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Gastrointestinal Disorders: Nausea in Adults

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Nausea is a common symptom that refers to the unpleasant sensation experienced prior to vomiting. It may be a "simple," transient symptom, secondary to a self-limited condition such as viral gastroenteritis, requiring only symptomatic relief. Nausea may also be a part of a more complex medical problem. Nausea is a symptom, not a diagnosis. Attempt to determine the underlying cause when possible (Table 1). Nausea may be self-limited or may be defined as chronic if it lasts >1 month. Many causes of nausea are iatrogenic but approaches to its treatment are dependent on the associated diagnosis, for example, postoperative nausea and vomiting (PONV), chemotherapy-induced nausea and vomiting (CINV), metabolic, gastrointestinal, vestibular or neurologic causes such as motion sickness.[1] This chapter does not address treatment of nausea in children or cancer chemotherapy– or radiation therapy–induced nausea and vomiting (see Cancer Chemotherapy Toxicity: Chemotherapy-induced Nausea and Vomiting and Cancer Chemotherapy Toxicity: Management of Side Effects of Chemotherapy and Radiation Therapy).

Table 1: Common Causes of Nausea

N	*Neurologic:* cerebrovascular accident, increased intracranial pressure, migraine, neoplasm, pain, trauma (head injury) and vestibular causes (e.g., labyrinthitis, Ménière's disease, motion sickness)
A	*Alcohol and other drugs:* drug-related adverse effects (e.g., antibiotics, cancer chemotherapy, hormones, opioids, NSAIDs, antiarrhythmics); drug toxicity (e.g., anticonvulsants, digoxin); drug initiation and withdrawal (e.g., benzodiazepines, narcotics, SSRIs), acute glaucoma
U	*Usually accompanies:* anesthesia, severe heart failure, hypercalcemia, hyponatremia, hypothyroidism, malignancy including metastasis, myocardial infarction, noxious odours, pain, radiation therapy, uremia, common infections such as otitis media or urinary tract infections in the elderly
S	*Stress and psychiatric:* anxiety, depression, fear, grief, pain, eating disorders, functional nausea *Surgical:* including nasogastric tube placement
E	*Enteral:* viral gastroenteritis; constipation; diseases of the liver (including hepatitis), cholecystitis and pancreatitis; functional gastrointestinal disorders (chronic idiopathic nausea, chronic intestinal pseudo-obstruction, gastroparesis, irritable bowel syndrome, nonulcer dyspepsia); gastroesophageal reflux; ingestion of allergens or irritants, toxins and bacterial food poisoning; GI motility disorders; obstruction *Endocrine:* Addison's disease; diabetic ketoacidosis; hormonal effects of pregnancy
A	*Anticipatory nausea:* in patients on cancer chemotherapy or situations in which patients are conditioned by previous experience of nausea and vomiting

Goals of Therapy

- Rule out acute emergencies or causes that require hospitalization and/or surgery
- Diagnose and remove or treat the underlying cause of the nausea
- Correct any consequences of persistent nausea (with or without vomiting) such as electrolyte abnormalities or dietary compromise. Control nausea and provide patient comfort (nausea can be more distressing to some patients than actual vomiting and interferes significantly with quality of life)
- Prevent the development of anticipatory nausea
- Balance the benefit of symptomatic treatment with possible adverse effects and cost of medications
- Control nausea so patients can resume treatment of other conditions

Investigations

- History[1]
  - determine if the nausea is acute or chronic
  - ascertain the frequency and severity of nausea as well as the timing in relation to meals, time of day, emotions or stresses
  - explore possible underlying causes, simple versus complex or chronic

- establish the onset, progression and temporal sequence of associated events, e.g., surgery
- identify other symptoms, e.g., headache, pain, vertigo
- clarify the relationship between nausea and vomiting; if present, determine the amount and nature of the vomitus
- complete an appropriate GI functional inquiry including frequency and nature of bowel movements, early satiety, postprandial symptoms, abdominal pain or weight loss
- inquire about diet history including any new foods, food allergies or intolerances and if potentially infected food has been consumed
- establish any exposure to, or other symptoms of, infection such as gastroenteritis or exposure to others who are ill
- in all women of reproductive age, inquire about last menstrual period to rule out pregnancy
- obtain a thorough medication history including use of prescription, nonprescription, herbal or recreational drugs as well as alcohol, nutritional supplements and vitamins
- inquire about recent changes to drug regimens (dose increases or withdrawal) and correlation with nausea
- inquire about past history of migraine headaches, endocrine disorders, malignancy
- explore possible psychosocial stressors, conflicts, sources of emotional pain or loss
- inquire about the patient's feelings, concerns, ideas, functional impairment and expectations of treatment

- Physical examination
  - vital signs including blood pressure, pulse, respiratory rate and temperature
  - determine severity and consequences of symptoms—assess hydration including JVP, mucous membranes, skin turgor and postural changes in blood pressure and heart rate
  - assess systems related to the probable underlying cause when apparent, e.g., perform neurologic exam for a migraine patient, examine for bowel obstruction if the patient has a malignancy or is postsurgical, check for nystagmus in vertigo-associated nausea, inspect fundi for papilledema
  - if no specific cause is identified in the history, use the physical exam to rule out other potential causes, e.g., abdominal mass

- Other investigations
  - laboratory investigations are determined by the history and physical exam
  - test females of childbearing age for pregnancy
  - electrolytes may be indicated if metabolic disturbances are suspected, e.g., test for hypercalcemia in a patient with a malignancy, glucose in a diabetic patient, hypokalemia or hyponatremia in a patient on diuretics, serum lipase/amylase levels if pancreatitis is suspected
  - CBC and differential if an infective cause is suspected
  - serum creatinine and urea to determine if there is a renal cause and assess degree of dehydration
  - drug levels in select cases, e.g., digoxin, anticonvulsants
  - thyroid function or fasting cortisol levels may be helpful to rule out endocrine disorders
  - x-rays may also be indicated; an abdominal series if a bowel obstruction is suspected or an upper GI with motility studies if gastroesophageal reflux or gastroparesis is suspected
  - ultrasound of the liver, gallbladder or pancreas may be useful in some patients
  - upper GI endoscopy or CT of the abdomen may be required in select patients as determined by the history and physical

Therapeutic Choices

Nonpharmacologic Choices

- Ensure adequate oral hydration in nonsurgical patients.
- Some forms of complementary therapies have been used, e.g., acupuncture, neurostimulation therapy at the wrist, hypnosis.[2]
- A Cochrane systematic review of acupuncture point stimulation concluded that there was possible benefit for a variety of causes of nausea and vomiting.[3]
- Dietary interventions may be important for nausea associated with certain food intolerances.
- Recommend consumption of frequent small meals and snacks rather than large meals at infrequent intervals.
- Consult a dietitian when necessary.
- Advise patients to avoid smells and foods that cause nausea.
- Recommend controlled breathing for motion sickness.
- Relaxation therapy and cognitive behaviour therapies may be useful in the treatment of nausea associated with irritable bowel syndrome and anticipatory nausea.[1]
- Gastric electric stimulation may be effective for refractory gastroparesis.[4]
- Engage the patient in the decisions around treatment. Not every patient will want treatment; watchful waiting is an alternative to medication for these individuals.
- Reassure patient when the underlying cause is self-limited.

Pharmacologic Choices

Although antiemetics are widely prescribed (Table 2), there is a paucity of randomized, controlled trials examining their effectiveness, with the exception of serotonin ($5\text{-}HT_3$) antagonists for CINV (see Cancer Chemotherapy Toxicity: Chemotherapy-induced Nausea and Vomiting) and PONV. When selecting a drug, consider if the nausea is acute or chronic, review concurrent medications and attempt to identify the underlying cause of nausea (Figure 1 - Management of Nausea). Many patients cannot tolerate oral medications when nauseated, and alternative routes of administration (im, sc, rectal or transdermal) may be more effective.

In an emergency room setting, iv **droperidol** is more effective than iv **metoclopramide**, iv **prochlorperazine** or saline for relief of moderate to severe nausea and/or vomiting of any etiology.[5] However, due to concerns regarding QT interval prolongation and severe cardiac arrhythmias, use iv droperidol only for the prevention or treatment of post-operative nausea and vomiting (PONV) when other treatments are ineffective or inappropriate and at the lowest effective dose. **Promethazine** has similar efficacy but is more sedating when compared to **ondansetron** for undifferentiated nausea managed in emergency settings.[6]

Standardized ginger (*Zingiber officinale*) is an alternative to established antiemetics in the management of pregnancy-induced[7,8] and post-operative[9] nausea and vomiting.[SORT B] Useful Info?

A preventive approach may be appropriate in certain situations, for example, in the management of motion sickness.

If nausea is associated with gastroesophageal reflux (see Gastrointestinal Disorders: Gastroesophageal Reflux Disease) or peptic ulcer disease (see Gastrointestinal Disorders: Dyspepsia and Peptic Ulcer Disease), treat the underlying cause.

Choices During Pregnancy and Breastfeeding

Nausea and vomiting of pregnancy (NVP) is common and can often be controlled effectively. Up to 85% of all pregnant women experience varying degrees of nausea and vomiting, usually in the first 16 weeks of pregnancy. NVP can occur throughout the day despite the common expression "morning sickness." Less than 2% of pregnant patients go on to hyperemesis gravidarum, which may require hospitalization and intravenous therapy. Assess and treat NVP in all pregnancies to avoid significant psychosocial morbidity resulting in disruption of work, home life, relationships, nutritional status and well-being. Consider other causes of nausea and vomiting not due to pregnancy as in the nonpregnant patient. A full assessment is especially appropriate for those pregnant women who first experience nausea and vomiting after the first trimester or have additional symptoms such as pain or fever which do not normally accompany NVP.

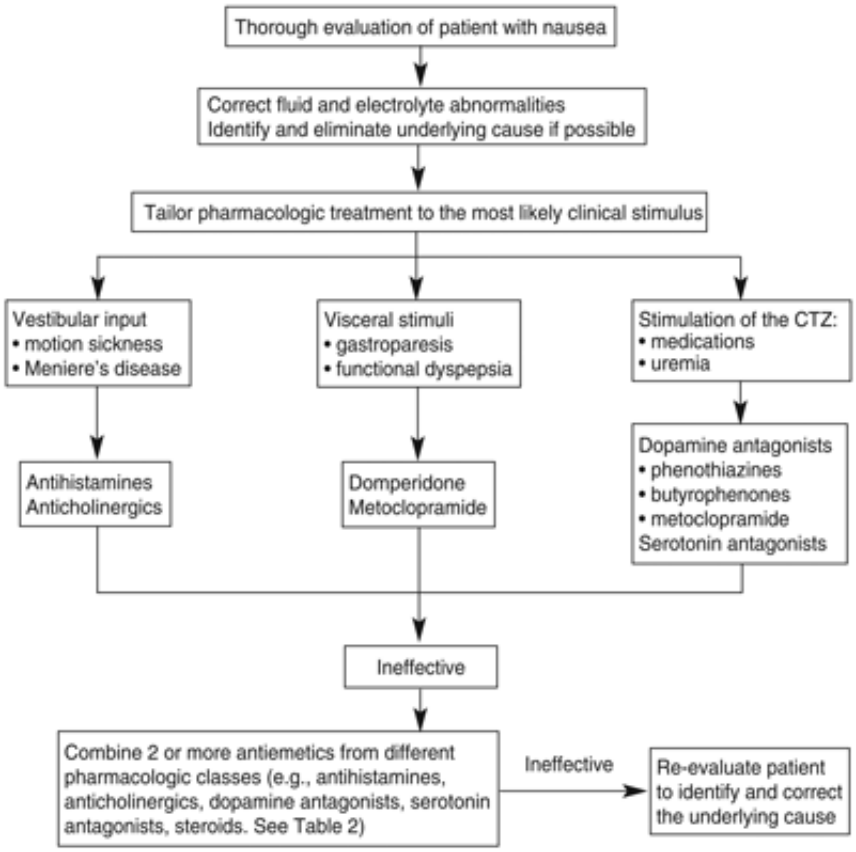
Management of NVP is similar to that in the non-pregnant patient. In Canada, **Diclectin** (doxylamine + pyridoxine) is the only medication approved solely for the treatment of NVP. Other agents including **dimenhydrinate**, **chlorpromazine**, **prochlorperazine**, **promethazine**, **metoclopramide**, **ondansetron** or **methylprednisolone** could also be tried if necessary (Figure 2 - Treatment of Nausea and Vomiting During Pregnancy[a]). These drugs can also be used safely while breastfeeding.

A discussion of general principles on the use of medications in these special populations can be found in Drug Use During Pregnancy and Drug Use During Breastfeeding. Other specialized reference sources are also provided in these appendices.

Therapeutic Tips

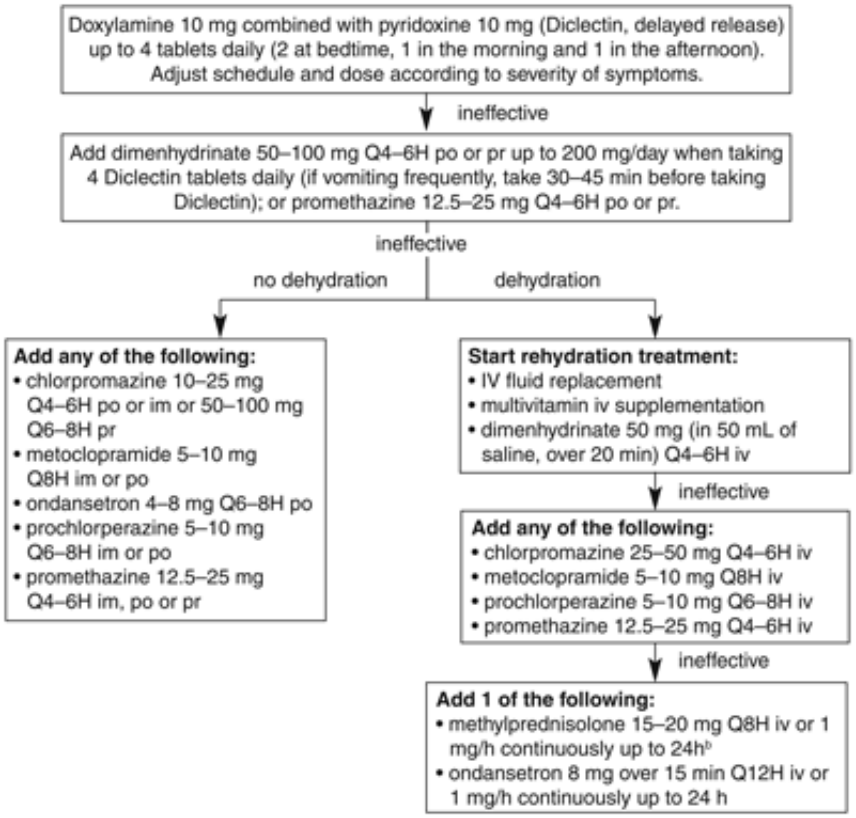
- Preemptive treatment may reduce nausea with certain procedures (e.g., insertion of a nasogastric tube).
- When a more complex cause is suspected, antiemetics may provide some symptomatic relief. However, when possible, determine and treat the underlying cause.[10]
- Start with a low dose and increase the dose slowly when prescribing for the elderly.
- Combination therapy may be required and has been found to be most useful in chemotherapy-induced nausea.
- If management of a nauseated patient fails to provide some symptomatic relief, reassess the patient and look for other causes.
- Know a few medications well. If one medication fails, try a different class of antinauseant or try an alternative route of administration.
- Consider the use of an alternative (non-oral) route of administration if drug absorption is likely to be delayed.
- Start with less expensive choices unless there is a preferred antiemetic for a specific disorder. For example, **ondansetron** is more effective than **metoclopramide** for nausea and vomiting in uremic patients.[11]

Figure 1 - Management of Nausea



Abbreviations: CTZ=chemoreceptor trigger zone

Figure 2 - Treatment of Nausea and Vomiting During Pregnancy[a]



[a] Use of this algorithm assumes that other causes of nausea and vomiting during pregnancy have been ruled out. At any step, when indicated, consider total parenteral nutrition.

[b] Corticosteroids are not recommended during the first 10 wk of pregnancy because of possible ↑ risk for oral clefts.

Table 2: Drugs Used to Treat Nausea

Class	Drug	Adult Dose	Adverse Effects	Drug Interactions	Cost[a]
Antacids	*aluminum hydroxide/ magnesium hydroxide combinations* Diovol, various others	GI-related nausea: 15–30 mL Q2–4H PRN po	Diarrhea (magnesium-containing), constipation (aluminum-containing).	May ↓ bioavailability of some drugs (e.g., digoxin); separate dosing by 2 h.	$
Anticholinergics	*scopolamine* Transderm V	Motion sickness: 1.5 mg (1 transdermal patch) Q72H PRN	Constipation, dry mouth. Confusion (especially in the elderly).	Additive sedation with alcohol or other sedating medications.	$
Antihistamines	*dimenhydrinate* Gravol Preparations, generics	Motion sickness or gastroenteritis: Short acting formulations: 50–100 mg Q4–6H PRN po/pr/im/iv (maximum 400 mg/day) Long acting formulation: 100 mg Q8–12H PRN po (maximum 300 mg/day)	Sedation, anticholinergic effects, confusion. The elderly may be particularly susceptible.	Additive sedation with alcohol or other sedating medications. May ↑ absorption of digoxin.	po: $ rectal: $ iv: $$
Antihistamines	*diphenhydramine* Benadryl Preparations, generics	Motion sickness or gastroenteritis: 25–50 mg TID–QID PRN po 10–50 mg TID–QID PRN im/iv	Sedation, anticholinergic effects, confusion. The elderly may be particularly susceptible.	Additive sedation with alcohol or other sedating medications. May ↑ absorption of digoxin. Inhibits CYP2D6 and can ↑ serum levels of many drugs including antidepressants and cardiovascular drugs.	po: $ iv: $$$
Antihistamines	*doxylamine succinate/ pyridoxine* Diclectin	Nausea and vomiting of pregnancy: 2 tablets QHS po, plus 1 tablet QAM po, plus 1 tablet mid afternoon po The 4 tablets may be	Diarrhea, disorientation, drowsiness, epigastric pain, headache, insomnia, irritability, nervousness, palpitation, urinary	Monoamine oxidase inhibitors may prolong and intensify the effects of doxylamine. There is an increased risk of antimuscarinic side	$$

		The 4 tablets may be scheduled differently according to timing, duration, severity and frequency of the symptoms experienced by the patient. Since Diclectin is a delayed release formulation it should not be prescribed on an as needed basis and should be taken daily on a regular basis for optimal effect.	palpitation, urinary retention, vertigo	antimuscarinic side effects when doxylamine is given with other antimuscarinic drugs. Doxylamine may increase the CNS depressant effects of other drugs (e.g., alcohol, barbiturates, opioid analgesics).	
Antihistamines	*hydroxyzine* Atarax, generics	Motion sickness or gastroenteritis: 25–100 mg TID–QID PRN po/im	Sedation, anticholinergic effects, confusion. The elderly may be particularly susceptible.	Additive sedation with alcohol or other sedating medications. May ↑ absorption of digoxin.	po: $ iv: $$$
Benzamides	*domperidone* [b] generics	Gastroparesis, functional dyspepsia: 10 mg QID po	Diarrhea, abdominal cramps and distention, headache, hyperprolactinemia.	Additive sedation with alcohol or other CNS depressants.	$
Benzamides	*metoclopramide* generics	Drug-induced nausea, migraine-related nausea, gastroparesis: 10–20 mg TID–QID PRN po/sc/iv	Diarrhea, abdominal cramps and distention, headache, hyperprolactinemia, drowsiness, fatigue, EPS.	Additive sedation with alcohol or other CNS depressants.	po: $ iv: $$$
Butyrophenones	*droperidol* generics	PONV only: Adults: 0.625–1.25 mg Q4–6H iv Elderly: 0.625 mg Q4–6H iv Children over 2 years: 20–50 µg/kg (maximum 1.25 mg) Q4–6H iv	Sedation, extrapyramidal effects. QTc interval prolongation and severe arrhythmia.	Additive sedation with alcohol or other CNS depressants.	iv: $$
Butyrophenones	*haloperidol* generics	Drug-induced nausea, PONV: 0.5–5 mg Q12H PRN po/im/iv	Sedation, extrapyramidal effects.	Additive sedation with alcohol or other CNS depressants.	$
Herbal products	*Ginger (zingiber officinale)* licensed natural	Nausea and vomiting of pregnancy: 250 mg QID[12, 13]	Abdominal discomfort, diarrhea, heartburn, pepper-	May inhibit *in vitro* CYP2C19; clinical significance	$

	licensed natural health product Gravol Natural Source, others	250 mg QID[12] , [13] , [14] , [15] or 500 mg BID[16] po PONV: 1000-1500 mg 1 hour before induction of anesthesia po[17] , [18] , [19] , [20] , [21]	heartburn, pepper-like irritant effect in the mouth and throat.	significance unknown.	
Phenothiazines	*chlorpromazine* generics	Labyrinthitis: 10–25 mg Q4–6H PRN po 25–50 mg Q3–4H PRN im/iv	Sedation, anticholinergic effects, EPS. Hypotension with im/iv administration.	Additive sedation with alcohol or other CNS depressants.	po: $ iv: $$$
Phenothiazines	*perphenazine* generics	PONV: 2–4 mg Q8H PRN po/im/iv	Sedation, anticholinergic effects, EPS. Hypotension with im/iv administration.	Additive sedation with alcohol or other CNS depressants.	$
Phenothiazines	*prochlorperazine* Apo-Prochlorazine, other generics	Drug-induced nausea, migraine-related nausea, PONV, vertigo-related nausea: 5–10 mg TID–QID PRN po/pr 5–10 mg BID–TID PRN im/iv	Sedation, anticholinergic effects, EPS. Hypotension with im/iv administration.	Additive sedation with alcohol or other CNS depressants.	po: $ rectal/iv: $$
Phenothiazines	*promethazine* generics	Motion sickness or gastroenteritis: 12.5–25 mg Q4–6H PRN po/im/iv	Sedation, anticholinergic effects, confusion. The elderly may be particularly susceptible.	Additive sedation with alcohol or other sedating medications. May ↑ absorption of digoxin.	$$
Serotonin Antagonists [b]	*dolasetron* Anzemet	PONV and CINV: 50–100 mg once daily po Contraindicated for the prevention and treatment of PONV in adults. Not recommended in patients with severe renal impairment because of the possibility of prolonged QTc interval.	Headache, diarrhea, fatigue, bradycardia, QTc and PR interval prolongation.	Cimetidine ↑ blood level of active metabolite. Rifampin ↓ blood level of active metabolite. Atenolol ↓ clearance of active metabolite.	$$$$$

Serotonin Antagonists[b]	*granisetron* Kytril, generics	PONV and CINV: 1–2 mg once or twice daily po 10 µg/kg iv infused over 5 minutes	Headache, constipation, diarrhea, weakness, QTc prolongation.		$$$$$
Serotonin Antagonists[b]	*ondansetron* Ondissolve ODF, Zofran, Zofran ODT, generics	PONV and CINV: 4–8 mg one to three times daily po/iv	Headache, constipation, diarrhea, sedation, bradycardia, dizziness. Transient ECG changes have been reported.	May ↓ analgesic effect of tramadol. CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin) ↓ ondansetron's blood concentrations.	$$$

a. Cost of 1-day supply; includes drug cost only.
b. Non-sedating.

Dosage adjustment may be required in renal impairment; see Appendices: Dosage Adjustment in Renal Impairment.

Abbreviations: CINV=chemotherapy-induced nausea and vomiting; ECG=electrocardiogram; EPS=extrapyramidal symptoms; PONV=postoperative nausea and vomiting

Legend: $ <$5 $$ $5–10 $$$ $10–20 $$$$ $20–30 $$$$$ $30–40

Suggested Readings

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