



# Functional Gastroenterology Bolus

by Steven Sandberg-Lewis, ND, DHANP

## Understanding Chronic Nausea and Gastroparesis

Chronic nausea with or without vomiting is an often poorly understood problem. I have seen many patients who have suffered for years, sometimes with no clear diagnosis or poorly managed on symptomatic treatment measures. Typical medications include Zofran (ondansetron), which blocks 5-HT<sub>3</sub> receptors.

The vomiting reflex has three phases:

1. The first is nausea. Nausea involves inhibition of gastric tone, reverse peristalsis beginning in the jejunum, and reflux of duodenal contents into stomach. This is what is occurring in the patient who has nausea alone.
2. The second phase is retching. This includes orad (toward the mouth) compression of the stomach by the diaphragm and external abdominal muscles, but the lower and upper esophageal sphincters are closed.
3. The third and final phase is vomiting. This causes orad propulsion of the contents of the upper GI tract through the open pyloric and esophageal sphincters.

The three phases are controlled by the brain's vomiting center, which is located just inferior to the fourth ventricle. Nausea/vomiting is triggered when sensory neurons convey distention or irritation of gastrointestinal organs (e.g., appendicitis, bowel obstruction, biliary tract obstruction), but also by cerebral events such as emotion, pain, and vestibular rotation.<sup>1</sup>

Certain extra-gastrointestinal stimuli alter body chemistry and may activate the chemoreceptor trigger zone in the brainstem. These include irritation of the diaphragm from lung infections or inferior wall myocardial infarctions, uremia (in acute or chronic kidney disease), toxins, and certain drugs (e.g., ipecac, digitalis).

The key additional underlying issues I have found in chronic nausea include gastroparesis, chronic liver issues, yeast overgrowth, small intestine bacterial overgrowth, hypochlorhydria, and gluten intolerance.

Gastroparesis is a delay in gastric emptying that can lead to prolonged distention and nausea with or without vomiting. Causes of gastroparesis include diabetes (up to 40% of DM1 patients; 10-20% of DM2 patients). Glycosylated hemoglobin

levels may correlate with the presence of gastroparesis.<sup>2,3</sup> The mechanism is generally considered to be autonomic neuropathy. If a diabetic has any other form of neuropathy (e.g., decreased deep tendon reflexes, peripheral neuropathy), they will likely also experience altered gastrointestinal motility.

Other causes of gastroparesis include hypothyroidism, traumatic brain injury, systemic lupus erythematosus, progressive systemic sclerosis (scleroderma), Parkinson's disease, and stroke. Drugs that often lead to delayed gastric emptying include tobacco, calcium channel blockers, L-dopa, hyoscyamine, anticholinergics, and opiates. Other symptoms of gastroparesis include heartburn, regurgitation, belching, early satiety, and epigastric cramping.

Testing for gastroparesis may include the upper GI barium series ("barium swallow"), which reveals evidence of emptying by the findings of gastric dilatation, delayed emptying of barium, retained gastric debris (bezoars) or retained gastric fluid.<sup>4</sup> Electrogastrogram (EGG) or R-R interval testing with the electrocardiogram (EKG) measure the basic electrical rhythm alterations in gastroparesis.<sup>1</sup>

Most commonly employed is the gastric emptying study (gastric scintigraphy).<sup>2</sup> An isotope-labeled solid test meal is eaten by the patient, and four hourly x-ray images are used to calculate the gastric emptying time. The test meal contains technetium-99 sulphur-colloid bound to egg. This is in the form of a sandwich or added to scrambled eggs or a mashed potato. Additionally, for gluten- or egg-sensitive patients, gluten-free oats may be used.<sup>5</sup> Following ingestion of the test meal, scintigraphy should be performed for at least two hours; and by extending the test out to four hours the most accurate results are seen. If there is greater than 10% residual gastric content of the test meal at the fourth hour, gastroparesis is diagnosed. A smartpill or capsule endoscopy may also give evidence for delayed gastric emptying.<sup>6</sup>

Treatments for gastroparesis include diabetes management (if this is the cause), mindfulness at mealtimes, diet, replacement of acid and/or enzymes, therapeutic exercises, and botanical or prescription prokinetics.

## Diet

Diet modifications may include smaller meals, reduced dietary fiber and fat, avoidance of red meat, reduced portions of protein and fat at evening meals and smaller evening meals in general. Other important considerations may include adequate hydration, reduced alcohol consumption, reduction or avoidance of cruciferous vegetables and gluten-free or grain-free diets.<sup>7</sup> Meticulous attention to detail with respect to a prescribed low carbohydrate diet has been found to reverse glycation of the vagus nerve, thereby gradually normalizing gastric emptying in diabetics.<sup>8</sup>

## Botanical Medicine

Aloe vera juice may be used in doses from 0.5 - 8 ounces 15-30 minutes before meals.<sup>8</sup> If SIBO is a current co-condition, lower polysaccharide liquid preparations may be preferred. Papain or bromelain extracts may be very useful before meals.

Prokinetic herbs may improve gastric emptying and significantly relieve nausea. *Zingiber officinalis* (ginger) is a standby for relief of nausea and 500-1000 mg. may be used at bedtime or before or with meals. The mechanism behind ginger's prokinetic action is in part due to 5-HT<sub>3</sub> receptor inhibition.<sup>9</sup> Amy Rothenberg, ND, has found excellent nausea relief for her patients undergoing chemotherapy by using a candy called "Gin-Gins double strength."<sup>10</sup> Iberogast is a German liquid prokinetic herbal formula. It has been studied for the treatment of functional dyspepsia and found to be more effective than metoclopramide. Using guinea pig tissue in vitro, it was found to have a relaxing effect on the muscles of the gastric fundus and a prokinetic effect in the antrum.<sup>11</sup> Adults may take 20 drops before meals and at bedtime, or occasionally the full dose of 60 drops at bedtime is even more effective.

## Prescription Prokinetics

Prescription prokinetics may also be employed. The one I have used most commonly is low-dose erythromycin (sub-antibiotic dosage), which is a motilin receptor agonist. Motilin activates gastric emptying and the migrating motor complex of the upper GI tract. Erythromycin can be compounded as a 50 mg capsule for adults, given as a pediatric suspension, or the commercial 250 mg tablet can be divided into fourths (with a pill cutter) providing a dose in the 50-65 mg range.<sup>12</sup> Some patients with a history of "allergy" to erythromycin may have experienced the cramp-like effects of standard dosage erythromycin and are not in fact allergic to it. If there is no history of rash or true allergic response to the drug, they may have a very effective prokinetic response to the lower dose discussed above. If the patient has a history of QT interval prolongation – or is currently taking other medications that can cause QT interval prolongation – any dosage of erythromycin should be used with caution. (See [www.crediblemeds.org](http://www.crediblemeds.org) for a list of drugs with QT interval effects.) Other prescriptions used are dopamine receptor modulators such as Reglan (metoclopramide) and domperidone (available through compounding pharmacies or Canadian pharmacies). I have never prescribed either of these. The chemoreceptor trigger zone in the brainstem employs dopamine D<sub>2</sub> and serotonin (5HT<sub>3</sub>) receptors to control the vomiting reflex, therefore drugs that modulate these receptors affect nausea and

vomiting. Metoclopramide, a dopamine and serotonin receptor modulator, is reported to cause side-effects including CNS side-effects in up to 40% of patients. Domperidone is said to have fewer side effects perhaps because it is a peripherally acting selective dopamine modulator. All these prescriptions should be checked for QT interval interactions with other medications. A screening EKG is recommended prior to starting these.<sup>13</sup>

Carmello Scarpignato, MD, notes that some highly constipated patients may have abdominal pain or other responses to prescription prokinetics.<sup>14</sup> He suggests using a standard colonoscopy bowel prep protocol to clear retained colonic material prior to initiating a prokinetic for these patients. I have found that colonic hydrotherapy is also useful for many of these cases.

For stimulation of digestive juices, vinegar or bitters may be used before meals. Betaine HCL may also be an effective treatment when taken with meals. Its necessity and dosage may be determined by Heidelberg radio-telemetry capsule testing or - if this is not available – a cautious clinical titration. Plant pancreatic enzymes before meals or porcine-based enzymes after meals may also prove helpful. Stool elastase or chymotrypsin testing may be used to assess the need for the latter.

Understanding the underlying causes of chronic nausea allows for targeted, specific treatment for this troubling problem.

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