



Investigating adults with recurrent nausea and vomiting

In this series, we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

MATTHEW HALL
MB BS, FRACP

Dr Hall is a Visiting Medical Officer, Sutherland Hospital, Caringbah, and a Gastroenterologist in private practice, Caringbah, NSW.

Series Editor
CHRISTOPHER S. POKORNY
MB BS, FRACP

Dr Pokorny is a Member, Board of Continuing Education, Royal Australasian College of Physicians, and a Gastroenterologist in private practice, Sydney, NSW.

Recurrent nausea and vomiting is a frequent clinical problem that is often managed by the GP. The history and examination will often suggest the cause and direct initial investigations. Empirical therapy with antiemetics or acid suppression can be used early or late in the diagnostic–therapeutic algorithm.

This article focuses on a practical approach to nausea and vomiting in general practice, which is summarised in the flowchart on page 56. It does not discuss nausea in a palliative care setting or nausea associated with pregnancy.

Terminology

A clear understanding of terms is important when interpreting the patient's history. Nausea is the unpleasant sensation, in the throat or epigastrium, of the imminent need to vomit; patients often describe feeling 'queasy' or 'sick to the stomach'. Vomiting is the contraction of the abdominal and chest wall muscles, resulting in the forceful expulsion of gastric contents. Vomiting is important to differentiate from regurgitation, where liquids and/or solids return to the mouth without forceful muscular contraction. Retching, or 'dry heaves', is spasmodic contractions without the expulsion of gastric contents, and rumination is the chewing

and re-swallowing of food that has been regurgitated within minutes of eating.

History

As always, a thorough history includes establishing the nature and associations of the symptoms as well as past history and current medications.

The pattern of symptoms and any relation to meals, particular foods or the time of day, can influence the next step in management. For example, nausea associated with heartburn suggests reflux and may lead to an early trial of a proton pump inhibitor (PPI); nausea associated with bloating after fatty meals may indicate gastroparesis, prompting limitation of fatty foods. (It is not uncommon for fatty meals to exacerbate gastroparesis.)

During history taking, nongastrointestinal causes such as neurological, functional or psychiatric abnormalities, should be kept in mind. Also, alarm symptoms, such as bleeding and weight loss, should be specifically sought and should prompt early investigation.

Medication history

The presentation of a patient with nausea is a good opportunity to review all prescribed and over-the-counter medications, including herbal

IN SUMMARY

- Recurrent nausea and vomiting is a common clinical problem that is managed by the GP.
- Often, the pattern of symptoms or associated symptoms will guide investigations and management.
- If the cause is not clear, screening blood and urine tests may suggest the underlying aetiology.
- Neurological, psychiatric and functional causes should not be overlooked.
- Alarm symptoms such as weight loss, bleeding or an abdominal mass should prompt rapid referral.

remedies. Patients should be specifically asked about alcohol and illicit drug intake, both of which can cause nausea and vomiting.

In regard to prescription medications, most patients will notice within a month if a new drug is causing nausea or vomiting, but sometimes months elapse before nausea occurs. Certain drug groups, such as the opiate analgesics, have more potential to cause nausea than have others. Also, nausea may be caused by elevated circulating levels of some drugs, such as digoxin, and this may occur because the required dosage has changed over time, such as in the elderly, or in people with renal impairment.

It is worthwhile emphasising that because NSAIDs may cause peptic ulceration (Figure 1), patients with nausea or vomiting taking these preparations should undergo early gastroscopy.

Drugs less obviously associated with nausea include oral contraceptives, oral hypoglycaemics, antihypertensives and antiarrhythmics. A trial without the medication (using an alternative if needed) may relieve the nausea, thus identifying the cause.

Specific symptom enquiry

Direct questioning on specific gastrointestinal, neurological and psychological symptoms should be undertaken as these may suggest a cause and indicate the next appropriate step whether it is an investigation or empirical therapy.

Heartburn or dyspepsia

Nausea and/or vomiting associated with heartburn or dyspepsia is suggestive of gastro-oesophageal reflux disease. A two-month trial of a PPI is appropriate. If the patient fails to improve, gastroenterology referral and gastroscopy are the next steps.

Regurgitation

Regurgitation is characteristic of reflux disease. It also is typical in less common oesophageal disorders, such as achalasia, Zenker's diverticulum and oesophageal stricture. A barium swallow and/or endoscopy is used to confirm these less common diagnoses, which should be considered if a trial of PPIs is unsuccessful.

Cramping pain

Generally, nausea due to obstruction of the stomach or small intestine is associated with

cramping abdominal pain and relief by vomiting. Gastric outlet obstruction is often intermittent, and the vomitus is not bile stained. On the other hand, small intestinal obstruction is usually acute, and the colicky pain is more severe. Plain abdominal films and CT of the abdomen and pelvis are the initial investigations if obstruction is suspected.

Occasionally, severe constipation may contribute to the sensation of nausea and, rarely, mesenteric ischaemia, retroperitoneal fibrosis or peritoneal carcinomatosis may cause nausea and abdominal pain.

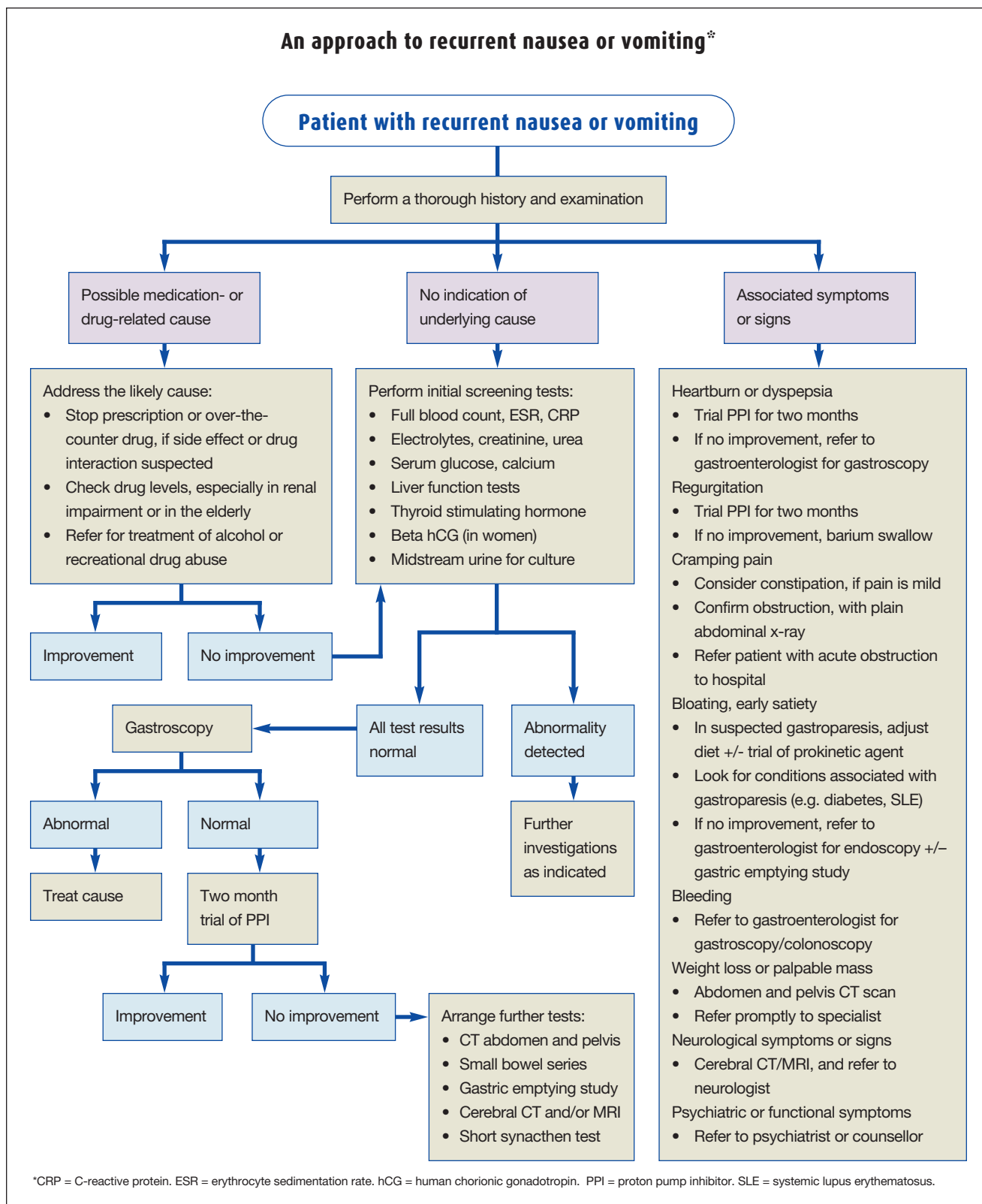
Bloating and early satiety

Delayed or impaired gastric emptying due to altered motility (gastroparesis) may cause nausea, which usually occurs at least one hour after meals. The associated symptoms are early satiety and postprandial abdominal bloating or fullness. Gastroparesis is not typically associated with abdominal pain.

Patients diagnosed with functional dyspepsia (i.e. those who have upper abdominal discomfort with exclusion of common organic pathology) often report nausea and vomiting. Gastroparesis is documented in a large proportion of these patients,

This image is unavailable due to copyright restrictions

continued



regardless of whether ulcer-, reflux- or dysmotility-like symptoms predominate.

If gastroparesis is suspected, associated conditions, such as diabetes mellitus, scleroderma, amyloidosis, systemic lupus erythematosus and polymyositis–dermatomyositis, vagotomy and pancreatic adenocarcinoma, should be sought. Gastroparesis can be confirmed by a gastric emptying study.

CNS symptoms

Nausea and vomiting can be caused by disturbances of the central nervous system (CNS). The classic brain tumour headache that is severe and occurs in the early morning is uncommon. Long tract or cranial nerve signs usually accompany tumours of the brain stem, and projectile vomiting suggests raised intracranial pressure. Any of these symptoms or signs should prompt early CNS imaging. Rare causes of nausea include seizure disorders and brain stem demyelination. In addition to their local effects, brainstem and posterior fossa lesions may also produce gastroparesis.

Labyrinthine disorders (usually associated with vertigo) and migraine can also cause nausea and vomiting. It is important to remember that migraine may not always occur with headache.

Psychiatric and functional symptoms

Nausea, early satiety, dyspepsia and bloating often occur with functional disorders. Also, psychological stress, anxiety and depression may present nonspecifically with nausea. Psychogenic vomiting results from emotional responses to unpleasant smells, tastes or memories and tends to occur in young women.

The possibility of anorexia or bulimia nervosa should also be considered. Vomiting in anorexia and bulimia nervosa tends to occur during or shortly after a meal. Evaluation for an eating disorder includes enquiring about binge eating and purging as well as about dissatisfaction with body shape and weight. Detailed

psychiatric assessment may be necessary to further assess and treat the patient.

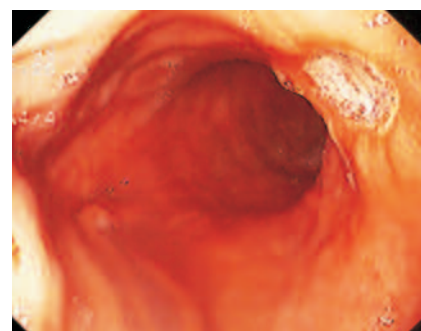
Physical examination

Possible consequences of recurrent vomiting are assessed firstly, including nutritional status, dentition and level of hydration. During general examination, the doctor should particularly seek lymphadenopathy, jaundice, thyrotoxicosis and the pigmentation of Addison's disease. Abdominal examination should concentrate on distension, hernial orifices and masses, and neurological examination should include assessing for postural hypotension and cranial nerve and long tract abnormalities, fundoscopy (for papilloedema) and assessment of gait. A flat affect would suggest depression.

Initial screening tests

Often, a likely cause for nausea and vomiting is not apparent from the history and examination. A possible systemic cause for the nausea is next sought, with screening blood and urine tests. The screening tests are listed below.

- **Electrolytes.** Electrolyte abnormalities, particularly hyponatraemia, often cause nausea. Hyponatraemia can result from diuretic use or from the syndrome of inappropriate antidiuretic hormone secretion (SIADH). SIADH is often drug induced; commonly associated drugs are selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, carbamazepine, phenothiazines and some oral hypoglycaemics. Other commonly used drugs such as omeprazole can, rarely, cause SIADH. Potentially causative drugs should be ceased or substituted. SIADH should prompt further assessment for hypothyroidism, Addison's disease and primary lung cancer. (Hypokalaemia, hypomagnesaemia, hypophosphataemia and metabolic alkalosis can result from persistent vomiting and should be corrected.)
- **Renal function.** Elevated creatinine and/or urea may be a consequence of severe dehydration, in which case an inpatient



COURTESY OF DR CHRIS POKORNY, SYDNEY

Figure 1. NSAID-induced gastric ulcer. Patients who are taking NSAIDs and experience nausea or vomiting need early gastroscopy, because NSAIDs can cause ulceration.

evaluation is necessary. Renal failure, from any cause, may itself cause nausea and is often due to drug toxicity. Diuretics, ACE inhibitors and NSAIDs are commonly responsible and should be ceased until renal function recovers; then, the dosage or indication should be reviewed. Urinary tract infection and obstruction should be sought with midstream urine samples and renal ultrasound.

- **Serum glucose.** Diabetes may present with nausea due to metabolic abnormalities, and these patients are also susceptible to infections, which may be associated with nausea. Diabetes is also a common cause of gastroparesis.
- **Serum calcium.** Hypo- or hyperparathyroidism are uncommon causes of nausea but have specific and effective treatments. An elevated serum calcium may also draw attention to an adverse drug reaction with vitamin D analogues or alert to the possibility of malignancy.
- **Full blood count.** Anaemia (particularly iron deficiency) would heighten the suspicion for gastrointestinal mucosal disease such as peptic ulcer or gastric or colonic malignancy and prompt endoscopic assessment.
- **Liver function tests.** Acute or chronic viral hepatitis may present with nausea. Also, abnormal liver function tests may increase the suspicion of an adverse drug reaction or gall bladder disease.

continued

- **Thyroid stimulating hormone.** Hypo- or hyperthyroidism are uncommon causes of nausea but are important to identify.
- **Inflammatory markers.** The erythrocyte sedimentation rate (ESR) and level of C-reactive protein (CRP) may suggest organic disease and indicate that further investigation is needed.
- **Serum or urine beta hCG.** All women of child bearing potential should have pregnancy excluded before proceeding with further investigation, particularly as

tests may involve radiation.

- **Urine dipstick test.** A urine dipstick test, although not diagnostic, can give immediate results in the doctor's surgery and may be helpful in assessing hydration. The results may be suggestive of hyperglycaemia, renal impairment or infection.
- **Midstream urine.** Urinary tract infection is an uncommon cause of severe symptoms, but specific therapy is available.

Table. Commonly used medications in patients with recurrent nausea and vomiting

Drugs	Some side effects	Comments
Phenothiazines Prochlorperazine (Stemetil, Stemizine)	Relatively frequent: – sedation – postural hypotension – extrapyramidal reactions (such as dystonia and tardive dyskinesia) Rare: – neuroleptic malignant syndrome – blood dyscrasias – cholestatic hepatitis	Available in oral, parenteral and rectal forms Acts centrally
Substituted benzamides Metoclopramide (Maxalon, Pramin) Domperidone (Motilium)	Metoclopramide can cause: – hyperprolactinaemia – dystonia, dyskinesia, opisthotonos – oculogyric crises, particularly in children and the elderly Domperidone can cause: – hyperprolactinaemia	Available in oral and parenteral forms Both act centrally and peripherally, having prokinetic activity thus useful in gastroparesis Domperidone does not significantly enter the central nervous system, despite acting centrally, but is more costly
Butyrophenones Haloperidol (Haldol decanoate, Serenace)	Relatively frequent: – sedation – extrapyramidal reactions Infrequent: – tardive dyskinesia – neuroleptic malignant syndrome	Available in oral and parenteral forms Mainly central action Can be used as second line or add-on therapy Small doses (0.5 to 1.0 mg twice daily) may be effective
Antihistamines Promethazine (Avomine, Phenergan)	Relatively frequent: – drowsiness, dry mouth Less frequent: – blurred vision	Useful in some people with nausea

Further investigation

The choice of further investigation may be guided by the history and examination, or initial screening tests (above). However, if there are no clues, the following tests are often performed in the order listed below to exclude treatable causes. Empirical treatment and treatment directed at test findings are usually conducted along with progressive investigation.

Gastroscopy

Upper gastrointestinal mucosal disease, such as reflux oesophagitis, peptic ulcer disease and gastritis, is a frequent cause of nausea. Gastroscopy is the most accurate method to diagnose mucosal disease and, importantly, many patients with these conditions will respond to acid suppression.

At least 50% of patients with gastro-oesophageal reflux disease will not have endoscopically visible lesions. Hence if reflux is suspected, despite a negative gastroscopy, a two-month trial of a PPI can be given. During gastroscopy, if there are no findings, a small bowel biopsy should be obtained, because coeliac disease may present with nonspecific upper gastrointestinal symptoms.

Plain abdominal x-ray

Abdominal x-ray is unlikely to be helpful apart from confirming the clinical suspicion of bowel obstruction.

CT scan

CT scanning with oral and intravenous contrast has a high sensitivity and positive predictive value (both around 90%) for

detecting small bowel obstruction and its causes. Obstruction is suggested, on a scan, by an abrupt transition from dilated to collapsed loops of small bowel. CT can also detect extraluminal masses, such as pancreatic, hepatic and retroperitoneal malignancy, and can reveal intra-abdominal abscess cavities. CT is sensitive for identifying intestinal strangulation and volvulus, which require early surgery. It is usual to perform an abdominal and pelvic CT scan with contrast.

Small bowel series

Small bowel series is now considered second line to CT scanning, and is reserved for when the clinical suspicion for obstruction persists after a nondiagnostic CT scan. Small bowel series may be more accurate than CT scans in determining the level of obstruction.

Cerebral imaging

Most intracranial lesions will be associated with physical signs that should prompt an early cerebral CT. If the above investigations are negative, however, a brain CT scan with intravenous contrast should be performed to look for cerebral lesions. CT is not definitive for detecting posterior fossa lesions and, if negative, a brain MRI should be ordered.

Gastric emptying study

Radio-isotopic gastric emptying studies are easy, accurate and noninvasive. They are most sensitive when performed with a solid test meal. A gastric emptying study is often used to support the diagnosis of gastroparesis and to justify the trial of a prokinetic drug. However, controlled studies have not shown this test to have a major impact on management decisions, nor will it exclude mucosal or structural disease.

Short synacthen test

Addison's disease may not necessarily be associated with pigmentation, electrolyte abnormalities or postural hypotension. If all tests are negative at this point, a

short synacthen test is done to exclude Addison's disease.

Treatment

The initial treatment involves correcting any fluid and electrolyte abnormalities, assessing the need for hospitalisation and treating the underlying cause, if it is known.

Most patients are managed in the out-patient setting and trials of medication are often conducted concurrently with investigations. Antiemetics are the usual initial empirical therapy (see the Table on page 60). These can be used when symptoms occur, or in anticipation of symptoms, such as 30 minutes before a meal. Trials of antiemetic therapy should be for a few days and be abandoned if there is not a response or if there are side effects. If there is not a rapid response to antiemetics, a trial of a PPI would be the next therapeutic step.

In patients with nausea and vomiting associated with typical features of gastro-oesophageal reflux disease, a trial of acid suppression (usually PPIs) should occur early in the management. Also, because isolated and unexplained nausea may also be due to reflux, a trial of a PPI at standard doses for one to two months is safe and frequently effective in patients in whom no other cause is found or suspected.

In suspected or documented gastroparesis, initial management should be dietary measures such as small frequent meals and avoidance of fatty foods. In patients with diabetes, better control of diabetes may improve gastric emptying. If these measures are not helpful, prokinetic agents should be considered (e.g. metoclopramide or domperidone; see the Table on page 60). Cisapride (Prepulsid) is the prototypical pro-motility drug, but because of cardiac toxicity it is available only on authority prescription for documented gastroparesis. This drug should not be used in patients with a history of arrhythmia or heart disease, or a family history of sudden death. ECG assessment

of the QT interval is needed before and during treatment on an ongoing basis. The drug should not be initiated or should be discontinued if the QT segment is prolonged. Cisapride occasionally causes mild diarrhoea and cramping abdominal pain. Benefits in gastroparesis have been documented for up to one year.

Refractory nausea and vomiting

Patients who have been extensively investigated and in whom no cause was found are labelled as having functional nausea and vomiting. Uncontrolled studies suggest that up to 50% of these people improve with low-dose tricyclic antidepressants (for example, amitriptyline [Endep, Tryptanol] 10 to 50 mg day), analogous to improvements documented in patients with irritable bowel syndrome. Anticholinergic and sedative side effects are common.

Rare syndromes

Rare syndromes such as rumination and cyclic vomiting are beyond the scope of this article.

Conclusion

Recurrent nausea and vomiting can be a challenging clinical problem. A detailed history and physical examination can tailor the investigational approach. A stepwise approach to identify common and readily treated conditions can be conducted concurrent with trials of empirical therapy and drug 'holidays' from medications that may be contributing to symptoms. If a patient does not improve despite a trial of PPIs and the cause remains unclear, specialist referral is warranted. **MT**

Further reading

1. Talley NJ, Martin CJ. Clinical gastroenterology: a practical problem-based approach. Sydney: MacLennan & Petty, 1996.
2. American Gastroenterological Association medical position statement: nausea and vomiting. *Gastroenterology* 2001; 120(1): 261-262.