

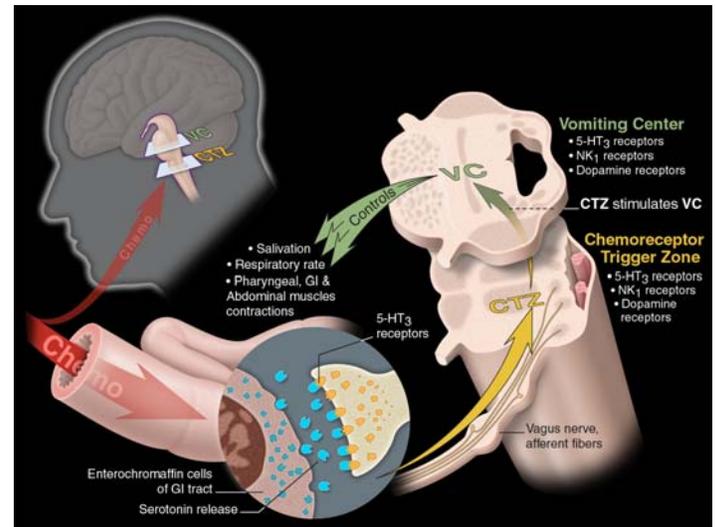
Nausea is defined as a subjective unpleasant sensation of discomfort in the stomach and the back of the throat associated with flushing, tachycardia, sweating, increased salivation and inclination to vomit.

Opioid-induced nausea occurs through three mechanisms:

- 1) Direct stimulation of the chemoreceptor trigger zone (CTZ)
- 2) Increased vestibular sensitivity
- 3) Delayed gastric emptying

What are management approaches?

- Establish the etiology and consider other treatable causes such as constipation or other medications
- Schedule anti-emetics. Start with a low-cost drug such as a dopamine receptor antagonist (e.g., prochlorperazine); use 5HT₃ antagonists for more refractory cases. Antihistamines or scopolamine may be helpful for patients who note increased nausea from motion.
- Adjust the opioid dose. If good pain relief is achieved but associated with nausea, it may be possible to lower the dose, still retain good analgesia, but eliminate the nausea. Most patients develop rapid tolerance to the emetic effects, so that within 3-7 days, at a constant opioid dose, the emetic effect will abate.
- Switch to a different opioid. Since all mu agonist opioids cause nausea, there is little rationale for changing drugs; however, patients may be more sensitive to one opioid compared to another, thus a change is warranted when the above options are not effective.



Drugs Used to Treat Nausea

Category	Drug	Mechanism	Dosing
Phenothiazines	Prochlorperazine ¹ (Compazine [®])	Dopamine receptor antagonist	5-10mg PO; 5-10mg IV; 25mg rectally every 8 hr
Substituted Benzamides	metoclopramide (Reglan [®])	dopamine receptor antagonist increases gastric motility	10-20mg PO or IV every 3-4hr
Serotonin (5HT ₃) Antagonists	dolasetron, ondansetron (Zofran [®]), granisetron	5HT ₃ receptor antagonist	ondansetron 8-16 mg PO or 4 mg IV once per 24 hr
Butyrophenones	droperidol ² (Inapsine [®])	Dopamine receptor antagonist	0.625mg-2.5mg every 3-4hr

Butyrophenones	haloperidol (Haldol®)	Dopamine receptor antagonist	1-4 mg PO or IV every 6 hr
Antihistamines	Promethazine ³ (Phenergan®)	Dopamine receptor antagonist	25mg PO every 6hr, 12.5-25mg IV every 4-6hr
Benzodiazepines	lorazepam (Ativan®)	Unknown	0.5-1mg PO; 0.5-1mg IV every 4-6hr
Muscarinic receptor antagonist	scopolamine (Transderm Scōp®)	acetylcholine receptor antagonist	1.5mg patch to mastoid every 72 hr
Neurokinin-1 Receptor Antagonist	aprepitant (Emend®)	Substance P/neurokinin 1 (NK) antagonist	RESTRICTED to CHEMOTHERAPY 125mg PO day one prior to chemo, then 80 mg daily in the morning for 2 more days

1. *Phenothiazines can cause extrapyramidal symptoms including dystonia and/or tardive dyskinesia*
2. *There is an increased risk of cardiotoxicity and prolongation of the QT interval with droperidol. Droperidol should not be used in patients with known or suspected QT prolongation; it should also be used with extreme caution in patients at risk of arrhythmias, including those with impairment of cardiac function, hypokalaemia or other electrolyte imbalance. Reduced doses should be used in elderly or debilitated patients.*
3. *Extravasation of promethazine may result in severe tissue damage. Dilute with 10-20 mL normal saline, make sure line is in a large vein, and then give through a running IV line – administer slowly – over several minutes. It must be given IV push if administration is through a peripheral line.*

References:

- [Fast Fact and Concept #025: Opioids and Nausea](http://www.eperc.mcw.edu/). Weissman, David E. <http://www.eperc.mcw.edu/>
- Ishihara M, Iihara H, Okayasu S et al. Pharmaceutical interventions facilitate premedication and prevent opioid-induced constipation and emesis in cancer patients. Support Care Cancer 2009 Nov 18 [Epub ahead of print].
- Swegle JM, Logemann C. Management of common opioid-induced adverse effects. Am Fam Physician 2006;74(8):1347-1354.
- Redmond M, Glass P. Opiate-induced nausea and vomiting: what is the challenge? Anesth Analg 2005;101:1341-1342.



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