro, Inc.; 2018.

24. Zhang L, Lu S, Feng J, et al. A randomized phase III study evaluating the efficacy of single-dose NEPA, a fixed antiemetic combination of netupitant and palonosetron, versus an aprepitant regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC). *Ann Oncol.* 2018;29:452–458. [PubMed: 29092012]

25. Navari RM, Qin R, Ruddy KJ, et al. Olanzapine for the prevention of chemotherapy-induced nausea and vomiting. *N Engl J Med.* 2016;375:134–142. [PubMed: 27410922]

26. Yanai T, Iwasa S, Hashimoto H, et al. A double-blind randomized phase II dose-finding study of olanzapine 10 mg or 5 mg for the prophylaxis of emesis induced by highly emetogenic cisplatin-based chemotherapy. *Int J Clin Oncol.* 2018;23:382–388. [PubMed: 29039073]

27. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Management of immunotherapy related toxicites. v3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Last accessed September 1, 2021.

28. Ernst A, Weiss SJ, Park S, et al. Prochlorperazine versus promethazine for uncomplicated nausea and vomiting in the emergency department: A randomized, double-blind clinical trial. *Ann Emerg Med.* 2000;36:89–94. [PubMed: 10918098]

29. Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. *N Engl J Med.* 2016;374:1356–1367. [PubMed: 27050207]

30. Molassiotis A, Lee PH, Burke TA. Anticipatory nausea, risk factors, and its impact on chemotherapy-induced nausea and vomiting: Results from the Pan European Emesis Registry Study. *J Pain Symptom Manage.* 2016;51:987–993. [PubMed: 26891606]

31. Roila F, Molassiotis A, Herrstedt J, et al. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. *Ann Oncol.* 2016;27(Suppl 5):v119–v133. [PubMed: 27664248]

32. Jordan K, Gralla R, Jahn F, Molassiotts A. International antiemetic guidelines on chemotherapy induced nausea and vomiting (CINV): Content and implementation in daily practice. *Eur J Pharmacol.* 2014;722:197–222. [PubMed: 24157984]

33. Enblom A, Bergius Axelsson B, Steineck G, et al. One third of patients with radiotherapy-induced nausea consider their antiemetic treatment insufficient. *Support Care Cancer*. 2009;17:23–32. [PubMed: 18528717]

34. Polderman JA, Farhang-Razi V, Van Dieren S, et al. Adverse side effects of dexamethasone in surgical patients. *Cochrane Database Syst Rev.* 2018;8(8):CD011940. [PubMed: 30152137]

35. Wiesmann T, Kranke P, Eberhart L. Postoperative nausea and vomiting—A narrative review of pathophysiology, pharmacotherapy and clinical management strategies. *Expert Opin Pharmacother.* 2015;16:1069–1077. [PubMed: 25866213]

36. Shaikh SI, Nagarekha D, Hegade G, Marutheesh M. Postoperative nausea and vomiting: A simple yet complex problem. *Anesth Essays Res.* 2016;10:388–396. [PubMed: 27746521]

37. Apfel CA, Karttila K, Abdalla M, et al. A factorial trial of six intervention for the prevention of postoperative nausea and vomiting. *N Engl J Med.* 2004;350:2441–2451. [PubMed: 15190136]

38. Diemunsch P, Gan TJ, Philip BK, et al. Single-dose aprepitant vs. ondansetron for the prevention of postoperative nausea and vomiting: A randomized, double-blind phase III trial in patient undergoing open abdominal surgery. *Br J Anaesth.* 2007;99:202–211. [PubMed: 17540667]

39. Park SK, Cho EJ. A randomized, double-blind trial of palonosetron compared with ondansetron in preventing postoperative nausea and vomiting

after gynaecological laparoscopic surgery. *J Int Med Res.* 2011;39:399–407. [PubMed: 21672343]

40. Okafor D, Kaye AD, Kaye RJ, Urman RD. The role of neurokinin-1 (substance P) antagonists in the prevention of postoperative nausea and vomiting. *J Anaesthesiol Clin Pharmacol.* 2017;33:441–445. [PubMed: 29416232]

41. Janicki PK, Schuler HG, Jarzembowski TM, Ross M II. Prevention of postoperative nausea and vomiting with granisetron and dolasetron in relation to CYP2D6 genotype. *Anest Analg.* 2006;102:1127–1133.

42. Singh PM, Borle A, Makkar JK, et al. Haloperidol versus 5-HT_3 receptor antagonists for postoperative vomiting and QTc prolongation: A noninferiority meta-analysis and trial sequential analysis of randomized controlled trials. *J Clin Pharmacol.* 2018;58(2):131–143. [PubMed: 28914976]

43. De Oliveira GS Jr, Bialek J, Marcus RJ, McCarthy R. Dose-ranging effect of systemic diphenhydramine on postoperative quality of recovery after ambulatory laparoscopic surgery: A randomized, placebo-controlled, double-blinded, clinical trial. *J Clin Anesth.* 2016 Nov;34:46–52. [PubMed: 27687344]

44. Som A, Bhattacharjee S, Maitra S, et al. Combination of 5-HT3 antagonist and dexamethasone is superior to 5-HT3 antagonist alone for PONV prophylaxis after laparoscopic surgeries: A meta-analysis. *Anesth Analg.* 2016;123(6):1418–1426. [PubMed: 27870735]

45. Kranke P, Bergese SD, Minkowitz HS, et al. Amisulpride prevents postoperative nausea and vomiting in patients at high risk: A randomized, double-blind, placebo-controlled trial. *Anesthesiology*. 2018;128(6):1099–1106. [PubMed: 29543631]

46. Fan Z, Ma J, Ma X, et al. The efficacy of dexamethasone on pain and recovery after total hip arthroplasty: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore).* 2018;97(13):e0100. [PubMed: 29595631]

47. Paul AA, George SK, Ranjan RV, et al. Randomised control study of palonosetron versus dexamethasone in preventing postoperative nausea and vomiting flowing ear and nose surgeries under general anesthesia. *J Clin Diagn Res.* 2018;12(11):UC10–UC13.

48. Singh PM, Borle A, Panwar R, et al. Perioperative antiemetic efficacy of dexamethasone versus 5-HT3 receptor antagonists: A meta-analysis and trial sequential analysis of randomized controlled trials. *Eur J Clin Pharmacol.* 2018;74:1201–1214. [PubMed: 29858921]

49. Liu G, Gong M, Wang Y, Xiang Z. Effect of methylprednisolone on pain management in total knee or hip arthroplasty: A systematic review and meta-analysis of randomized controlled trials. *Clin J Pain*. 2018;34(10):967–974. [PubMed: 29595528]

50. Candiotti KA, Kranke P, Bergese SD, et al. Randomized, double-blind, placebo-controlled study of intravenous amisulpride as treatment of established postoperative nausea and vomiting in patients who have had no prior prophylaxis. *Anesth Analg.* 2019;128(6):1098–1105. [PubMed: 31094774]

51. Kranke P, Thompson JP, Dalby PL, et al. Comparison of vestipitant with ondansetron for the treatment of breakthrough postoperative nausea and vomiting after failed prophylaxis with ondansetron. *Br J Anaesth.* 2015 Mar;114(3):423–429. [PubMed: 25488303]

52. Yazbeck-Karam VG, Siddik-Sayyid SM, Barakat HB, Korjian S, Aouad MT. Haloperidol versus ondansetron for treatment of established nausea and vomiting following general anesthesia: A randomized clinical trial. *Anesth Analg.* 2017;124(2):438–444. [PubMed: 28002167]

53. Gan TJ, Kranke P, Minkowitz HS, et al. Intravenous amisulpride for the prevention of postoperative nausea and vomiting: Two concurrent, randomized, double-blind, placebo-controlled trials. *Anesthesiology.* 2017;126(2):268–275. [PubMed: 27902493]

54. Wang L, Dong Y, Zhang J, Tan H. The efficacy of gabapentin in reducing pain intensity and postoperative nausea and vomiting following laparoscopic cholecystectomy: A meta-analysis. *Medicine (Baltimore).* 2017;96(37):e8007. [PubMed: 28906382]

55. Ahn EJ, Kang H, Choi GJ, Baek CW, Jung YH, Woo YC. The effectiveness of midazolam for preventing postoperative nausea and vomiting: A systematic review and meta-analysis. *Anesth Analg.* 2016;122(3):664–676. [PubMed: 26516802]

56. Brainard A, Gresham C. Prevention and treatment of motion sickness. *Am Fam Physician*. 2014;90:41–46. [PubMed: 25077501]

57. Flaxman SM, Sherman PW. Morning sickness: A mechanism for protecting mother and embryo. *Q Rev Biol.* 2000;75:113–148. [PubMed: 10858967]

58. Simpson SW, Goodwin TM, Robins SB, et al. Psychological factors and hyperemesis gravidarum. *J Womens Health Gend Based Med.* 2001;10:471–477. [PubMed: 11445046]

59. Matthews A, Haas DM, O'Mathúna DP, Dowswell T. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev.* 2015;(9):CD007575.

60. Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea and vomiting of pregnancy. *Obstet Gynecol.* 2018;131:e15–e30. [PubMed: 29266076]

61. Herrell HE. Nausea and vomiting of pregnancy. *Am Fam Physician*. 2014;89(12):965–970. [PubMed: 25162163]

62. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 187: Neural tube defects. *Obstet Gynecol.* 2017;130:e279–e290. [PubMed: 29189693]

63. Koren G, Clark S, Hankins GD, et al. Maternal safety of the delayed-release doxylamine and pyridoxine combination for nausea and vomiting of pregnancy: A randomized placebo controlled trial. *BMC Pregnancy Childbirth*. 2015;15:59. [PubMed: 25884778]

64. Abas MN, Tan PC, Azmi N, Omar SZ. Ondansetron compared with metoclopramide for hyperemesis gravidarum: A randomized controlled trial. *Obstet Gynecol.* 2014;123(6):1272–1279. [PubMed: 24807340]

65. Phenergan [package insert]. Philadelphia, PA. Wyeth Pharmaceuticals Inc. 2004.

66. Danewa AS, Shah D, Batra P, et al. Oral ondansetron in management of dehydrating diarrhea and vomiting in children aged 3 months to 5 years: A randomized controlled trial. *J Pediatr.* 2016;169:105–109. [PubMed: 26654135]

67. Nino-Serna LF, Acosta-Reyes J, Veroniki AA, Florez ID. Antiemetics in children with acute gastroenteritis: A meta-analysis. *Pediatrics*. 2020;145(4):e20193260. [PubMed: 32132152]

68. Danewa AS, Shah D, Batra P, et al. Oral ondansetron in management of dehydrating diarrhea and vomiting in children aged 3 months to 5 years: A randomized controlled trial. *J Pediatr.* 2016;169:105–109. [PubMed: 26654135]

69. The 2019 American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2019 updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019;67(4):674–694. [PubMed: 30693946]

70. Reuben DB, Herr KA, Pacala JT, et al. *Geriatrics at Your Fingertips 2021*. 23rd ed. New York, NY: The American Geriatrics Society; 2021.

SELF-ASSESSMENT QUESTIONS

1. Which of the following medications would be considered first-line in the prevention of nausea and vomiting related to motion sickness?

   A. a. Scopolamine

   B. b. Ondansetron

   C. c. Cetirizine

D. d. Ginger

2. Which of the following treatments is contraindicated in children less than 2 years old due to the risk of fatal respiratory depression?

   A. a. Metoclopramide

   B. b. Promethazine

   C. c. Probiotics

   D. d. Ondansetron

3. GJ is an 82-year-old male who just had a knee replacement and is experiencing postoperative nausea and vomiting (PONV). The provider would like to use a safe medication in this older patient. Which of the following is the best recommendation for GJ?

   A. a. Promethazine

   B. b. Metoclopramide

   C. c. Scopolamine

   D. d. Ondansetron

4. An appropriate nonpharmacologic recommendation for a pregnant patient with nausea and vomiting includes:

   A. a. Eating large meals

   B. b. Eating two times a day

   C. c. Using ginger

   D. d. Smelling trigger odors

5. MJ is a 32-year-old Black female who is pregnant with her first child and nonpharmacologic therapies are no longer helping her nausea and vomiting. Which of the following is the recommended first-line therapy for the treatment of nausea and vomiting in a pregnant woman?

   A. a. Meclizine

   B. b. Metoclopramide

   C. c. Ondansetron

   D. d. Doxylamine

6. A 35-year-old female patient is found to be at high risk for developing PONV. Which of the following would be the best therapy for prevention of PONV in this patient?

   A. a. Haloperidol + Droperidol

   B. b. Ondansetron + Dexamethasone + Midazolam

   C. c. Dexamethasone + Droperidol +Haloperidol

   D. d. Rolapitant + Promethazine

7. Which of the following 5-HT_3-RA has the longest duration of action?

   A. a. Granisetron

B. b. Ramosetron

C. c. Ondansetron

D. d. Palonosetron

8. A patient undergoing chemotherapy is having a difficult time taking their oral ondansetron during chemotherapy treatments, and has no IV access. Which of the following 5-HT_3-RA medications could be used in this patient?

A. a. Tropisetron

B. b. Granisetron

C. c. Palonosetron

D. d. Fosaprepitant

9. Which of the following is considered a risk factor for developing postoperative nausea and vomiting?

A. a. Use of local anesthetics

B. b. Positive smoking history

C. c. History of motion sickness

D. d. Age >70 years old

10. When should dexamethasone be administered for prevention of postoperative nausea and vomiting in relationship to the operative procedure?

A. a. The night prior to the procedure

B. b. 1 hour prior to the procedure

C. c. At the end of the procedure

D. d. After the induction of anesthesia

11. What antiemetic can be used to treat nausea and vomiting, but when used chronically it can cause hyperemesis syndrome?

A. a. Lorazepam

B. b. Ondansetron

C. c. Promethazine

D. d. Cannabinoids

12. Which agent is considered the first-line treatment for pregnancy-associated nausea and vomiting?

A. a. Pyridoxine + doxylamine

B. b. Droperidol

C. c. Scopolamine

D. d. Olanzapine + dexamethasone

13. The _____ diet can help decrease the symptoms of nausea and vomiting.

A. a. DASH

B. b. BRAT

C. c. Keto

D. d. Raw food

14. Which NK-1 antagonist requires dosing on multiple days post-chemotherapy?

A. a. Aprepitant

B. b. Netupitant-palonosetron

C. c. Rolapitant

D. d. Fosaprepitant

15. What laboratory abnormalities may be found secondary to nausea and vomiting?

A. a. Elevated WBCs

B. b. Low platelets

C. c. Low sodium

D. d. Elevated CRP

SELF-ASSESSMENT QUESTION-ANSWERS

1. **A.** Scopolamine is effective for the prevention of motion sickness and is considered first-line for this indication. The usefulness of scopolamine in preventing motion sickness was enhanced with the development of the transdermal system (patch) that increased patient satisfaction and decreased untoward side effects. The patch should be placed several hours before the anticipated motion exposure.

2. **B.** The use of promethazine is contraindicated in patients less than 2 years old and should be used with caution in older children due to the potential risk of fatal respiratory depression.

3. **D.** Ondansetron may be considered a preferred antiemetic in older adults; however, consider drug–drug interactions and potential adverse effects before prescribing.

4. **C.** Dietary changes and/or lifestyle modifications such as eating smaller, more frequent meals every 1 to 2 hours, and avoiding foods or odors that trigger symptoms are recommended. Ginger is beneficial in reducing nausea but not vomiting.

5. **D.** Persistent nausea and/or vomiting leads to the consideration of drug therapy at a time when teratogenic potential of each agent must be considered. Pyridoxine (vitamin B6), with or without doxylamine, is recommended as first-line therapy. The US Food and Drug Administration (FDA) approved a delayed-release formulation of doxylamine and pyridoxine hydrochloride (Diclegis[R]) as a prescription product.

6. **B.** Patients at highest risk of vomiting (> 2 risk factors) should receive three or more prophylactic antiemetics from different pharmacologic classes. Of the available 5-HT3-RAs, ondansetron is still considered the “gold standard” agent and has the most data supporting its use at the end of surgical procedures. When evaluating 2 drug regimens, the combination of a 5-HT3- RAs plus dexamethasone 4-8 mg is considered the cornerstone of therapy. Considering other regimens, the addition of low dose midazolam has shown to have increased efficacy.

7. **D.** Palonosetron has a significantly longer half-life compared to other 5-HT3-RAs. The half lives are as follows: Granisetron (9 hours); Ramosetron (5.8 hours); Ondansetron (6 hours); Palonosetron (40 hours).

8. **B.** Granisetron is the only option that is also available as a transdermal patch.

9. **C.** The answer is a history of motion sickness. General or volatile anesthetics put patients at a higher risk of PONV. Patients who do not smoke are actually at a higher risk of PONV than those who do, and patients less than 50 years old are at a higher risk. This leaves a history of PONV or motion sickness that increases the risk for PONV.

10. **D.** Dexamethasone should be administered after the induction of anesthesia.

11. **D.** There is also concern that chronic cannabis use can lead to cyclic nausea and vomiting, which is called cannabinoid hyperemesis syndrome. This syndrome is primarily treated by supportive care, frequent hot showers, and cannabis cessation.

12. **A.** Glucocorticoids, like methylprednisolone, may be used in patients with severe NVP or hyperemesis gravidarum, but should be used only after 10 weeks of gestation due to the increased risk of cleft lip.

13. **B.** Changes in diet such as restricting oral intake, eating smaller meals, avoiding spicy or fried foods, and instead eating bland foods such as with the BRAT diet (Bananas, Rice, Applesauce, and Toast) can help alleviate symptoms.

14. **A.** Aprepitant requires dosing on days 1-3 surrounding chemotherapy.

15. **C.** Various electrolyte derrangements may occur as a result of vomiting, including hyponatremia, or low sodium levels.