

# Nausea and Vomiting

## Introduction

The management of nausea and vomiting for individuals receiving palliative care can be complex. Many of the published guidelines and recommendations are based on a theoretical understanding of the mechanisms of nausea and vomiting and there is little robust clinical evidence to support practice.

Nausea and vomiting are distinct entities, principally representing behavioural adaptive mechanisms to avoid the ingestion of toxins. However, there are clearly other physical (eg vestibular upset) and psychological (eg fear, anticipation) triggers that can lead to the experience of nausea, vomiting or both. As there may be several potential contributory factors to consider in any one individual, it may be useful to parallel the approach taken with pain management in palliative care and consider the concept of 'total nausea'.

Anti-emetic drug therapy is primarily for the control of nausea so that it is often inappropriate to treat every episode of vomiting. All anti-emetics have the potential to produce significant side effects, eg hyoscine hydrobromide crosses the blood brain barrier and may cause sedation, agitation or confusion. Anti-dopaminergics should be avoided in patients with Parkinsons Disease.

As well as managing the actual nausea and vomiting, it is essential that the consequences are considered. Individuals with protracted nausea and vomiting are likely to have poor control of other symptoms (particularly if they are unable to manage their usual medication) and usually have reduced oral intake of food and fluid – contributing to weight loss and fatigue. The potential for significant dehydration and hypokalaemia must be borne in mind along with the potential for increased adverse drug reactions from relatively commonly prescribed medication such as non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme , and diuretics which may require to be temporarily discontinued until vomiting is controlled.

The effect on family and carers of looking after someone with nausea and / or vomiting can be profound. The patient and their family will therefore usually require emotional and spiritual care as well as physical support.

## Regurgitation

Obstruction of the oesophagus and consequent regurgitation can be reported as vomiting. It is important to differentiate regurgitation from vomiting to avoid delay in seeking endoscopic intervention if it is appropriate. Regurgitation will never be relieved by anti-emetics but associated persistent nausea may respond to the appropriate medication.

## Assessment

- History – A separate history for both nausea and vomiting:
  - triggers, volume, pattern
  - exacerbating and relieving factors, including individual and combinations of drugs tried and routes used
  - bowel habit
  - medication.
- Examination:
  - general review for signs of dehydration, sepsis and drug toxicity
  - central nervous system
  - abdomen (eg organomegaly, bowel sounds, succussion splash).
- Blood investigations – clinical biochemical screen:
  - urea and electrolytes test
  - liver function tests
  - calcium
  - blood glucose.
- Dip urine for possible infection.

## Management

- Correct the correctable (eg renal function, [hypercalcaemia](#), [constipation](#))
- Consider non-pharmacological measures first (see non-pharmacological management below)
- Choose an anti-emetic appropriate to a likely identified cause
- A combination of anti-emetics may be appropriate
- A broad spectrum anti-emetic may be indicated if multiple concurrent factors are present
- Adjuvant steroid and/or benzodiazepine may be combined with the prescribed anti-emetic drug(s)
- Try to avoid the concurrent prescribing of prokinetic (eg metoclopramide - caution in use of prolonged higher doses, monitor for extrapyramidal side effects) and anticholinergic (eg cyclizine) medication, seek specialist advice.
- Consider the route of administration of medication as:
  - the oral route may not provide adequate absorption or be available as a result of nausea (which inhibits gastric emptying) or vomiting.
  - buccal or sublingual medication administration may be helpful but may trigger symptoms of nausea or vomiting in susceptible individuals.
  - the parenteral route may reduce tablet burden which may be a contributing factor to nausea.

## Non-pharmacological management

Prescribing a seemingly appropriate anti-emetic is no substitute for non-pharmacological measures. Correcting the correctable and attention to detail with oral care and hygiene (commonly altered taste and thrush) are important (see [Mouth care](#) guideline). Regularising bowel habit - [constipation](#) may be a relatively common cause of nausea.

Other measures include:

- regular small palatable portions rather than large meals
- avoid food preparation and cooking smells
- calm and reassuring environment
- acupressure bands (eg Seaband®)
- acupuncture
- psychological approaches.

## Medication

### Pharmacological management

Almost all causes of nausea and vomiting can be placed in the following categories, and each are associated with management with a specific drug or class of drugs.

Causes*	Drug class
Clinical toxicity or metabolic/biochemical upset (see flow chart)	Dopamine receptor antagonist (eg  haloperidol,  levomepromazine or  prochlorperazine)
Motility disorders (including drug-induced and paraneoplastic gastroparesis)	Prokinetic (eg metoclopramide - caution in use of prolonged higher doses, monitor for extrapyramidal side-effects or  domperidone)
Intracranial disorders eg raised intracranial pressure, vestibular dysfunction, motion disorders	Anticholinergic or antihistamine (cyclizine or  hyoscine hydrobromide),  steroid,  levomepromazine or  prochlorperazine.
Gastric/oesophageal irritation	Antifungals/antivirals  Antacids/inhibition of acid production
Multifactorial/unknown/refractory including higher centres (pain, fear, anxiety)	Use appropriate anti-emetics for known causes; consider adding benzodiazepine  Levomepromazine, benzodiazepine

\* Chemotherapy and/or radiotherapy-induced nausea and vomiting – refer to Oncology guidelines.

## Clinical toxicity or metabolic/biochemical upset (stimulation of chemoreceptor trigger zone (CTZ))

### Clinical picture

- Persistent often severe vomiting
- Little relief from vomiting or retching



### Cause

- chemical stimulation of CTZ

### By

- drugs, including cytotoxics and opioids (also delay gastric emptying), NSAIDs, syrupy liquids, antibiotics, antidepressants, anticonvulsants, digoxin/cardiac drugs, alcohol
- carcinomatosis/chronic inflammation (cytokine induced)
- metabolic eg uraemia, hypercalcaemia, hyponatraemia, ketoacidosis, infection, Addison's disease, circulating toxins, hormone imbalance



### Treatment

- treat metabolic imbalances
- dopamine antagonist eg **fQT** haloperidol 500 micrograms to 1.5mg orally or 500 micrograms to 1mg subcutaneously daily (start with lower doses in renal failure and elderly and frail patients) or metoclopramide (caution in use of prolonged higher doses, monitor for extrapyramidal side-effects) 10mg four times/day orally or subcutaneously.
- **fQT** levomepromazine 2.5 to 5mg subcutaneous injection 12 hourly or 5 to 15mg in 24 hours by continuous subcutaneous infusion (unlicensed use). Consider change to [oral route](#) if symptoms resolve.
- cytotoxic/chemotherapy induced – 5HT3 eg **QT** ondansetron 4mg orally (or subcutaneously) twice daily (check local policy)



For persistent problems, seek specialist advice

## Motility disorders

### Clinical picture

- Intermittent large volume vomit, usually relieves symptoms temporarily
- Early satiation
- Reflux, hiccup
- Often little nausea until immediately prior to vomit



### Cause

- gastric stasis
- gastric outlet obstruction - pseudo-obstruction - intestinal

### By

- autonomic neuropathy (paraneoplastic)
- drugs (opioid, anticholinergic)
- metabolic (eg hypercalcaemia)
- mechanical obstruction, tumour, nodes, enlarged liver (leading to squashed stomach)

Exclude complete bowel obstruction – see [separate guideline](#)



### Treatment - prokinetic

- metoclopramide 10 to 20mg orally four times a day or 30 to 80mg/24 hours by subcutaneous infusion (unlicensed route/dose/duration) Caution in use of prolonged higher doses, monitor for extrapyramidal side-effects.
- **QT** domperidone 10mg three times a day orally.
- specialists may recommend **fQT** erythromycin (potent prokinetic) 250mg three to four times daily

If extrinsic compression consider steroid – **f** dexamethasone 4 to 8mg daily reducing after 3 days, aiming to stop or lowest maintenance dose - or stent



For persistent problems, seek specialist advice

## Intracranial disorders eg raised intracranial pressure, vestibular dysfunction, movement-related nausea

### Clinical picture

- Headache
- Altered conscious level
- Vertigo - dizziness with nausea
- Movement-related sickness



### Cause

- raised intracranial pressure (ICP), vestibular nerve or inner ear stimulation

### By

- space occupying lesion
- base of skull tumour
- ototoxicity
- middle ear problems
- traction of heavy, obstructed gut on peritoneum during body movement



### Treatment

- If raised ICP suspected, cyclizine 25 to 50mg orally or subcutaneously (unlicensed route) three times per day or **[†]** hyoscine hydrobromide 150 to 300 micrograms orally, 200 to 400 micrograms subcutaneously or 1mg/72 hours via transdermal patch. Observe for anti-cholinergic side effects.
- Steroid – **[†]** dexamethasone 8mg daily reducing after 3 days, aiming to stop or lowest maintenance dose
- If inner ear cause suspected – cinnarizine 30mg orally initially then 15mg three times a day
- Second line – **[†QT]** levomepromazine 3 to 6mg orally daily (**[QT]** levomepromazine 6mg tablet is an unlicensed preparation) or **[QT]** prochlorperazine 3mg buccal or 5 to 15mg orally



For persistent problems, seek specialist advice

## Gastric/oesophageal irritation

### Clinical picture

- Constant nausea
- Worse on eating
- Reflux symptoms
- Gastric colic



### Cause

- Stimulation of vagus

### By

- Tumour
- Toxins
- Inflammation
- Infection (eg candida, herpes simplex)
- Foreign body (eg stent)



### Treatment

- Anticholinergics eg [Hyoscine](#) hydrobromide 200 to 400 micrograms subcutaneously or 1mg/72 hours via transdermal patch
- Antifungals/antivirals/antibiotics
- Inhibition of acid production eg rantiidine 150mg twice daily, proton pump inhibitor (PPI)

Note: prokinetic agents may trigger oesophageal spasm



For persistent problems, seek specialist advice

## Multifactorial/unknown/refractory including higher centres (pain, fear, anxiety)

Cause unclear



### Treatment

- metoclopramide increasing to 30 to 80mg/24 hours by subcutaneous infusion (unlicensed route). Caution in use of prolonged higher doses, monitor for extrapyramidal side-effects
-  levomepromazine (unlicensed use) 3 to 6mg twice daily orally or 2.5 to 5mg twice daily by subcutaneous injection or occasionally
- 5 to 15mg in 24 hours by continuous subcutaneous infusion but likely to cause sedation
- trial of  dexamethasone 8mg daily, reducing after 3 days aiming to stop or to lowest maintenance dose

Consider higher centre origin eg pain, fear, anxiety

- benzodiazepines eg lorazepam 500 micrograms to 1mg, diazepam 2 to 5mg



For persistent problems, seek specialist advice

Remember co-anti-emetics:

- infection causing pharyngeal irritation should be treated with appropriate antibiotics, antifungals or antivirals
- nebulised saline to aid clearance of thick respiratory secretions
- nausea associated with the use of NSAIDs or frank gastritis or peptic ulcer may require treatment with a PPI.

nausea associated with anticipation or anxiety may respond to benzodiazepines

## Practice Points

- For persistent vomiting, attention to hydration and nutritional status is essential ( see '[Subcutaneous fluid](#)' guidance).
- Nausea may be the cause of lack of efficacy of anti-emetics and other oral drugs.
- Occasionally nausea and vomiting may be refractory to treatment.
- Check that the correct anti-emetic been chosen, at the correct dose and given by the correct route for an adequate length of time.
- Consider treating all possible causes with cause-specific anti-emetic by non-oral route for 24 hours before introducing benzodiazepines in addition to anti-emetics.
- Despite logical and appropriate treatment, the patient may continue to vomit especially if there is a duodenal/gastric outflow obstruction or high small bowel obstruction.
- Prokinetic agents may trigger oesophageal spasm
- If surgical intervention for an obstructing lesion is neither appropriate nor possible, then interventional radiological stenting may be an option. The passage of a nasogastric tube followed by the placement of a venting gastrostomy can be preferable to the persistent vomiting associated with upper bowel obstruction.
- Patients can sometimes be very content and accepting of an occasional vomit or a pattern of daily vomiting when it is not accompanied by continuous intermittent nausea.

### Patient/carer information

- Advise patients/carers that nausea is a profoundly unpleasant sensation often felt in the stomach and frequently heralds the approach of vomiting.
- There are many causes but it can be a consequence of being generally unwell and rarely because they have eaten something that does not agree with them.
- Relaxation can help as anxiety can make nausea worse.
- Continue to take pain medication as severe pain can make nausea worse.
- It is better to eat small portions more frequently rather than less frequent large meals.
- Plenty of fresh air can be helpful as well as avoiding strong cooking smells; cold rather than hot meals may be helpful.
- Pay particular attention to oral hygiene.
- Watch out for signs of oral thrush.
- Let healthcare professionals know if vomiting is interfering with care of wound dressings, bed sores or ostomy appliances.
- Provide dietary advice (refer to patient information leaflet: <http://www.nhsinform.co.uk/PalliativeCare/symptomcontrol/eatingproblems/feelingsick>)
- It is important to take anti-emetic medication regularly and follow instructions.

## Practice Points

### Professional

Palliative Care Drug Information online: <http://www.palliativedrugs.com/index.html>

### Patient

Patient leaflet on 2010palliativecare website: Managing sickness & vomiting

<http://www.2010palliativecareguidelines.scot.nhs.uk/documents/Managing%20sickness%20and%20vomiting.pdf>

## Appendix A Receptor Site Affinities

Receptor site affinities of selected anti-emetics									
	<i>D<sub>2</sub></i> <i>antagonist</i>	<i>H<sub>1</sub></i> <i>antagonist</i>	<i>Muscarinic</i> <i>antagonist</i>	<i>5HT<sub>2</sub></i> <i>antagonist</i>	<i>5HT<sub>3</sub></i> <i>antagonist</i>	<i>NK<sub>1</sub></i> <i>antagonist</i>	<i>5HT<sub>4</sub></i> <i>agonist</i>	<i>CB<sub>1</sub></i> <i>agonist</i>	<i>GABA</i> <i>mimetic</i>
Domperidone !	**								
Haloperidol	***			*/-					
Metoclopramide	**				*		**		
Cyclizine		**	**						
Hyoscine <i>Hydrobromide</i>			***						
Chlorpromazine	***	***	**	**					
Levomepromazine	**	***	**	***					
Olanzapine	**	*	**	**	*				
Prochlorperazine	***	**	*	**/**					
Promethazine	**/**	**	**						
Lorazepam									***
Nabilone								***	
Aprepitant						***			
Ondansetron/ Granisetron !!					***				

Pharmacological activity: blank = none or insignificant; \* = slight; \*\* = moderate; \*\*\* = marked.

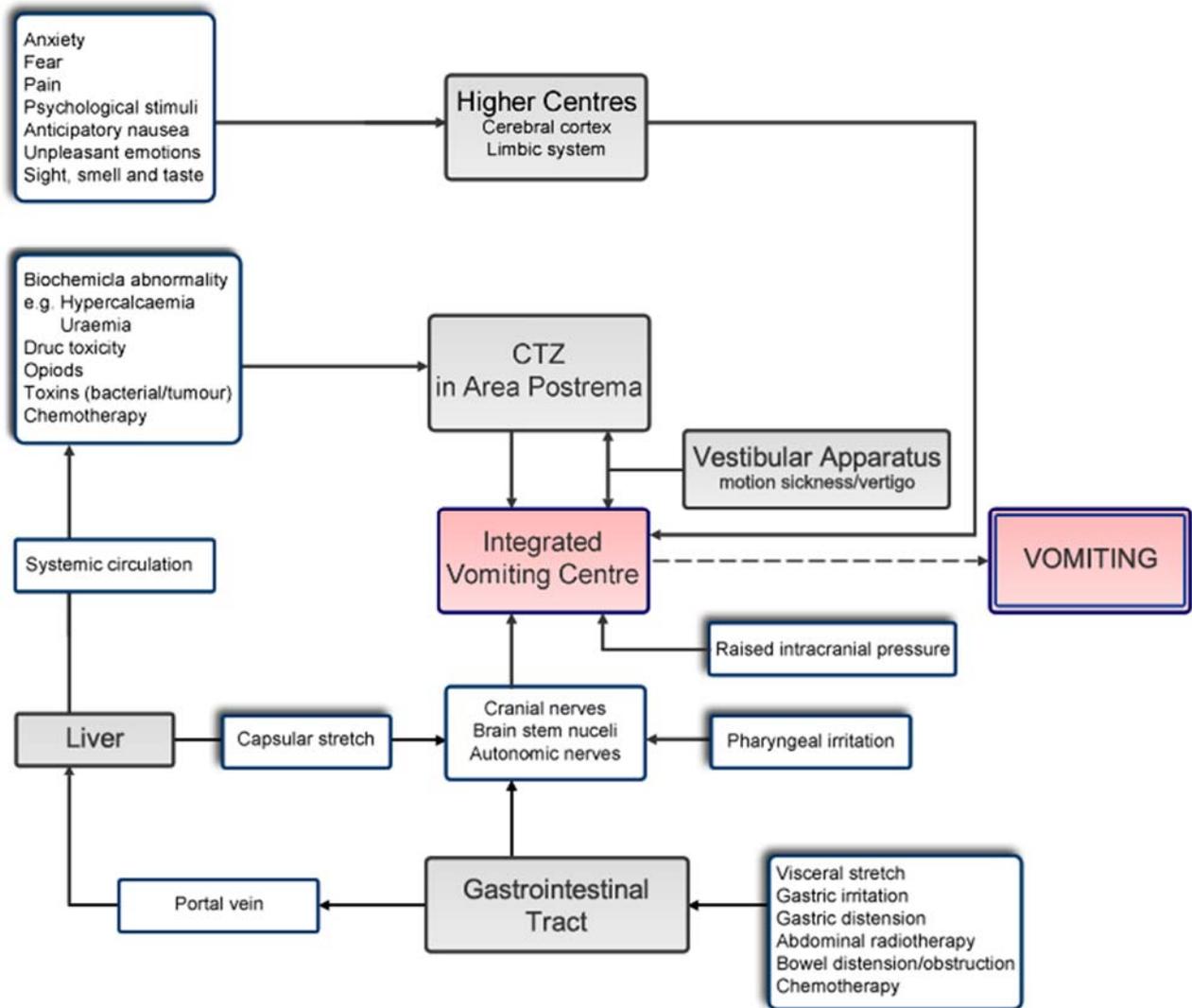
**! domperidone** does not normally cross the blood-brain barrier; minimal risk of extrapyramidal effects, watch for interactions.

**!! ondansetron/granisetron** – watch for interactions

Metoclopramide - Caution in use of prolonged higher doses, monitor for extrapyramidal side effects.

Adapted from Twycross, R. and Wilcock A. (eds) Palliative Care Formulary 4th Edition 2011.

## Appendix B – Receptor Site Chart



## References

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