Nausea is an unpleasant sensation of sickness and wanting to vomit, vomiting is the forceful ejection of stomach contents via the mouth. Nausea and vomiting are protective reflexes to prevent toxins from entering the body. They are common and distressing symptoms that may present acutely or be chronic, and their effective management represents an ongoing challenge to physicians.

There are many causes of nausea and vomiting, which are listed in Table 1. Population-based data show that vomiting occurs once a month in 2–3 percent of the general population.

Viral gastroenteritis and bacterial food poisoning are the most common causes of acute nausea and vomiting. It should also be appreciated that the ratio of organic to functional disease increases considerably with advancing age, with malignancy being very rare below the age of 45.

The vomiting centre is located in the central medulla and co-ordinates the complex events behind vomiting (see Figure 1). It projects to the vagus nerve and spinal motor neurones, which innervate the abdominal muscles. The chemoreceptor trigger zone (CTZ) is located in the area postrema in the posterior aspect of the medulla and is an important source of stimulation for the vomiting centre.

The vomiting centre contains muscarinic and histamine receptors while the CTZ is rich in dopamine (D₂) and 5-HT₃ receptors, hence explaining how drug antagonists provide their antiemetic effect. In addition 5-HT₃ has a peripheral effect on the gastrointestinal tract. The vomiting centre also receives afferents from the sensory vestibular system and higher cortical centres such as the limbic cortex.

The causes of nausea and vomiting are multifarious and a full clinical history is required before commencing treatment. Our Drug review discusses the diagnosis and the available drug options and their properties, followed by sources of further information.
Nausea and vomiting are clinically identifiable symptoms that are often self-limiting. A full clinical history should be taken including an exhaustive drug and alcohol history as this may yield the diagnosis. It is crucial to determine if the vomiting is a medical emergency requiring hospitalisation. Circulatory shock, renal failure, hypokalaemia and other electrolyte disturbances, cardiac dysrhythmias and hollow viscus perforation are all possible serious sequelae.

A thorough clinical examination should be performed, looking for signs of dehydration and malnourishment. Abdominal examination detects any masses or surgical scars and auscultation can identify tinkling or absent bowel sounds. Dental inspection may reveal loss of enamel, indicating bulimia or severe reflux disease.

Mental and neurological assessment (with MRI of the brain) should be performed in chronic unexplained vomiting, although it is rare for intracranial pathology to present solely with vomiting.

The nature of the vomitus should be examined and may provide a clue to the aetiology. For example, early frank food vomiting is likely to be due to gastric outlet obstruction, whereas bilious or faeculent vomitus suggests a more distal bowel obstruction.

Blood tests should be taken to check serum urea, electrolytes (sodium, potassium, calcium, phosphate and magnesium), liver function tests, amylase, glucose, thyroid function tests and morning cortisol level.

Arterial blood sampling may reveal an acute metabolic alkalosis due to loss of stomach acid; however, metabolic acidosis may be present in cases of severe hypovolaemia. An ECG should be performed to check for QT prolongation and possible dysrhythmias.

Multiple stool cultures should be taken to check for gastrointestinal infections. Testing for Helicobacter pylori should be performed with either stool cultures or hydrogen breath tests.

Gastroscopy detects mucosal lesions, and biopsies can be taken to check for coeliac disease, eosinophilic enteritis and infections. Retained food at the time of examination suggests gastroparesis and contrast studies or nuclear medicine gastric emptying scans can confirm the diagnosis.

In persistent vomiting, radiological investigations should also be performed. Abdominal X-ray has the advantage of being quick and cheap and can diagnose gross small/large bowel obstruction. However, it is neither sensitive nor specific. Cross-sectional imaging such as CT of the abdomen is highly sensitive in detecting bowel obstruction and pancreatobiliary pathology.

Pregnancy is an important cause to remember and a urinary pregnancy test should always be performed in fertile women. Nausea is associated with more than 50 per cent of pregnancies and occurs early, peaking at around nine weeks of gestation. Its cause is

---

**Table 1. Causes of nausea and vomiting**

<table>
<thead>
<tr>
<th>Abdominal causes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanical obstruction</strong></td>
</tr>
<tr>
<td>gastric outlet obstruction (eg pyloric stenosis), small bowel obstruction</td>
</tr>
<tr>
<td><strong>Motility disorders</strong></td>
</tr>
<tr>
<td>chronic intestinal pseudo-obstruction, achalasia and oesophageal dysmotility, functional dyspepsia, gastroparesis (eg diabetes)</td>
</tr>
<tr>
<td><strong>Other intra-abdominal causes</strong></td>
</tr>
<tr>
<td>acute appendicitis, acute cholecystitis, acute hepatitis, acute mesenteric ischaemia, artery syndrome, Crohn's disease, gastric and duodenal ulcer disease, pancreatitis and pancreatic cancer, peritonitis and peritoneal carcinoma, retroperitoneal and mesenteric pathology, superior mesenteric</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin and other NSAIDs, antidiabetic agents, antigout drugs, antibiotics, cancer chemotherapy, cardiovascular drugs, CNS drugs, immunosuppressant drugs, opiates, oral contraceptives</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infectious causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute gastroenteritis (viral and bacterial), systemic infections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metabolic and endocrine causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute intermittent porphyria, Addison’s disease, diabetes mellitus and ketoacidosis, hyperparathyroidism and other causes of hypercalcaemia, hyperthyroidism, hypoponatraemia, hypoparathyroidism, pregnancy, uraemia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nervous system causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>autonomic disorders, demyelinating disorder, hydrocephalus (congenital malformations, raised intracranial pressure, low-pressure hydrocephalus), intracerebral lesions with oedema (abscess, haemorrhage, infarction, cancer), meningitis, migraines, otitis media, seizure disorders, vestibular and labyrinthine disorders (labyrinthitis, Meniere’s disease, motion sickness), visceral neuropathy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>anxiety and depression, alcohol abuse, cardiac disease (congestive cardiac failure, MI, ischaemia, radiofrequency ablation), collagen vascular disorders (scleroderma, systemic lupus, erythematosus), cyclic vomiting syndrome, eating disorders, functional disorders, intense pain, paraneoplastic syndrome, postoperative state, postvagotomy, radiation therapy, starvation</td>
</tr>
</tbody>
</table>

**Recommended diagnosis**

Nausea and vomiting are clinically identifiable symptoms that are often self-limiting. A full clinical history should be taken including an exhaustive drug and alcohol history as this may yield the diagnosis. It is crucial to determine if the vomiting is a medical emergency requiring hospitalisation. Circulatory shock, renal failure, hypokalaemia and other electrolyte disturbances, cardiac dysrhythmias and hollow viscus perforation are all possible serious sequelae.

A thorough clinical examination should be performed, looking for signs of dehydration and malnourishment. Abdominal examination detects any masses or surgical scars and auscultation can identify tinkling or absent bowel sounds. Dental inspection may reveal loss of enamel, indicating bulimia or severe reflux disease.

Mental and neurological assessment (with MRI of the brain) should be performed in chronic unexplained vomiting, although it is rare for intracranial pathology to present solely with vomiting.

The nature of the vomitus should be examined and may provide a clue to the aetiology. For example, early frank food vomiting is likely to be due to gastric outlet obstruction, whereas bilious or faeculent vomitus suggests a more distal bowel obstruction.

Blood tests should be taken to check serum urea, electrolytes (sodium, potassium, calcium, phosphate and magnesium), liver function tests, amylase, glucose, thyroid function tests and morning cortisol level.

Arterial blood sampling may reveal an acute metabolic alkalosis due to loss of stomach acid; however, metabolic acidosis may be present in cases of severe hypovolaemia. An ECG should be performed to check for QT prolongation and possible dysrhythmias.

Multiple stool cultures should be taken to check for gastrointestinal infections. Testing for Helicobacter pylori should be performed with either stool cultures or hydrogen breath tests.

Gastroscopy detects mucosal lesions, and biopsies can be taken to check for coeliac disease, eosinophilic enteritis and infections. Retained food at the time of examination suggests gastroparesis and contrast studies or nuclear medicine gastric emptying scans can confirm the diagnosis.

In persistent vomiting, radiological investigations should also be performed. Abdominal X-ray has the advantage of being quick and cheap and can diagnose gross small/large bowel obstruction. However, it is neither sensitive nor specific. Cross-sectional imaging such as CT of the abdomen is highly sensitive in detecting bowel obstruction and pancreatobiliary pathology.

Pregnancy is an important cause to remember and a urinary pregnancy test should always be performed in fertile women. Nausea is associated with more than 50 per cent of pregnancies and occurs early, peaking at around nine weeks of gestation. Its cause is
unknown and it should be regarded as a normal manifestation of pregnancy but may require pharmacotherapy.\(^7\)

Hyperemesis gravidarum refers to severe symptoms that lead to complications. Multiparous overweight women are most at risk.\(^8\)

**Management**

Appropriate treatment for nausea and vomiting should be directed towards the underlying cause. Simple measures should be sought first before commencing medical treatment.

Acute dehydration and shock should be corrected with intravenous fluids. Electrolytes such as potassium should be replaced intravenously as necessary. Nasogastric tubes should be placed to decompress and aid drainage of the upper gastrointestinal tract in cases of acute gastrointestinal obstruction.

If required, nutritional support can be provided via either the enteral or parenteral route. Enteral nutrition can be given by nasogastric/nasojejunal tubes depending on the cause of vomiting. Jejunal feeding has the advantage of bypassing gastric obstruction and can be used in gastroparesis.

Where possible, enteral feeding is preferred to the parenteral route as the latter is associated with more complications and is usually reserved as a short-term measure. Pabrinex (B vitamins and ascorbic acid) should be administered to replenish vitamin B stores.

Mechanical causes of obstruction should be reviewed by a surgical team urgently as surgery may be indicated. Cases such as postoperative ileus may be managed conservatively with intravenous fluids and nasogastric decompression.

A withdrawal of suspected/known emesis-inducing drugs should be trialled. If the symptoms improve then

---

*Figure 1. Areas of the brain and triggers involved in the vomiting reflex, with sites of action of antiemetic and prokinetic agents*
further investigations can be avoided. Higher cortical conditioning may occur such as in the chemotherapy patient who experiences anticipatory nausea and vomiting upon sighting/smelling cytotoxic drugs they are about to receive. ³

Pharmacotherapy
Pharmacotherapy consists of centrally acting antiemetics and peripherally acting prokinetics to aid gut emptying. Deciding which drug to use can be difficult and many are available in the physician’s armamentarium.

A recent review of the Cochrane database has shown the following drugs to be particularly effective: cyclizine, 5-HT₃ antagonists, dexamethasone and metoclopramide. Recent Canadian guidelines for the management of postoperative nausea and vomiting have also recommended these drugs as first line. Suitable second-line treatment would be a combination of these drugs.⁹

The route of administration is important to consider as persistent vomiting will not allow for adequate drug absorption via the oral route. Alternative routes include per rectum, subcutaneous, intramuscular and intravenous.

Dopamine antagonists
A summary of the most commonly used dopamine agonists is provided in Table 2.

Phenothiazines act on the CTZ to inhibit dopamine receptors. Prochlorperazine (5–10mg two to three times daily or 12.5mg intramuscularly) is relatively well tolerated and less sedating than chlorpromazine. Due to side-effects including orhotstagic hypotension and extrapyramidal symptoms, it is less commonly used compared to other antiemetic drugs.

Metoclopramide (10mg three times daily) is a D₂ antagonist that also has a prokinetic action on the gut. It enhances the absorption of many drugs, which can be advantageous in certain therapeutic scenarios, eg

---

**Table 2. The most commonly used dopamine antagonists and their properties**

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Usual oral dose and frequency</th>
<th>Oral bio-availability</th>
<th>Pharmacokinetics</th>
<th>Half-life</th>
<th>Drug interactions</th>
<th>Side-effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prochlorperazine</td>
<td>5–10mg 2–3 times daily</td>
<td>&lt;10%</td>
<td>extensive first-pass metabolism</td>
<td>7h</td>
<td>other drugs causing hypotension</td>
<td>sedation, extrapyramidal reactions and hypotension</td>
<td>available in several formulations including buccal tablets, oral liquid and injection</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>10mg 3 times daily</td>
<td>&gt;90%</td>
<td>undergoes first-pass metabolism; clearance is by hepatic metabolism; only 20% is excreted in the urine unchanged</td>
<td>4h</td>
<td>antipsychotics</td>
<td>extrapyramidal reactions, restlessness and stimulation of prolactin release</td>
<td>also available as an injection can be used as a prokinetic agent; contraindicated in gastrointestinal patients with an obstruction, perforation or haemorrhage</td>
</tr>
<tr>
<td>Domperidone</td>
<td>10–20mg 3–4 times daily</td>
<td>13-17%</td>
<td>undergoes extensive presystemic metabolism</td>
<td>12–16h</td>
<td>none significant</td>
<td>stimulates prolactin release reduced libido</td>
<td>less likely to cause extrapyramidal side-effects and sedation also available as suppositories and oral liquid but not as an injection also has prokinetic properties</td>
</tr>
</tbody>
</table>
migraine treatment. Side-effects are mild but it has been associated with severe dystonic reactions, particularly in the young and in females.

Domperidone (10mg three times daily) is similar to metoclopramide but does not cross the blood-brain barrier. It is therefore less likely to cause extrapyramidal side-effects.

Cyclizine (50mg three times daily) acts by centrally blocking histamine (H1) receptors. It is cheap but adverse effects include dry mouth, blurred vision and tachycardia.

5HT3 antagonists
These include ondansetron (8mg three times daily) and were originally developed for use in chemotherapy. They act centrally on the CTZ and are highly effective. They are widely used in the postoperative setting where as many as 80 per cent of high-risk patients may be affected by nausea and vomiting.10 They have the advantage of being able to be administered in soluble wafer form. Side-effects may include bradycardia and headache.

Corticosteroids
Dexamethasone is cheap and effective.11 Its mechanism of action is not fully understood but may be due to the release of endorphins, which elevate mood and stimulate appetite.12 It is not suitable for long-term use due to the risk of adrenal suppression and Cushing’s syndrome. There is no evidence that a single dose raises blood glucose levels or affects sleeping patterns.

Other drugs
Betahistine is first-line treatment for vertigo and Meniere’s disease. It acts by reducing endolymphatic pressure in the vestibular system.

The tricyclic antidepressant amitriptyline (10–30mg nightly; unlicensed indication) may be of benefit in chronic nausea and vomiting,2 particularly in the presence of functional abdominal pain.

Proton-pump inhibitors are a cheap and highly effective treatment for nausea and vomiting associated with dyspepsia.

Pregnancy
Most antiemetic drugs are thought to be safe when taken in pregnancy, though their use, especially in the first trimester, should be minimised. Specific evidence regarding the safety of promethazine, 5-HT3 antagonists and metoclopramide exists.1 Steroids, erythromycin and ginger root have also been shown to be effective.1

Alternative therapies
Alternative treatments such as acupuncture may be effective,9 though may not be readily available or easy to use. Recently, a small trial using aromatherapy was found to be ineffective.13

Conclusion
Nausea and vomiting are common symptoms that often resolve spontaneously. It is crucial to determine the cause and tailor the investigations and treatment accordingly.

Significant points to remember are that a comprehensive drug history should be taken and potentially offending drugs withdrawn, pregnancy tests should always be performed in fertile women, and organic causes are more common in patients aged >45 and warrant urgent further investigation.

A trial of pharmacotherapy may be cost-effective and provide symptomatic relief, especially in patients aged <45, and intracranial pathology is a rare but important cause of chronic nausea and vomiting for which radiological imaging should be performed.

Nutritional requirements should be assessed and met, and psychiatric assessment and cognitive behavioural therapy may be beneficial in some cases.

References

Declaration of interests
None to declare.

Dr Goel is a gastroenterology registrar and Dr Wilkinson is a gastroenterology consultant, St Thomas’ Hospital, London