14: Nausea, vomiting, and Helicobacter pylori

R.W. McCALLUM, S.H. CALDWELL & B.J. MARSHALL

Introduction

The many causes of nausea and vomiting are summarized in Fig. 14.1. Although all of these conditions are potential etiologies in the acute setting, a longer history of episodic or cyclical symptoms will usually narrow the differential diagnosis. Usually such patients have received various empiric therapeutic trials and only resistant chronic cases present to the consulting gastroenterologist.

In general, we define "chronic" as persistent symptoms for 3 months or longer. Commonly, patients who fit into this category describe recurring bouts of nausea and vomiting with intermittent periods of normal or near-normal function. Such patients are often diagnostic and therapeutic challenges. Many fall into the realm of non-ulcer dyspepsia, and about half of these are found to harbor chronic bacterial gastritis. Below, we will review the spectrum of chronic nausea and vomiting with attention to the possible role of *Helicobacter pylori* in this setting.

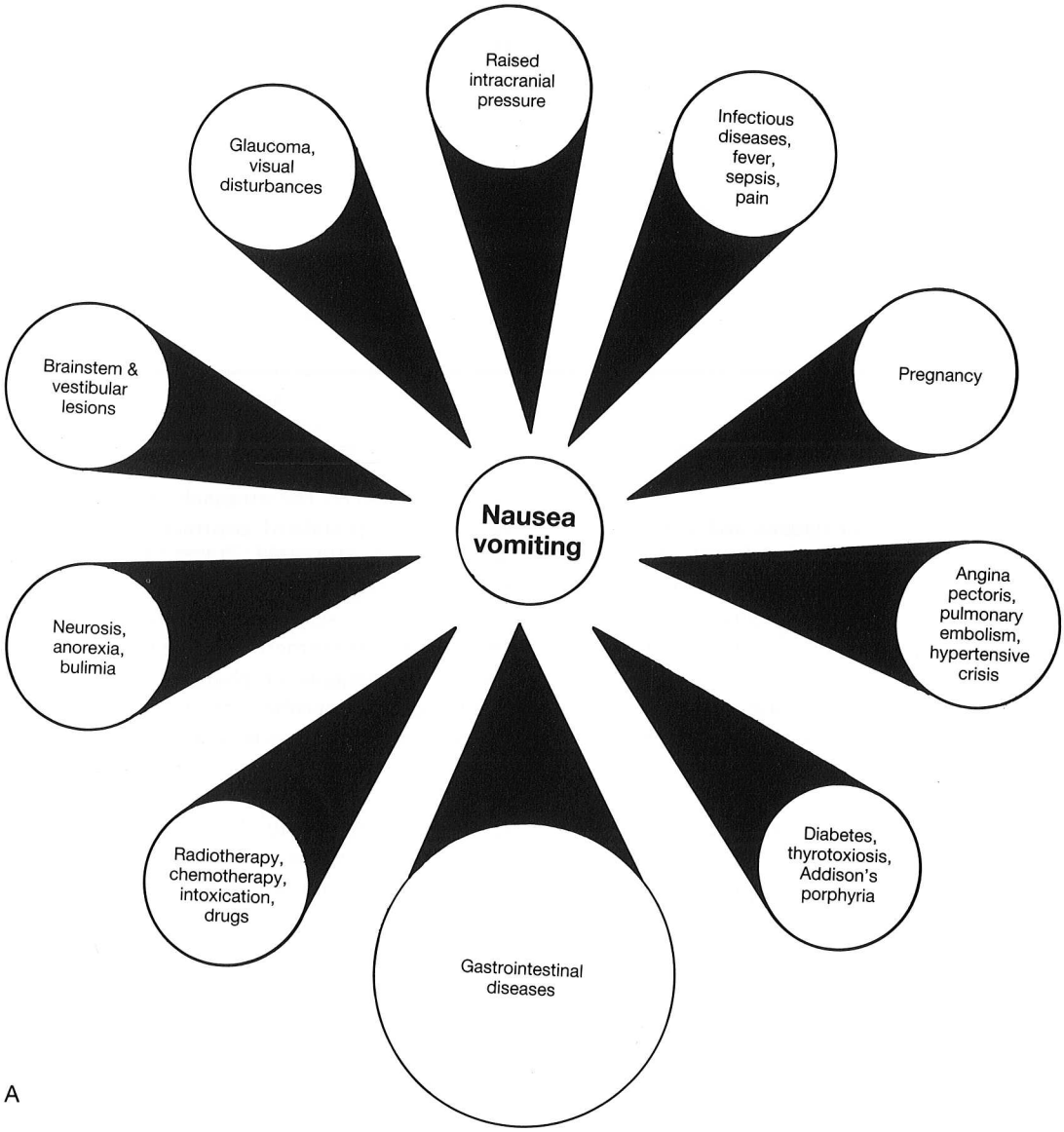
Nausea and vomiting

Nausea is an unpleasant, upper abdominal sensation that usually, but not always, precedes the act of vomiting or forceful expulsion of the gastric contents. Nausea is a component of the involuntary autonomic nervous system and is usually associated with tachy- or bradycardia, tachypnea, hypersalivation, and pupillary dilation. It may be associated with frank abdominal pain. The subsequent act of vomiting is a coordinated interaction of the viscera and central nervous system (CNS), which results in increased pyloroduodenal tone, elevation of the gastric cardia, loss of the normal pressure gradient between the stomach and esophagus, and forceful sustained contraction of the abdominal muscles (Fig. 14.2). Distinguished from vomiting is the act of gastroesophageal reflux, which is seldom associated with nausea, and involves movement of the gastric contents into the esophagus or pharynx as a result of less forceful, sometimes passive, changes in the gastroesophageal pressure gradient.

A related condition is regurgitation and rumination. The latter term describes the effortless regurgitation of food within minutes of its ingestion and without accompanying nausea. Rumination is not forceful, although it may lead to continued "vomiting," even to a dehydration level, but not accompanied by esophagitis. It is to be distinguished from bulimia, which is vomiting induced by the patient, often in a secretive manner.

The nature of the patient's complaints and the medical history usually provide important clues as to the etiology of recurrent nausea and vomiting. A history of prior psychiatric illness is helpful but seldom adequate to draw firm conclusions. Neurosis is common among patients with chronic gastrointestinal symptoms, but it is rarely clear which problem is "cause" and which is "effect," so that psychosomatic disorders are best left as a diagnosis of exclusion.

Obviously, a history of prior ulcer disease or gastric surgery is significant and may have bearing on both diagnostic and therapeutic strategies. The medical history should also emphasize other medical illnesses for which the patient may be on potentially toxic medications, such as theophylline preparations or digoxin. Often, by the time these patients



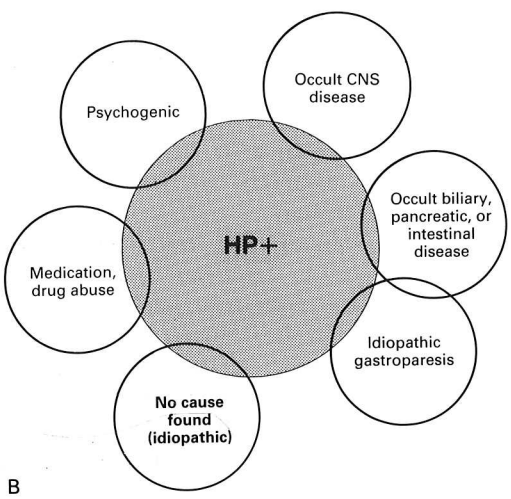


Fig. 14.1 Etiology of nausea and vomiting. A, main causes of vomiting. B, likely diagnoses and association with *H. pylori* in patients with chronic symptoms.

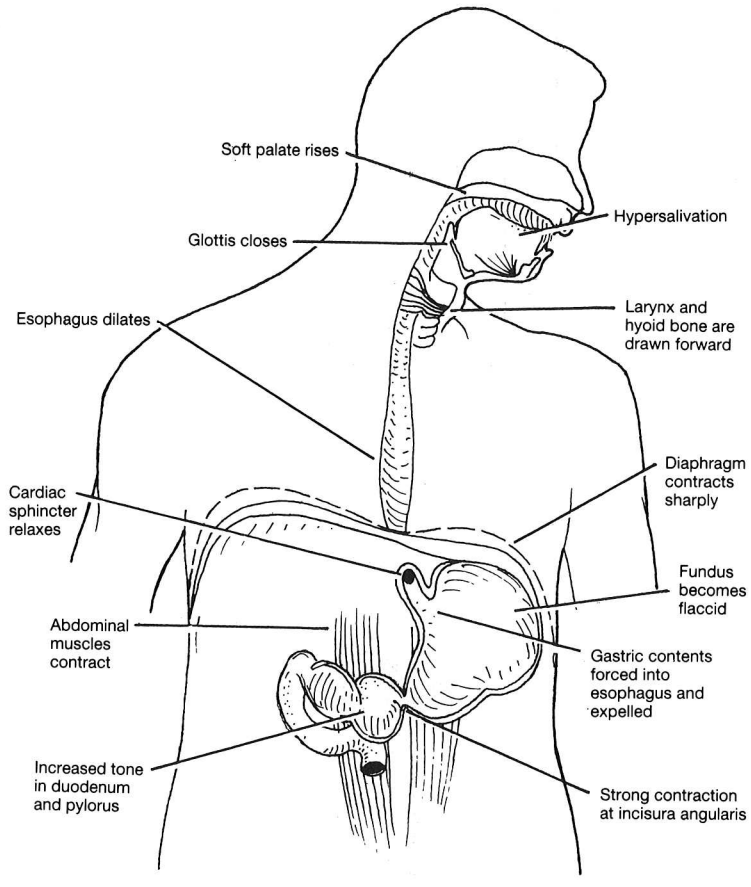


Fig. 14.2 The act of vomiting in man.

reach the gastroenterologist, they are on numerous medications, and a few minutes spent reviewing the side-effects of these drugs can be rewarding.

Once the patient's background has been established, special attention to the details of their symptoms should be given. In particular, the character of the vomitus, associated symptoms, the relation to abdominal pain, and especially the relation to meals, are important variables. Prominent symptoms of headache, vertigo, or visual disturbance indicate a problem outside of the gastrointestinal tract, as do exertional symptoms, association with shortness of breath, or frank chest pain, which suggest a cardiopulmonary disorder.

The appearance of the vomitus is often indicative of the underlying problem. The presence of undigested food is suggestive of a mechanical problem, such as gastric outlet obstruction or stricture. Grossly bloody vomitus may be the result of peptic ulcer or of a Mallory–Weiss tear. Foul-smelling and partially fermented food suggests either a mechanical obstruction or a gastric motility disorder. In rare cases, fistulae between colon and proximal gut can cause this. Pain may be associated with peptic ulcer, biliary tract disease or pancreatitis, particularly when there is a close association between meals, upper abdominal pain, and recurrent nausea and vomiting. Prominent morning symptoms are seen with pregnancy and, perhaps more commonly, with chronic alcoholism, although the latter may also be associated with chronic *H. pylori* infection [1].

The examination and laboratory evaluation of the patient should be directed by the medical history (see also Fig. 14.3). Of particular importance is the need to assess the

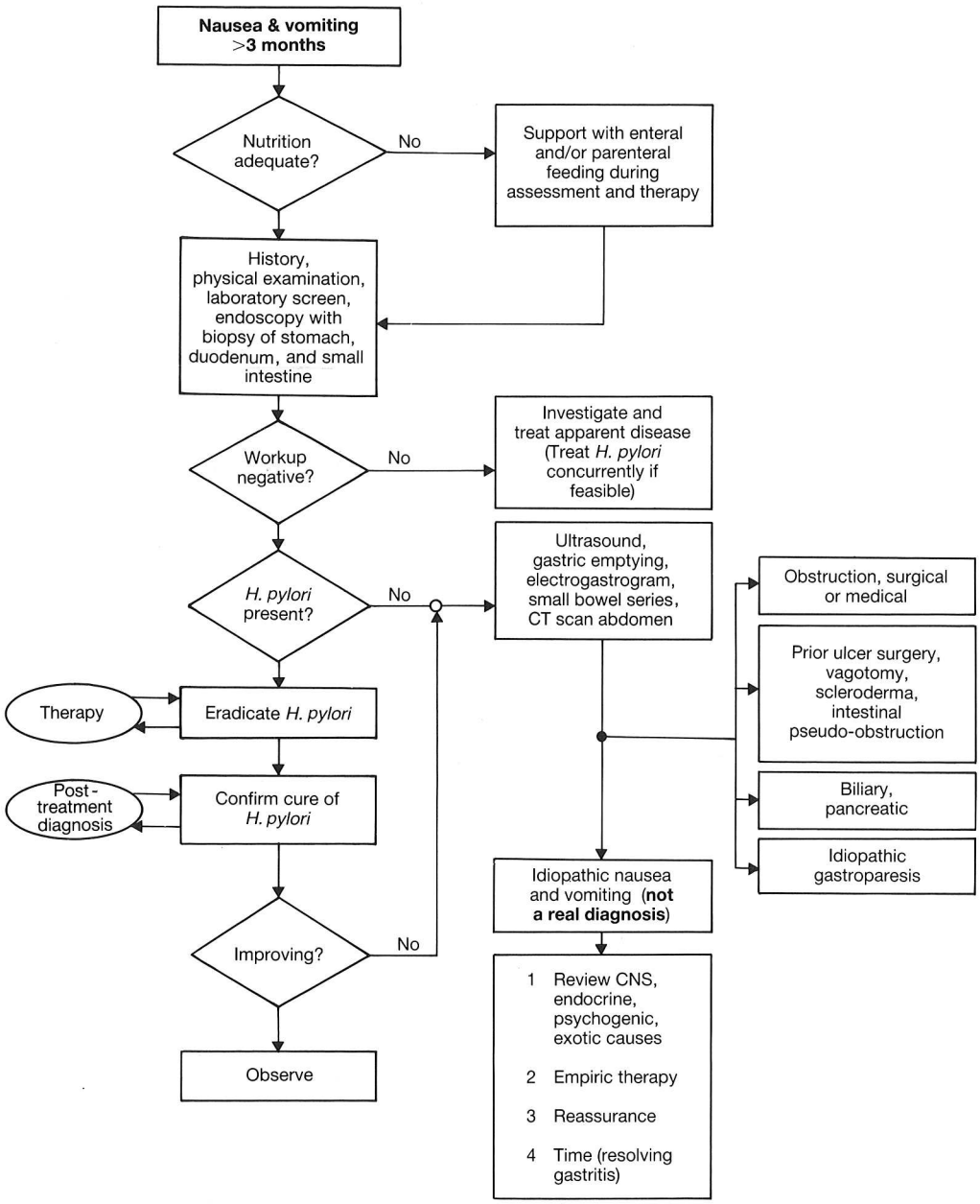


Fig. 14.3 Management of chronic nausea and vomiting.

nutritional status of the patient, as this may be severely compromised and often dictates the need for direct supportive measures prior to, or during, the initial work-up. A brief neurologic examination, with attention to the cranial nerves and optic fundi, may reveal a previously unrecognized CNS lesion. The abdominal examination should determine the presence of distension, a gastric succussion splash, tenderness, or organomegaly, which may require various imaging studies to characterize further. Fecal occult blood may offer a clue to under-

lying peptic ulcer or malignancy, but is often non-specific and may be unrelated to the presenting symptoms.

In general, we perform screening laboratory tests to assess serum electrolytes (sometimes a clue to the severity of the symptoms or an underlying adrenal disorder), cortisols, blood glucose, liver transaminases, blood counts, sedimentation rate, thyroid function, nutritional indices, and pancreatic enzymes, as well as drug levels if necessary. Sometimes, tests for alcohol or occult drug use are helpful. A chest X-ray, to exclude the possibility of a paraneoplastic syndrome related to small cell carcinoma of the lung, is appropriate where paraneoplastic syndrome is being considered in a middle-aged or older patient. Abdominal flat plate X-rays can identify dilated loops of bowel in pseudo-obstruction settings. Beyond these initial diagnostic measures, further evaluation often includes endoscopic studies, gastric motility tests, and/or abdominal and biliary imaging tests.

Non-ulcer dyspepsia

Many patients with chronic nausea and vomiting fall into the category of non-ulcer dyspepsia (NUD). Among patients with the latter syndrome, approximately 25% have, as prominent symptoms, nausea and vomiting [2] and, at this hospital, about 9% of NUD patients have these symptoms as major complaints. Dyspepsia refers to vague upper abdominal discomfort which is often meal-related. The term "non-ulcer dyspepsia" refers to the presence of these symptoms in the absence of peptic ulcer, and excluding other obvious abnormalities of the pancreas or biliary tree. Aside from anatomic abnormalities, however, many of these patients have *H. pylori* infection, histologic gastroduodenitis and, in some, gastric motility disorders. These three entities, and their possible relationships to each other and to chronic nausea and vomiting, are discussed below.

The spectrum of NUD

Non-ulcer dyspepsia has been conceptually divided into five groups [3, 4]. Among these, the first four are diagnostic categories and the last comprises the 25% or so of individuals who cannot be classified into a distinct category. The first group consists of patients with prominent symptoms of acid reflux, with meal-related or positional epigastric or retrosternal burning, which may be relieved with antacids. The second group has symptoms of classic duodenal ulcer without a demonstrable ulcer crater, i.e. Moynihan's disease. The third group consists of patients with prominent bloating during meals, early satiety, and distension, which are suggestive of a primary dysmotility disorder. The fourth group consists of patients with various mixed upper and lower gastrointestinal symptoms, overlapping with the irritable bowel syndrome and including aerophagia, bloating, distension, abdominal colic, food intolerances, and altered bowel habit.

Although these categories are useful to conceptualize the clinical problem, their relationship to underlying pathophysiologic mechanisms has not yet been fully refined. The NUD syndrome is discussed further in Chapter 13.

H. pylori, motility and non-ulcer dyspepsia

Helicobacter pylori has been implicated in a number of upper gastrointestinal illnesses. Persistent infection after duodenal ulcer healing increases the risk of ulcer relapse [5]. In NUD patients, gastric infection with *H. pylori* occurs in 30–50% [6]. Infection with *H. pylori* is strongly associated with histologic antral gastritis [7]. Eradication of the organism may improve symptoms in a significant number of patients with chronic dyspepsia [8]. Many of these patients complain of chronic nausea, or even intermittent vomiting, associated with their dyspepsia; however, the mechanism by which chronic bacterial gastritis might cause symptoms has not been elucidated. Studies before the discovery of *H. pylori* suggested a relationship between chronic histologic gastritis and gastric hypomotility [9], and recently an association between *H. pylori* infection and delayed orocecal transit time has been reported among patients with NUD [10]. On the other hand, *H. pylori* is not more

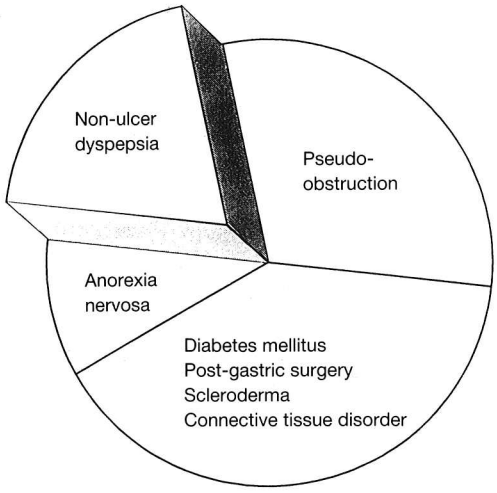


Fig. 14.4 Gastric motor disorders; associated conditions.

Table 14.1 Twenty consecutive patients presenting with known gastroparesis were prospectively evaluated for *H. pylori* infection. The prevalence of *H. pylori* infection in this group was not different to that of 21 age-, sex-, and race-matched patients presenting for routine upper endoscopy for symptoms of dyspepsia

	Gastroparetics	Consecutive endoscopies
n	20	21
Age	43 ± 10	47 ± 13
Range	26–74 years	28–73 years
Females	20	21
HP+	4 (20%)	7 (33%)

common in patients with symptomatic gastroparesis than in dyspeptic controls [11, 12].

Delayed gastric emptying may be a cause of upper abdominal pain [13]. Abnormal gastric motility has been found to be common among patients with dyspepsia [14]. About 20% of patients with delayed gastric emptying have symptoms which allow them to be classified into a category of NUD (Fig. 14.4) and, in our population, about one-third of patients with NUD have delayed gastric motor function. Vomiting is often a prominent symptom among these patients.

Is chronic *H. pylori* infection associated with gastroparesis?

We have recently reported our findings in two groups of patients — one with idiopathic gastroparesis associated with recurrent nausea, vomiting, and abdominal discomfort, and another group of patients with NUD and *H. pylori* infection [15]. The groups were studied for the presence of infection, and underwent gastric emptying studies using a ^{99m}Tc–sulfur–

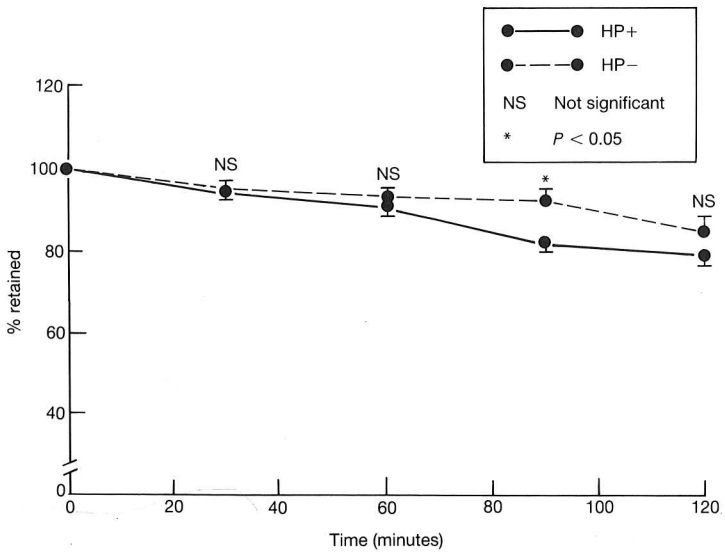


Fig. 14.5 The percentage of retained isotope (^{99m}Tc) among infected (n = 4; HP+) versus uninfected (n = 16; HP−) consecutive gastroparetic patients. There was no significant difference at 30, 60, and 120 minutes ($P > 0.1$, Student's T-test). At 90 minutes, the infected patients retained significantly less isotope ($P < 0.05$, Student's T-test).

Table 14.2 Nineteen consecutive patients with chronic dyspepsia and *H. pylori* infection underwent ^{99m}Tc-labeled chicken-liver gastric emptying tests. The results of the solid-phase gastric emptying tests were compared to 16 uninfected, asymptomatic volunteers

	HP+ (dyspeptics)	HP− (normals)
n	19	16
Age	38 ± 9	24 ± 4
Range	24–55 years	20–40 years
Females	12	11

colloid-labeled chicken-liver test meal. Among 20 consecutive patients with idiopathic gastroparesis (Table 14.1), four (20%) were infected with *H. pylori*. Solid-phase gastric emptying was delayed in all patients, but less so in the infected group (Fig. 14.5). Symptom scores were similar between infected and uninfected patients, and the prevalence of *H. pylori* in this group was not significantly different from a group of age-matched patients presenting with NUD.

In another group of 19 patients with proven *H. pylori* infection and NUD (Table 14.2), solid-phase gastric emptying was significantly more rapid in infected patients compared to 16 healthy, uninfected controls (Fig. 14.6). This relationship persisted when this group of patients was reanalyzed, using only male patients and controls to exclude possible menstrual cycle effects. Although orocecal transit time may be prolonged in *H. pylori* infection [10], our data and those of others [11, 12, 15] do not suggest an association between *H. pylori* and delayed gastric emptying. On the contrary, our results suggest increased emptying of solids among infected, symptomatic patients. These findings have yet to be correlated to the extent of underlying histologic disease, and they have not been reconciled with the apparent frequent presence of recurrent vomiting among symptomatic patients, as discussed further below. However, decreased gastric compliance related to chronic gastritis accompanying the *H. pylori* infection could be a contributing factor.

Evidence for a relationship between *H. pylori* and vomiting

The usual division between NUD and peptic ulcer disease may be invalid in patients with *H. pylori*, because many such NUD patients give a history of prior ulcer disease, and some go on to develop peptic ulcer disease [16]. In addition, ulcer patients sometimes have milder but persistent dyspeptic symptoms, even nausea and vomiting, in between actual clinical ulcer episodes [17, 18]. These authors believe that gastritis in NUD is the more benign end of the *H. pylori* clinical spectrum, which starts asymptomatic gastritis, includes NUD syn-

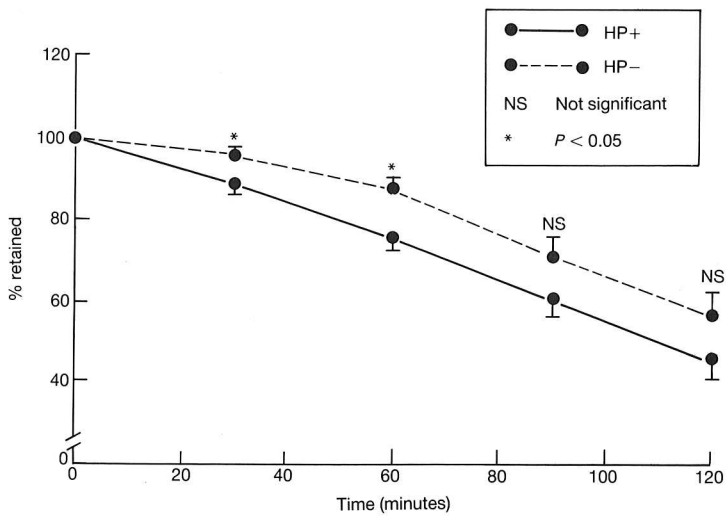


Fig. 14.6 The percentage of retained isotope (^{99m}Tc) in 19 dyspeptic patients with *H. pylori* infection (HP+) versus 16 uninfected, asymptomatic volunteers (HP−). Gastric emptying in the infected group was significantly faster in the early post-prandial period ($P < 0.05$, Wilcoxon Rank Sum).

drome, and ends with severe mucosal ulceration of the duodenum and/or stomach.

At the turn of the century, when acute *H. pylori* infections may have been common in children, Osler described acute gastritis with hypochlorhydria as a short-lived vomiting illness, which at times progressed to chronic dyspepsia [19]. Subsequent reports of acute gastritis with hypochlorhydria [20], now known to be due to *H. pylori*, usually describe a transient illness consisting of epigastric pain, nausea, and vomiting. In the epidemic of *H. pylori* reported by Ramsey *et al.* [21], the onset of hypochlorhydria was accompanied by an upper gastrointestinal illness lasting a week or so. In the self-administration experiment reported by Marshall *et al.* [22], early morning nausea and concurrent gnawing hunger pains were felt. These symptoms are very similar to those reported by patients with duodenal ulcer, who often have nausea and epigastric gnawing relieved by eating small snacks. In the self-administration experiment reported by Morris & Nicholson [23], nausea and vomiting occurred from day 4 until around day 7 after ingestion of the bacterium. Similarly, nausea and vomiting were prominent in apparent acute *H. pylori* episodes reported by several other authors [24, 25, 26].

Children with *H. pylori* often present with unexplained vomiting [27]. Pediatric *H. pylori* may also cause radiologic enlargement of the gastric folds [28] and a Menetrier-like protein-losing enteropathy [29], which responds well to eradication of the bacterium.

Recent reports suggest that *H. pylori* is a common cause of chronic nausea and vomiting. Mohiuddin *et al.* [30] studied 10 consecutive patients with unexplained intractable symptoms. The mean duration of the syndrome was 12 months (range 5–60) and no cause had been found after exhaustive work-up. Many of the patients carried a psychiatric diagnosis, reflecting an absence of discernible organic disease. Endoscopy was normal in the 10, but nine were found to have active gastritis and *H. pylori* on biopsy. Suppressive therapy with bismuth subsalicylate resulted in complete remission in six patients and substantial improvement in the other three. Those patients who had lost weight immediately regained it once the vomiting had ceased.

In a double-blind study of *H. pylori* treatment in duodenal ulcer disease, Marshall *et al.* [31] reported that three patients continued to have nausea and vomiting after healing of their ulcer. All three had received H2 receptor antagonists and *H. pylori* had not been eradicated. They immediately responded to antibacterial therapy with colloidal bismuth subcitrate, and achieved permanent remission after eradication of the bacterium. Although this was a small subset of patients, and not statistically significant, it did suggest that in patients with duodenal ulcer disease, vomiting may be related to *H. pylori* and gastritis and not always to the ulcer crater.

At the University of Virginia, we have seen six patients with intractable vomiting in whom *H. pylori* was the only abnormality detected after extensive work-up. In these patients, therapy for *H. pylori* resulted in symptomatic cure, except for one patient subsequently found to have small intestinal Crohn's disease.

Pathogenic effects of *H. pylori*

The pathogenic aspects of the *H. pylori* organism have been reviewed elsewhere [32]. *H. pylori* organisms colonize the gastric epithelium in vast numbers and the majority of isolates are toxigenic [33]. *In vitro*, 30–60% of isolates from NUD patients will cause vacuolation of cultured epithelial cells [34]. Vacuolation also occurs when such cells are incubated with high concentrations of ammonia, or *H. pylori* (urease) and urea [35]. Ammonia collects in the gastric juice of patients with *H. pylori* and can reach concentrations of 50 mM, about 1000 times higher than that of the blood [36].

Other enzymes produced by *H. pylori* may also damage the gastric mucosa. Proteases digest the gastric mucus layer [37], phospholipases compromise the integrity of the mucus layer and may damage epithelial cell membranes [38], and a toxin inhibits acid production by parietal cells [39]. This "hypochlorhydric" toxin may be relevant to gastric emptying delays, because slower emptying is known to occur in hypochlorhydric states, such as drug-induced hypochlorhydria or pernicious anemia [40].

Finally, the presence of bacterial proteins incites an immune response, giving rise to activated complement, inflammatory mediators, and superoxide radicals generated from

phagocytic cells [41]. It is possible that the nausea and vomiting present in patients with *H. pylori*-associated disease are the normal response to stimulation of local chemoreceptors designed to trigger the expulsion of noxious gastric contents.

Management of nausea and vomiting

Chronic nausea and vomiting are a therapeutic challenge, since many patients cannot take the oral medication prescribed and in severe cases even the investigation of the problem is difficult. The flow chart in Fig. 14.3 suggests a management plan.

Initially, obvious known causes should be ruled out and *H. pylori* should be excluded. If no mucosal abnormality is found, further investigation may reveal a gastric motility disorder. In general, chronic nausea and vomiting associated with an identifiable motility disorder are more difficult to treat, and may never resolve. In some cases, underlying diseases such as diabetes, scleroderma, previous gastric surgery, or intestinal myoneuropathy will be irreversible causes. Therapy for these is a stepwise increase in measures starting with:

1 Low-residue soft or liquid diet, frequent small oral feeds, erect posture to assist gastric drainage.

2 Oral or parenteral antiemetic medications, known and experimental prokinetic agents (see Table 14.3).

3 Frequent small feeds, soft naso–gastric–jejunal feeding tube.

4 Percutaneous gastrostomy feeding tube, either into the stomach or via gastrostomy into the jejunum (depends on the amount of nausea

Table 14.3 Drugs used for the treatment of nausea and vomiting

Drug name	Mode of action	Dosage and administration	Side-effects
Metoclopramide, "Reglan", "Octamide"	Dopamine antagonist and anticholinergic with peripheral and central action. Speeds gastric emptying, increases LES tone, antinauseant	Oral, 10 mg t.i.d. 30–60 minute ac; SC or IV = 5–10 mg t.i.d.; for chemotherapy, infuse 2 mg kg^{-1} IV 2 hourly for 5 doses in 24 hours (2–3 hourly); halve dose in renal failure	Sedation, extrapyramidal reactions (give 50 mg diphenhydramine, "Benadryl," IM), amenorrhea, lactation
Chlorpromazine, "Thorazine"	The prototype phenothiazine, anticholinergic, dopamine antagonist, weak serotonin antagonist, central antiemetic, peripheral alpha blocker, psychotropic	Oral, 10–25 mg 4–6 hourly (may increase if no side-effects); suppositories, 100 mg 6–8 hourly; IM, 25–50 mg 4–6 hourly (deep IM); IV, 25–50 mg, dilute to 1 mg ml^{-1} as 1 mg $minute^{-1}$	Anticholinergic, alpha blocking, sedation, dopamine antagonist, galactorrhea, gynecomastia, cholestatic jaundice, extrapyramidal effects
Prochlorperazine, "Compazine"	A phenothiazine, some anticholinergic action, dopamine antagonist, central antiemetic, peripheral alpha blocker	Oral, IM, IV, 5–10 mg t.i.d., maximum dose around 40 mg day^{-1}; also available as suppositories, 25 mg b.i.d.	Sedation, extrapyramidal reactions, tardive dyskinesia (long-term use), amenorrhea, lactation, orthostatic hypotension, cholestatic jaundice
Thiethylperazine, "Torecan"	Related to phenothiazine, a centrally acting antiemetic	Oral, 10 mg t.i.d.; suppositories, 10 mg t.i.d.; IM, 10 mg t.i.d.	As for phenothiazines; anticholinergic, alpha blocking, dopamine antagonist, sedation, extrapyramidal effects

Table 14.3 (*continued*)

Drug name	Mode of action	Dosage and administration	Side-effects
Scopolamine, "Transderm Scop"	Centrally acting antiemetic via anticholinergic effect on vomiting center. Peripheral (GI) actions also present. 75% reduction in motion sickness. About 40-minute delay before effect is evident	Cutaneous patch attaches behind ear. One patch releases 0.5 mg scopolamine over 73 hours	Anticholinergic. Dry mouth, sedation (20%), blurred vision, glaucoma. Temporary exacerbation of symptoms after withdrawal
Diphenhydramine, "Benadryl," and diphenhydrinate, "Dramamine"	Antihistamine, anticholinergic, central antiemetic action	Oral, IM, and IV dose is 50 mg 3–6 hourly, maximum dose 400 mg day^{-1}	Anticholinergic, sedative, photosensitivity, GI side-effects, glaucoma
Promethazine, "Phenergan"	Phenothiazine derivative, an antihistamine, very weak dopaminergic action. Central antiemetic, sedative, weakly anticholinergic	Oral, 12.5–50 mg 4–6 hourly; suppository, same dose; IM, 25–50 mg 4–6 hourly (can cause gangrene if intraarterial, or necrosis if given SC); IV, 25–50 mg as 25 mg ml^{-1} or less, best if IV solution running, repeat 4–6 hourly	Sedation, dry mouth, blurred vision, glaucoma, hyper or hypotension, allergic reaction, photosensitivity, GI upset
Meclizine, "Antivert," "Bonine"	Antihistamine with weak anticholinergic action. Central antiemetic	Oral, 25–100 mg daily, as b.i.d. dose	Sedative, anticholinergic, glaucoma
Cyclizine, "Marezine"	Antihistamine, anticholinergic, central antiemetic	Oral, IM, or IV 50 mg 4–6 hourly	Sedative, anticholinergic, glaucoma
Hydroxyzine, "Vistaril"	Antihistamine, unrelated chemically to the phenothiazines, sedative, anticholinergic, central antiemetic action	Oral, 25–100 mg q.i.d. Well absorbed, onset of action 15–30 minutes	Anticholinergic, sedative
Benzquinamide, "Emete-con"	A benzoquinolizine chemically unrelated to phenothiazines. Central antiemetic. Antihistamine, weak anticholinergic, sedative. Half-life 40 minutes, used to prevent post-operative nausea and vomiting in anesthesiology. Has caused hypertension when given IV	IM, 50 mg repeated 3–4 hourly. Not usually used for a prolonged period. Halve dose in the elderly. IV, give 25 mg initially, then use IM (do not give IV to patients with cardiovascular disease)	Hypertension, hypotension, anticholinergic effects, arrhythmias, drowsiness, GI upset, fatigue, chills, fever

Table 14.3 (*continued*)

Drug name	Mode of action	Dosage and administration	Side-effects
Trimethobenzamide, "Tigan"	Central antiemetic with anticholinergic, dopamine antagonist and sedative effects	Oral, 250 mg 3–4 times daily; suppositories, 200 mg 3–4 times daily; IM, 200 mg 3–4 times daily (not recommended for intravenous use)	Extrapyramidal reactions, drowsiness, allergic reactions, convulsions, masking of other CNS signs. Injection is painful
Domperidone, "Motilium"	Peripherally acting dopamine antagonist. Prokinetic action (similar to metoclopramide) but less central effects	Oral, 20 mg ac and at bedtime	Some central action allows dopamine antagonism with consequent gynecomastia, and galactorrhea. Can be used (with caution) in Parkinson's disease
Cisapride	Facilitates acetylcholine release from gut myenteric plexus, also serotonin antagonism, very little central action, no dopamine antagonism and minimal anticholinergic action. Not primarily an antiemetic. Increases GI motility from stomach to colon. Half-life 7–10 hours	Oral 10–20 mg 6 hourly; IM, 4–8 mg (not yet available in the United States, consult *Physicians Desk Reference* (PDR))	Abdominal cramps, GI discomfort, diarrhea
δ-9-THC, "Marinol"	The active agent in cannabis. Central action. Psychotropic and antiemetic	Oral, 5–10 mg repeated at 2–4 hour intervals for 4–6 doses per day; mainly used in chemotherapy	About twice the side-effects of prochlorperazine in comparative studies. Drowsiness, dizziness, euphoria, dry mouth, ataxia, visual, hypotension. Psychological dependence
Nabilone, "Cesamet"	"	Oral, 1–2 mg b.i.d.	"
Erythromycin "Eryc," "Erythromycin base filmtabs"	Erythromycin base is a motilin receptor agonist. It enhances gastric motor activity *in vitro* and *in vivo*. Use as a prokinetic agent is being investigated	Oral, 250 mg q.i.d.; IV, 150–300 mg t.i.d. Experimental in this prokinetic role, clinical efficacy not proven. Not an antinauseant	Abdominal cramps, allergies, nausea. Omeprazole ramitidine may decrease side-effects

ac, *ante cebum*; GI, gastrointestinal; IM, intramuscular; IV, intravenous; LES, lower esophageal sphincter; SC, subcutaneous.

present, and necessary only in persons who cannot maintain adequate oral intake).
5 Surgical feeding jejunostomy, necessary when gastric emptying is very poor and enteric feeds are vomited.

Table 14.3 lists the drugs and doses used for the treatment of nausea and vomiting. The table includes some new "prokinetic" agents (i.e. they increase gastric motility), which are experimental and not yet fully evaluated in the United States. An interesting new agent is erythromycin, which stimulates motilin receptors in the upper gastrointestinal tract and increases gut peristalsis [42]. The clinical relevance of this effect is presently under investigation. Prokinetic drugs are not necessarily antiemetic, so their use is best restricted to those patients with documented gastroparesis.

Unlike *H. pylori*-negative (HP−) nausea and vomiting, *H. pylori*-positive (HP+) cases often respond well, albeit slowly, to antibacterial therapy. These patients may give a history of vomiting several times per week for months or even years, sometimes starting in childhood. Usually a psychiatric diagnosis has been entertained by previous physicians.

Since 20% of patients with known gastroparetic syndromes will have *H. pylori* (i.e. the usual population prevalence after age 30), one must keep in mind that eradicating *H. pylori* in this setting will not necessarily change the underlying gastric motor disturbance, and that symptoms of gastroparesis will continue.

Nevertheless, we have seen three patients with *H. pylori*-associated gastroparesis and vomiting who responded symptomatically to antibiotic therapy. In two of these, gastric emptying returned to normal; in a third it remained slightly delayed after 1 year.

Figure 14.7 shows the response to therapy in NUD patients at this hospital who had nausea and/or vomiting as a major symptom. Of 26 patients with nausea at least once per week, one worsened, seven were unchanged, and 18 (70%) improved. Of these 18, 11 had symptoms less than once per month at follow-up 15 months later.

For reasons unknown, most patients with nausea and vomiting are women. They are very well motivated and will attempt to complete even the most difficult antibiotic therapy.

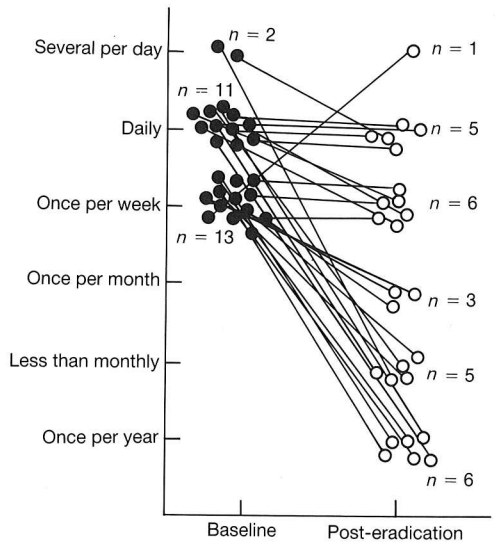


Fig. 14.7 Nausea and vomiting: symptom response in 26 patients after eradication of *H. pylori*.

As with all antibacterial therapy, the aim is to eradicate the underlying organism which, in the case of *H. pylori*, may involve more than one cycle of treatment. Nauseated patients may refuse a second course of antibiotic therapy if the first fails to eradicate *H. pylori*. Therefore, to ensure maximum success of the initial antibiotic course, we attempt to obtain culture and sensitivity of the organism prior to therapy, and may even ask the patient to return for endoscopic biopsy to achieve this purpose.

If the organism is sensitive to metronidazole, simple dual therapy usually eradicates *H. pylori* with minimum discomfort to the patient. If the organism is resistant to metronidazole (30% of cases), then alternative antibiotics are used in the first instance.

When medication is likely to be vomited back up, we recommend starting with liquid BSS in frequent small doses, and maintaining this until a partial clinical response is observed, when other agents can be added one by one. Metronidazole should be added last, since it is ineffective unless bacterial suppression is achieved with the initial therapeutic agents.

After treatment of *H. pylori* for 10–14 days (see Chapter 13), the patient and the physician must resist the temptation to give extra antibiotic therapy if a clinical response has not

occurred, because further antibiotic therapy will produce false-negative diagnostic tests for *H. pylori*. Negative endoscopic biopsy or breath test 1 month later is strong evidence for bacteriologic cure, but testing earlier than this is unreliable. The exception is the very unwell patient, in whom endoscopy and multiple biopsies for histology and culture at an earlier time may be worthwhile, since absence of *H. pylori* and healing of gastritis will prevent further unnecessary antibiotic treatment.

In our clinic, patients remain on their usual antiemetic therapy during antibacterial treatment, and may continue this after completing therapy for *H. pylori*. One month later a breath test is performed. If this is negative, we repeat it 3 months later to confirm long-term eradication of *H. pylori*.

After eradication of *H. pylori*, symptoms improve in many patients, although exacerbations and remissions often cause further concern. If a non-invasive *H. pylori* test is available, a negative result is reassuring and no extra intervention is necessary. If a breath test is unavailable, then endoscopy and biopsy should be repeated. Half of the patients successfully treated will improve immediately, while the others respond gradually over 3–12 months. Eventually, clinical relapses become uncommon and 75% cease their antiemetic medication. Older women, who may have had symptoms all their lives, seem to be the slowest to respond.

In patients with severe *H. pylori*-associated syndromes we routinely screen the spouse for the infection, and advise antibacterial therapy if infection is present. Because of the relapsing and remitting nature of the symptoms, fewer investigations will be performed during clinical relapses if we know the spouse is free of *H. pylori*.

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