



## THEME

Nausea and vomiting



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# Functional nausea and vomiting

## BACKGROUND

There is a group of patients who have unexplained chronic nausea and/or vomiting. In the past these patients were labelled as having psychogenic vomiting. However, there is little evidence that such a condition exists. Rather, these patients usually have a functional gastrointestinal disorder (functional nausea and vomiting).

## OBJECTIVE

This article describes the three important syndromes in adults that clinicians need to recognise: cyclic vomiting syndrome, functional vomiting, and chronic idiopathic nausea.

## DISCUSSION

Cyclic vomiting syndrome presents with stereotypical episodes of acute nausea and vomiting that may be severe. Patients are generally well between attacks. Cannabis use can cause a similar syndrome. Patients may respond to antimigraine therapy or low dose tricyclic antidepressant treatment. Functional vomiting is rare and presents with more frequent vomiting episodes. Rumination needs to be distinguished from functional vomiting by careful history taking. Tricyclic antidepressants are also useful in functional vomiting whether or not there is associated depression. Chronic idiopathic nausea refers to patients with bothersome nausea occurring several times a week usually not associated with vomiting. Its treatment is poorly defined but a trial of antidepressant therapy anecdotally can be helpful.

**Nausea and vomiting are relatively common complaints in the community, although patients and doctors sometimes confuse the terms (Table 1). In a study from a representative population living around the Mayo Clinic (USA), 3% of people reported nausea once per week, while nearly 2% had daily nausea. A total of 2% reported vomiting monthly or more frequently.<sup>1</sup> There is an important, albeit uncommon, group of patients who despite an intensive diagnostic evaluation have no clear cause found for their chronic nausea and/or vomiting. These patients are currently classified as having functional nausea and vomiting.<sup>2,3</sup>**

## Psychogenic vomiting

In the past, all chronic unexplained vomiting was typically labelled as 'psychogenic'. Classic papers were published on the topic, notably one in the 1930s<sup>4</sup> and another in the 1960s.<sup>5</sup> These authors assumed their patients had a psychogenic cause because nothing else was found, but no attempt was made to assign a modern psychiatric label or compare their patients with controls.

More recently, a Japanese study reported data from 59 patients with presumed psychogenic vomiting, and for the first time systematically evaluated personality and psychiatric status.<sup>6</sup> In this case series, all the patients were given a psychiatric diagnostic label and most (53%) had 'conversion disorder', while others (36%) were suffering from depression. However, there was no control group, and referral bias might explain the high rate of psychiatric labelling. A study from the Mayo Clinic subsequently did include appropriate controls,<sup>7</sup> and found that psychiatric diagnoses were similarly distributed in patients with chronic unexplained vomiting and organic disease controls.

Unexplained chronic gastrointestinal symptoms and psychiatric disease are both common, and even if they overlap, does not indicate a cause and effect relationship. Indeed, there is no convincing literature that supports the existence of a pure psychogenic aetiology for unexplained vomiting. This is not to say that it can't happen. Panic disorder, for example, can present with vomiting as one of its features, although this is probably uncommon.<sup>7</sup> Based on the available evidence (which for vomiting is limited),

consensus opinion has therefore favoured dropping the term psychogenic altogether.<sup>3</sup>

## Functional nausea and vomiting

There are three specific syndromes to recognise in practice: cyclic vomiting syndrome (CVS), functional vomiting (FV), and chronic idiopathic nausea (CIN) (Table 2). Before labelling a patient with a functional disorder, structural and biochemical causes must be ruled out with appropriate investigations.

## Cyclic vomiting syndrome in adults

Cyclic vomiting is a rare condition. It was first recognised in the paediatric population but is now known to occur in adults.<sup>8</sup> Adults typically develop CVS in middle age (around 35 years), although it can occur at any age.<sup>9,10</sup>

## Diagnosis

Patients typically present with acute episodes of nausea and vomiting without warning. Symptoms finally settle completely but recur weeks to months later.<sup>9,10</sup> Between episodes patients are asymptomatic. Episodes are stereotypical, ie. predictable in terms of symptom pattern, onset and duration. Typically adults have about four discrete episodes of nausea and vomiting per year with each episode or cycle lasting about 6 days (range 1–21 days). The patient is then symptom free often for months before the exact same type of episode recurs. Typically diagnosis is delayed for several years.

## Associated conditions

Up to one in 4 adults with CVS also has a history (or family history) of migraine headache.<sup>9,11</sup> It is important to ask about cannabis use. Patients may use cannabis to relieve nausea and vomiting. Cannabis use can also precipitate CVS in some cases and ceasing cannabis can lead to complete relief.<sup>12</sup> Many patients have compulsive bathing behaviours (multiple hot showers or baths often waking up during the night to do so). A urine drug screen can be helpful if you are suspicious and the patient denies cannabis use. Some patients have menstrual related cyclic vomiting.

## Investigations

Before making a firm diagnosis of CVS it is important to rule out motility disorders of the upper gastrointestinal tract as well as metabolic and central nervous system diseases.<sup>2,3</sup> Most authorities suggest upper endoscopy and small bowel X-ray or computed tomography enterography. Biochemical testing for electrolyte abnormalities, serum calcium, thyroid function tests and, if indicated, tests

**Table 1. Definitions of key terms**

|                                                                                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nausea – a painless, unpleasant, subjective feeling of wanting to vomit                                                                                   |
| Vomiting – the forceful expulsion of gastric or intestinal contents                                                                                       |
| Retching – abdominal muscle contractions with laboured rhythmic respiration                                                                               |
| Rumination – the effortless regurgitation of recently ingested food typically in the absence of nausea. Often the food tastes good and is re-swallowed.   |
| Rumination should be distinguished from vomiting even though patients will often refer to their problem as vomiting when they present with this condition |

**Table 2. Rome III classification of functional nausea and vomiting**

### Diagnostic criteria\* for nausea and vomiting disorders

#### Chronic idiopathic nausea

Must include all of the following:

- bothersome nausea occurring at least several times per week
- not usually associated with vomiting
- absence of abnormalities at upper endoscopy or metabolic disease that explains the nausea

\* criteria fulfilled for past 3 months with symptom onset at least 6 months before diagnosis

#### Functional vomiting

Must include all of the following:

- on average one or more episodes of vomiting per week
- absence of criteria for an eating disorder, rumination, or major psychiatric disease according to DSM-IV
- absence of self induced vomiting and chronic cannabinoid use and absence of abnormalities in the central nervous system or metabolic diseases to explain recurrent vomiting

\* criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis

#### Cyclic vomiting syndrome

Must include all of the following:

- stereotypical episodes of vomiting regarding onset (acute) and duration (<1 week)
- three or more discrete episodes in the previous year
- absence of nausea and vomiting between episodes

Supportive criterion:

- history or family history of migraine headaches

Source: Drossman DA, Corazziari E, Delvaux M, et al. Rome III: the functional gastrointestinal disorders. 3rd edn. McLean, Virginia: Degnon Associates, 2006

to exclude hypoadrenalism (Addison disease) are also relevant. Gastric emptying testing may be considered where available. In CVS, recent data suggests that gastric emptying is accelerated rather than delayed in a subset of patients.<sup>11</sup> There are mitochondrial diseases that can be associated with intermittent vomiting such as medium chain acyl-coenzyme A dehydrogenase deficiency.<sup>13</sup> This

is most often seen in children, but if there is any concern testing should be considered.

## Treatment

### Acute care

During an acute episode, patients with CVS may require hospital admission for intravenous fluids and intravenous antiemetic therapy. Another approach is to prescribe antimigraine therapy at the onset of an attack, particularly if there is a personal or family history of migraine. A triptan such as sumatriptan (a 5HT<sub>1</sub> agonist) can be effective for acute migraine and for CVS. Triptans can be given as a subcutaneous injection or nasal spray, or orally in the early stages of an episode. Remember triptans have a risk of inducing vascular problems in ischaemic heart disease, ischaemic stroke and uncontrolled hypertension.

### Prevention

For the prevention of attacks of cyclic vomiting, one of the most effective therapies appears to be low dose tricyclic antidepressant treatment.<sup>9,11</sup> This is based on anecdotal data as there are no clinical trials. However, use of drugs such as desipramine, nortriptyline or doxepin in a median dose of about 50 mg/day does seem to be helpful in practice and should be considered unless there is an active contraindication. In one uncontrolled study, 24 patients received amitriptyline up to 1 mg/kg/day for at least 3 months; 93% had a reduction in symptoms and 26% went into remission.<sup>11</sup> Beta blockers (eg. propranolol) may also help prevent episodes.

In a uncontrolled study, newer antiepileptic drugs, specifically zonisamide and levetiracetam, appeared beneficial as maintenance medications for almost three-fourths of patients evaluated.<sup>14</sup> Other drugs have been tried (eg. ketorolac, prochlorperazine) but all therapies are based on anecdotal evidence only.

In patients with menstrual related cyclic vomiting, the oral contraceptive pill can be helpful for prevention of episodes.

Psychiatric disease appears to be uncommon in patients with CVS.<sup>9</sup> If depression is present it should be treated on its own merits. Providing support is important (see *Resource*).

## Functional vomiting

Functional vomiting is thought to be very rare.

### Diagnosis

Functional vomiting is defined as recurrent unexplained vomiting at least once per week that is not cyclical.<sup>3,15</sup> Careful history taking will rule out rumination syndrome or an eating disorder. Rumination syndrome refers to

persistent or recurrent regurgitation of recently ingested food into the mouth; it is not vomiting (*Table 1*).<sup>16</sup> The patient either spits out the food or re-chews and swallows it. There is no preceding retching and typically no nausea. The regurgitant material is often pleasant tasting! While rumination was once thought to be rare in nonretarded adults, it may not be uncommon and is probably more frequent than FV. Rumination is a clinical diagnosis that is important to recognise as it is easily treated (*Table 2*). Rumination is thought to be an acquired habit. Habit reversal using a breathing technique to halt regurgitation can be easily taught to patients (diaphragmatic breathing) and can be curative.<sup>17</sup>

Eating disorders need to be excluded.<sup>3,18</sup> In particular, sensitively ask the patient questions that may reveal a distorted body image or self induced vomiting. Expert management with the help of a psychiatrist is required for bulimia or anorexia nervosa.

## Treatment

Management of FV remains difficult.<sup>18</sup> Maintenance of nutritional status and psychological support are essential. The role of psychiatric disease is unknown. Tricyclic antidepressants may be prescribed and anecdotally can help some patients whether or not there is associated depression.

Unfortunately, standard antiemetic therapies are usually not effective. Cognitive and social skills training may be helpful based on some limited data.<sup>19</sup> Others have suggested that self monitoring with suppression of the urge to vomit is useful.<sup>20</sup> Unfortunately, there is a lack of detailed clinical experience with this condition.

## Chronic idiopathic nausea

A group of patients present with nausea as their main symptom.<sup>2,3</sup> When this occurs several times per week in the absence of an organic cause it is known as CIN.<sup>3</sup>

## Presentation

Chronic idiopathic nausea is considered to be distinct from nonulcer (or functional) dyspepsia where epigastric pain or meal related symptoms tend to predominate rather than nausea. However, many patients with nausea also report other dyspepsia symptoms.

## Investigations

It is particularly important to exclude gastroesophageal reflux in this setting, which is easily treated but may be overlooked.<sup>21</sup> There may be no heartburn, so this possibility needs to be considered in difficult cases. Referral for oesophageal pH testing is usually diagnostic. An upper

gastrointestinal endoscopy will exclude a structural explanation and a 24 hour oesophageal pH test or an empiric trial of proton pump inhibitor therapy may be useful if endoscopy is negative.

Infection with *Helicobacter pylori* does not appear to be a major cause of nausea, although eradicating the bacteria if present is not unreasonable.<sup>2</sup> Gastroparesis may cause nausea and can be screened for with gastric scintigraphy by most nuclear medicine departments.<sup>18</sup>

## Treatment

The treatment of CIN is not well documented.<sup>3</sup> A prokinetic drug such as domperidone is worth trying initially; it has anti-nausea as well as prokinetic properties. Metoclopramide is an alternative but side effects limit its use. Anecdotally, tricyclic antidepressants are worth considering in difficult cases. Prochlorperazine or promethazine can be helpful in other cases. Ondansetron and other 5HT<sub>3</sub> antagonist drugs are expensive but can be useful in some refractory patients.<sup>18</sup>

## Conclusion

Unexplained or functional nausea and vomiting syndromes should be diagnosed with caution. Other explanations need to be carefully excluded. Cyclic vomiting syndrome can be easily diagnosed based on a typical history in the absence of a structural or biochemical explanation. These conditions are probably not psychogenic in origin.

Unfortunately, treatment remains empirical for all patients with functional nausea and vomiting. The class of drug that appears to be most useful across all of the syndromes is a tricyclic antidepressant; only low doses (or subantidepressant doses) need to be used in most cases. The duration of treatment however, remains poorly defined and the long term outcomes inadequately documented. However, a 3–6 month course seems reasonable followed by clinical observation after tapering off therapy.

## Resource

A patient based support organisation, the Cyclic Vomiting Syndrome Association, was founded in 1993 and provides up to date information for patients ([www.cvsanline.org](http://www.cvsanline.org)).

Conflict of interest: none declared.

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