Diagnosis and Management of Gastroparesis: The Stomach that Refuses to Empty

Improving Symptoms or Gastric Emptying

Henry P. Parkman, MD
Professor of Medicine
Director of GI Motility Laboratory
Gastroenterology Section
Temple University School of Medicine
Philadelphia, PA

Gastroparesis: A chronic disorder

A motility disorder of the stomach characterized by delayed gastric emptying without evidence of obstruction.

Diagnosis

- nausea, vomiting
- early satiety
- postprandial fullness/bloating
- upper abdominal pain
- loss of appetite
- constipation
Clinical Burden of Gastroparesis is High

**Nausea and Vomiting**
- Nausea is present in nearly all patients (95%)
- Nausea and vomiting decrease quality of life.
- Vomiting is more prevalent and severe in DG than IG.
- Symptoms of nausea and vomiting are important symptoms that each need to be specifically addressed.

Parkman et al. DDW 2015

**Abdominal pain**
- Pain has largely been ignored in gastroparesis
- Pain is the predominant symptom in one fifth of gastroparetics.
- Moderate-severe abdominal pain is prevalent in gastroparesis (66%), impairs quality of life, and is associated with idiopathic etiology, but not gastric emptying.
- Pain has at least as great an impact on disease severity and quality of life as nausea/vomiting.

Hasler et al. AJG 2011;106:1492-502

Trends of Gastroparesis-Related Hospitalizations
United States, 1995-2004

Figure 1. Number of hospitalizations with gastroparesis as the primary diagnosis in the United States, 1995-2004.

Hospitalizations: Gastroparesis as primary diagnosis increased +158%.
Gastroparesis as secondary diagnosis increased +136%.
Diabetes-related increased +53%
All hospitalizations increased +13%.

Wang, Fisher, Parkman DDW 2007 Poster Tuesday May 22, 2007
Etiologies of Gastroparesis

Diabetes
Postgastric surgery
Idiopathic

Other
Metabolic Disorders: Hypothyroidism
Medications: narcotics, anticholinergics
Rheumatologic: Scleroderma, SLE, RSD
Psychiatric: Eating disorders (anorexia, bulimia)
Generalized GI Motility Disorder:
  Intestinal pseudo-obstruction
  GERD

Diagnosis of Gastroparesis

Symptoms
  Gastroparesis vs functional dyspepsia, ulcer, cancer

Exclusion of organic lesions
  Upper Endoscopy or Upper GI Series

Delayed Gastric emptying
  Scintigraphy (solid phase)
Techniques to Evaluate Gastric Emptying

Scintigraphy: Standard test
Variable methodology clinically
Standardization of Meal / Imaging

Wireless Motility Capsule: Office Test, easily standardized
Gastric emptying/contractility
Empties with phase III MMC
Measures Whole Gut Transit

GE Breath Test: Office Based Tests, easily standardized
Used in US in research studies
Recently approved by FDA

Correlating Symptoms to Delayed Gastric Emptying

At TUH, 1499 patients undergoing Gastric Emptying Scintigraphy from September 2007 to January 2010.

GES was performed with ingestion of a liquid egg white meal with imaging at 0, 0.5, 1, 2, 3, and 4 hours. Patients completed the Patient Assessment of Gastrointestinal Symptoms questionnaire before GES.

629 of the 1499 patients (42%) had increased retention at 4 hours (>10%).

The symptoms correlating with gastric retention at 4 hours included:
- early satiety \( r=0.170; p<0.01 \)
- vomiting \( r=0.143; p<0.01 \)
- postprandial fullness \( r=0.123; p<0.01 \)
- loss of appetite \( r=0.122; p<0.01 \)

Pathikonda, Sachdeva Maurer AH, Parkman HP
J Clinical Gastro 2012
Chronic unexplained nausea/vomiting but normal gastric emptying

425 patients with chronic nausea and vomiting, 319 (75%) delayed, 106 normal GES.

Similar symptom severity indexes for nausea, retching, vomiting, stomach fullness, early satiety, postprandial fullness, loss of appetite, bloating, visibly larger stomach. Total GCSI scores were not correlated with gastric retention in either group.

Patients with or without delayed emptying did not differ in age, sex, or race, although those with normal gastric emptying were less likely to be diabetic.

No differences in health care utilization, quality of life, depression, trait anxiety scores. State anxiety scores were slightly higher among patients with delayed GE.

Patients with the syndrome were not adequately captured by Rome III diagnoses of chronic idiopathic nausea and functional vomiting.

CONCLUSIONS:

Patients with nausea and vomiting with normal gastric emptying represent a significant medical problem and are, for the most part, indistinguishable from those with gastroparesis. This syndrome is not categorized in the medical literature—it might be a separate clinical entity.

Assessment of Gastric Accommodation during Gastric Emptying

Impaired GA can be evaluated using current standardized solid-meal GES.

Impaired GA is associated with early satiety.

Impaired GA may explain early satiety in patients with normal GES.

Routine visual assessment of GA as a part of a GES study may allow for better correlation of symptoms to abnormalities of gastric motility.

Assessment of Gastric Accommodation during Gastric Emptying

Normal Fundic Accommodation

Impaired Fundic Accommodation
## Treatment of Gastroparesis

### General Items
- Avoid medications that can delay stomach emptying
- Glucose control for diabetic patients

### Diet
- low fiber and roughage
- low in fat (fat increases CCK and delays GE)
- Liquid nutrients are better tolerated over solid food
- small meals, usually multiple 4-6/day
- Nutrition Consultation

### Antiemetic Agents
- Compazine, Tigan (affect CNS vomiting center)
- Reduce N/V
- Ondansetron, a 5-HT-3 receptor antagonist

### Prokinetic Agents
- Metoclopramide, a dopamine receptor antagonist
- Speed gastric emptying
- Erythromycin, a motilin receptor agonist
- Domperidone, a dopamine receptor antagonist

## Commonly Used Prokinetic Agents

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metoclopramide</strong> (Reglan)</td>
<td>Approved for gastroparesis</td>
</tr>
<tr>
<td>Acts as prokinetic and antiemetic both may act for efficacy</td>
<td>Side Effects</td>
</tr>
<tr>
<td>Available po, IV, SQ</td>
<td>Acute/Chronic</td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>Potent gastrokinetic agent</td>
</tr>
<tr>
<td>Side Effects</td>
<td></td>
</tr>
<tr>
<td>Acute/Chronic</td>
<td>Tachyphylaxis (loss of effect)</td>
</tr>
<tr>
<td><strong>Domperidone</strong></td>
<td>Acts as prokinetic and antiemetic</td>
</tr>
<tr>
<td>Less side effects than Reglan</td>
<td>Not approved in the USA</td>
</tr>
<tr>
<td>Available with FDA IND</td>
<td></td>
</tr>
</tbody>
</table>
Metoclopramide to Treat Gastroparesis due to Diabetes Mellitus

Randomized, double-blind, controlled trial of metoclopramide in 10 patients with diabetic gastroparesis

Metoclopramide increased gastric emptying
Overall symptoms and symptoms of vomiting were reduced during metoclopramide treatment.
Poor correlation between improved gastric emptying and decreased symptoms.

Metoclopramide improves symptoms of diabetic gastroparesis:
Peripheral effect of gastric smooth muscle to increase gastric emptying
Central effect on chemoreceptor vomiting zone to decrease nausea.

Snape, Battle, et al.
Ann Intern Med 1982;96:444

Domperidone in the Management of Symptoms of Diabetic Gastroparesis

Single-Masked Study: 208/269 (77%) patients with diabetic gastroparesis improved on Domperidone 20 mg po QID
Randomized Placebo-Controlled, Double-Masked Withdrawal Phase: Placebo group had greater deterioration in total symptom scores compared to domperidone

Silvers, Kipnes, et al.
Clinical Therapeutics 1998;20:438
Erythromycin in the Short-Term and Long-Term Control of Dyspepsia Symptoms in Gastroparesis

25 patients with gastroparesis
Treated with low dose erythromycin suspension (50-100 mg TID)

Randomized, Placebo-Controlled Trial of Botulinum Toxin A for the Treatment of Gastroparesis

Botulinum toxin type A (Botox) binds to presynaptic acetylcholine terminals producing blockade at the level of the neuromuscular junction preventing cholinergic transmission and promoting muscle relaxation.

32 patients randomized to receive either Botox 200 units (n=16) or Saline 5 ml (n=16)
Outcomes in Gastroparesis using NIH GpR1

Patients with gastroparesis (diabetic or idiopathic) in GpR1 at the NIH Gp centers were seen every 4 months along with clinical care for their condition. Only 28% of 262 patients symptomatically improved at 48 weeks with decrease GCSI ≥1. These results emphasize chronic nature of gastroparesis. The disease burden remains high.

<table>
<thead>
<tr>
<th>Positive predictors</th>
<th>OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>age ≥ 50 years</td>
<td>3.35</td>
<td>0.001</td>
</tr>
<tr>
<td>GCSI score</td>
<td>2.87</td>
<td>0.001</td>
</tr>
<tr>
<td>antidepressant use</td>
<td>2.27</td>
<td>0.02</td>
</tr>
<tr>
<td>gastric retention &gt; 20% at 4 hours</td>
<td>2.22</td>
<td>0.02</td>
</tr>
<tr>
<td>initial infectious prodrome</td>
<td>2.22</td>
<td>0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Negative predictors</th>
<th>OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>anxiolytics</td>
<td>0.28</td>
<td>0.02</td>
</tr>
<tr>
<td>pain modulator use</td>
<td>0.34</td>
<td>0.01</td>
</tr>
<tr>
<td>abdominal pain (moderate/severe)</td>
<td>0.40</td>
<td>0.04</td>
</tr>
<tr>
<td>overweight/obese</td>
<td>0.43</td>
<td>0.01</td>
</tr>
<tr>
<td>depression</td>
<td>0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>smoking history</td>
<td>0.46</td>
<td>0.04</td>
</tr>
<tr>
<td>gastroesophageal reflux severity</td>
<td>0.66</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Pasricha et al. Gastroenterology 2015

Tricyclic Antidepressants for Chronic Vomiting in Diabetic Patients

24 diabetic patients treated with tricyclic antidepressants for nausea and vomiting after an unsatisfactory response to prokinetic therapy.

TCAs: Amitriptyline, nortriptyline, desipramine.

Starting doses 10-25 mg/day; final maintenance dose: 10-75 mg/day.

Sawhney, Prakash Lustman, Clouse. DDS 2007;52:418.
NORIG Trial: Main Outcomes

Nortriptyline did not improve overall symptoms, as defined by our primary outcome measure, in idiopathic gastroparesis over a 15 week period.

At 3 weeks:
Improvement in nausea and abdominal pain at nortriptyline (10 mg), but not sustained over time as dosing was increased.

At 15 weeks:
Higher doses of nortriptyline were associated with improvements in appetite, satiety, and body weight.

Continuous Glucose Monitoring (CGM) Plus Continuous Subcutaneous Insulin Infusion (CSII) Reduces Hypoglycemia in Diabetes (DM) with Gastroparesis (GP): A Multicenter Pilot Study (GLUMIT)

GLUMIT tested safety and efficacy of using CSII and CGM in 45 individuals with uncontrolled DM (A1c>8%) and GP (>10% 4 hr retention) (29% T1DM). CSII + CGM training was started prior to enrollment and continued throughout 24-week study. Patients were recommended to use dual wave boluses for meal boluses, adjust insulin dose based on sensor glucose trends and predictive alerts.

Diabetic Outcomes:
Baseline A1c levels (9.4±1.4 %) decreased by 1.1% at 24 weeks (P=0.0002 vs. baseline).

<table>
<thead>
<tr>
<th>Status</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia (&lt;70 mg/dl)</td>
<td>3.9%</td>
<td>1.7% (P&lt;0.0001)</td>
</tr>
<tr>
<td>Euglycemia (71-180 mg/dl)</td>
<td>51.8% (p=0.004)</td>
<td>51.8% (p=0.004)</td>
</tr>
<tr>
<td>Hyperglycemia (&gt;180)</td>
<td>44.0%</td>
<td>46.5% (p=0.04)</td>
</tr>
</tbody>
</table>

9 severe hypoglycemic events (third party assistance) occurred (2 during 2-8 week screening phase and 7 during 24 week treatment phase); 6 related to mismatches of insulin boluses/meal ingestion, 2 to insulin over-dosing, 1 no explanation.

Patients who had episodes of severe hypoglycemia had more severe GP at baseline, with nausea/vomiting scores 63.0% greater (p=0.002) and early satiety scores 18.2% greater (p=0.04) vs. those who did not have these episodes.

Summary: in DM patients with GP the CSII + CGM protocol for 6 months improved glycemic control with less time in hypoglycemia, more time in euglycemia and with an acceptable safety profile. Patients with more severe GP warrant more careful surveillance.
Pilot Study of the Safety, Feasibility, and Efficacy of Continuous Glucose Monitoring (CGM) and Insulin Pump Therapy in Diabetic Gastroparesis (GLUMIT-DG)

Diabetics with gastroparesis are advised to lower blood sugars to reduce symptoms. The potential of continuous glucose monitoring (CGM) coupled with intensive insulin regimens to safely reduce hyperglycemia and improve gastroparesis manifestations is unproved.

45 diabetics with gastroparesis, poorly controlled (A1c>8%) with gastroparesis (>10% 4 h retention); 29% type 1, 21±11 yr diabetes duration.

**Gastroparesis Outcomes:**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Change at wk 12</th>
<th>Change at wk 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total GCSI score</td>
<td>29.3±7.1</td>
<td>-7.2±8.2 (p&lt;0.001)</td>
<td>-6.6±8.8 (p&lt;0.001)</td>
</tr>
<tr>
<td>Nausea/Vomiting subscore</td>
<td>8.1±4.2</td>
<td>-2.9±4.0 (p&lt;0.001)</td>
<td>-2.8±4.1 (p&lt;0.001)</td>
</tr>
<tr>
<td>Fullness/Early satiety</td>
<td>14.1±3.6</td>
<td>-3.1±4.5 (p&lt;0.001)</td>
<td>-2.4±4.5 (p=0.002)</td>
</tr>
<tr>
<td>Bloating/Distention</td>
<td>7.1±2.3</td>
<td>-1.3±2.9 (p=0.001)</td>
<td>-1.5±2.5 (p=0.001)</td>
</tr>
<tr>
<td>Water load tolerance</td>
<td>430±207</td>
<td>0±243 (p=0.99)</td>
<td>-33±190 (p=0.31)</td>
</tr>
<tr>
<td>Liquid nutrient tolerance</td>
<td>420±258</td>
<td>15±117 (p=0.47)</td>
<td>59±176 (p=0.05)</td>
</tr>
</tbody>
</table>

**Conclusions:**

Symptom and nutrient tolerance benefits were maintained for the 24 week phase of intensive monitoring and therapy. This uncontrolled pilot study shows the feasibility and potential for dual benefits improving both diabetes control and lowering gastroparesis symptom burdens.

Refractory Gastroparesis

- Jejunostomy tube for feeding into small intestine bypassing gastroparetic stomach
- Gastrostomy tube for venting of stomach
- Gastric electric stimulation
  - Gastric pacing vs high frequency stimulation suppressing symptoms, particularly nausea, vomiting
- Pyloromyotomy/pyloroplasty
- Central line for Total Parenteral Nutrition (PICC)
  - If long term, problems with infection, thrombosis
- Gastrectomy (last resort)
  - near-total completion, for post surgical gastroparesis
Clinical Improvement with Enterra Gastric Electric Stimulation Treatment for Refractory Gastroparesis
The Temple Experience (2004-2006)

Overall, 14 of 28 (50%) patients felt improved.
Nausea/vomiting subscore improved
Abdominal pain did not change.

GCSI Scores: Subgroup Analysis

<table>
<thead>
<tr>
<th></th>
<th>N=10</th>
<th>N=2</th>
<th>N=12</th>
<th>N=4</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCSI Score</td>
<td>2.3</td>
<td>2.7</td>
<td>3.3</td>
<td>3.1</td>
</tr>
<tr>
<td>DM</td>
<td>N/V</td>
<td>Abd Pain</td>
<td>N/V</td>
<td>Abd Pain</td>
</tr>
</tbody>
</table>

Three Predictive Factors:
Diabetic patients better than idiopathic
Chief complaint of nausea/vomiting
Not taking narcotic analgesics.

Gastric Electric Stimulation for Refractory Gastroparesis:
A Prospective Analysis of 151 Patients at a Single Center

Results: Global Clinical Response

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Diabetes 85%</th>
<th>Idiopathic 68%</th>
<th>Other</th>
<th>All 75%</th>
</tr>
</thead>
</table>

Heckert, et al. DDS 2015
Laparoscopic pyloroplasty for gastroparesis results in sustained symptom improvement

Retrospective review of 28 patients underwent minimally invasive pyloroplasty as treatment for gastroparesis Jan 2007-Sept 2010. Laparoscopic Heineke-Mikulicz pyloroplasty performed in 26 patients. Laparoscopic assisted, flexible trans-oral endoscopic circular stapled pyloroplasty used 2 patients. GES T1/2 decreased from 320 to 112 min and normalized in 71%.

Improvements were seen at 1 month for nausea, vomiting, bloating, abdominal pain, and GER symptoms. Improvement persisted at 3 months for nausea, vomiting, bloating, abdominal pain and GERD symptoms. Prokinetic use was significantly reduced from 89% to 14%.

Minimally invasive pyloroplasty provides excellent outcomes for patients with gastroparesis. With technological advancements, a totally endoscopic pyloroplasty may be a less invasive option.


Assessing Pyloric Sphincter Pathophysiology using EndoFLIP in Patients with Gastroparesis

EndoFLIP is a novel technique that can be used to assess pyloric physiologic characteristics: pressure, diameter, length, cross sectional area, distensibility.

Early satiety and postprandial fullness were inversely correlated with diameter and cross-sectional area (CSA) of the pyloric sphincter.

No significant differences were seen comparing diabetic and idiopathic gastroparetics.

This technology may be of benefit to help select patients with pyloric sphincter abnormalities.

Malik, Sankinini et al. NGM 2015
On the Horizon for Gastroparesis

FDA Guidance on Gastroparesis (7/2015)
Diagnostic testing
   Intragastric meal distribution during scintigraphic testing
   Breath test for gastric emptying
New prokinetic agents
   Motilin receptor agonists
   Ghrelin receptor agonists
   5-HT4 receptor agonists
   Dopamine type 2 receptor antagonists
Antiemetic agents
   5HT3 receptor antagonists
   NK1 receptor antagonists
Surgical treatments
   Re-evaluation of gastric stimulation parameters
Endoscopic treatments
   Endoscopic pyloromyotomy
   Endoscopically placed gastric electric stimulation
Gastric Emptying: Regional Gastric Function

Gastric emptying reflects coordinated function of the fundus, corpus, antrum, pylorus, duodenum:
- Fundic relaxation and accommodation
- Antral contractions for trituration/grinding
- Pyloric sphincter opening for final emptying

General Principles for Treatment of Patients With Gastroparesis

Correct fluid, electrolyte, nutritional deficiencies

Identify and treat the underlying cause

Suppress or eliminate symptoms; primarily nausea, vomiting

Quigley, Hasler, Parkman. Gastroenterology 2000; 120:263
Gastric Neuromuscular Pathology in Gastroparesis: Analysis of Full Thickness Antral Biopsies

Histological abnormalities in gastroparesis: heterogeneous myenteric inflammation, decreased innervation, reduction of ICCs.

Harberson, Thomas, et al. DDS 2010

Regional gastric contractility alterations in a diabetic gastroparesis mouse model

Effect of Bethanechol and Potassium on Regional Mouse Gastric Contractility (in vitro circular muscle rings)
Delayed Gastric Emptying in Functional Dyspepsia: Improved Detection with 4 hour Gastric Emptying Test

Guo, Parkman, Maurer. DDS 2002;46:24-29.

Initiation of Enteral Nutrition
Surgical Jejunostomy

Severe weight loss
(weight loss > 10% of usual body weight over 6 months)

Repeated hospitalizations for refractory gastroparesis intravenous hydration and/or intravenous medication.

Better absorption of medications to gain therapeutic levels when vomiting prevents this.

Gastric decompression: Gastrostomy/jejunostomy tube(s).
### Understanding Gastric Pathophysiology

<table>
<thead>
<tr>
<th>Pathophysiology</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed gastric emptying</td>
<td>Gastric emptying scintigraphy</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>Breath test</td>
</tr>
<tr>
<td>Gastroparesis-Like Syndrome</td>
<td>Population studies</td>
</tr>
<tr>
<td>Regional gastric transit</td>
<td>Proximal gastric accommodation, emptying</td>
</tr>
<tr>
<td>Impaired accommodation</td>
<td></td>
</tr>
<tr>
<td>Whole gut transit abnormalities</td>
<td>Whole gut transit scintigraphy</td>
</tr>
<tr>
<td>Small bowel, Colon</td>
<td>Wireless motility capsule</td>
</tr>
<tr>
<td>Pyloric sphincter abnormalities</td>
<td>Pyloric manometry</td>
</tr>
<tr>
<td>Pylorospasm</td>
<td>EndoFLIP</td>
</tr>
<tr>
<td>Gastric myoelectric activity</td>
<td>EGG</td>
</tr>
<tr>
<td>Gastric Dysrhythmias</td>
<td></td>
</tr>
<tr>
<td>Sensation</td>
<td>Barostat</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Water loading</td>
</tr>
</tbody>
</table>

### Research Areas

- Understanding Normal Gastric Motility
- Understanding Pathophysiology in Gastroparesis
- Understand Symptom Generation
- Improving Diagnosis of Gastric Motility Disorders
- Improving Treatment for Gastroparesis
Simultaneous Assessment of Gastric Emptying & Volume: SPECT imaging

A. $^{111}$In labeled Egg Sandwich Meal

![Gastric Images after Intravenous $^{99m}$Tc and Egg Sandwich meal]

Botulinum Toxin A Injection into the Pylorus for Treatment of Idiopathic Gastroparesis
(Open Label Study in 10 Patients)

![Graphs showing % Gastric Retention and Total Symptom Score before and after Botox injection]


Botulinum Toxin A Injection into the Pylorus for Treatment of Idiopathic Gastroparesis
(Open Label Study in 10 Patients)

Miller, Parkman, Fisher et al. Am J Gastro 2002;97:1653
Randomized, Placebo-Controlled Trial of Botulinum Toxin A for the Treatment of Delayed Gastric Emptying

32 patients randomized to receive either Botox 200 units in 5 ml (n=16) or Saline 5 ml (n=16) into pylorus


Granisetron (5-HT3 Receptor Antagonist) Transdermal System Improves Refractory Nausea and Vomiting in Gastroparesis
Table 1: ANMS Gastroparesis Cardinal Symptom Index Daily Diary (ANMS GCSI-DD)

Participant Number: ______________________ Date:_______________  T i m e : ________________

Instructions: These questions ask about symptoms you may have each day. Please complete the daily diary at about the same time every evening.

For each symptom listed below, please mark with an X the box that best describes the worst severity of each symptom during the past 24 hours. Please be sure to answer each question.

None  Mild  Moderate  Severe  Very Severe

1. Nausea (feeling sick to your stomach as if you were going to vomit or throw up)

2. Not able to finish a normal-sized meal (for a healthy person)


4. Upper abdominal pain (above the navel).

The next question asks you to record the number of times either vomiting occurred in the last 24 hours. For vomiting, please record the number of times (throwing up with food or liquid coming out) that occurred in the last 24 hours. Record zero, if you have not vomited during the past 24 hours. If you vomited, write down the number of all vomits. If you vomited once, record one. If you vomited three times during the day, record three.

5. During the past 24 hours, how many episodes of vomiting did you have?

6. In thinking about your gastroparesis disorder, what was the overall severity of your gastroparesis symptoms today (during the past 24 hours)?

---

**ANMS GCSI-DD**

A PRO endpoint for clinical trials evaluating new treatments for either diabetic or idiopathic gastroparesis.

The ANMS GCSI-DD consists of five core symptoms (nausea, vomiting, early satiety, postprandial fullness, upper abdominal pain).

The ANMS GCSI-DD composite score (an average of the five core symptoms) is designed to detect clinical improvement in symptoms of gastroparesis to be used as a PRO endpoint for clinical trials.

---

**Botox Injection Into Pylorus for Gastroparesis**

Botulinum toxin type A (Botox) binds to presynaptic acetylcholine terminals; produces blockade at the level of the neuromuscular junction; preventing cholinergic transmission and promoting muscle relaxation.

---
Effect of Pyloric Botulinum Toxin Injection on Gastric Emptying in Gastroparesis

Assessing Vagal Integrity

[Graph showing pancreatic polypeptide levels over time]
EFFECT OF ALTERING GASTRIC EMPTYING ON POSTPRANDIAL PLASMA GLUCOSE CONCENTRATIONS FOLLOWING A PHYSIOLOGIC MEAL IN TYPE 2 DIABETIC PATIENTS

- Objective: The purpose of this study was to determine the effects of altering gastric emptying (GE) on postprandial plasma glucose concentrations after a physiologic meal in patients with type 2 diabetes mellitus (T2DM).

- Research Design and Methods: Nine T2DM patients underwent a double blind, randomized, three-way crossover study in which they received erythromycin 200 mg, morphine 8 mg, or normal saline (placebo) IV prior to ingestion of a radiolabeled, dual-isotope, solid-liquid meal. Gastric emptying rates of solids and liquids and serial plasma glucose, glucagon and serum insulin concentrations were measured at baseline and for 5 hrs after meal ingestion.

- Results: Erythromycin accelerated and morphine delayed solid and liquid phase GE compared to placebo (p<0.05). During the first hour, the postprandial plasma glucose concentrations were higher after erythromycin (p<0.05) and lower after morphine (p<0.05) compared to placebo. The peak postprandial plasma glucose concentration was higher after erythromycin (p=0.05) and lower after morphine (p<0.05) compared to placebo.

- Conclusions: Drug-induced acceleration of GE resulted in higher postprandial glucose concentrations, while delaying GE resulted in lower postprandial glucose concentrations after a physiologic meal in T2DM. These results suggest that administration of opioid analgesics or prokinetic agents to diabetic patients may alter glucose control. Modifying GE may be helpful in achieving glucose control in T2DM.
Diabetic Gastroparesis

Associated with long-standing Insulin-Dependent Diabetes (T1DM). Also seen in T2DM (NIDDM).

Frequently occurs with other diabetic complications
neuropathy, retinopathy, nephropathy
Gastroparesis is analogous to neuropathy of vagus nerve

May cause difficulty with glycemic control: hypoglycemia

Hyperglycemia also delays gastric emptying
Idiopathic Gastroparesis
Symptomatic gastroparesis with no underlying abnormality

Most common form of gastroparesis

Typically occurs in young/middle age women

Symptoms often fluctuate

Suggested cause in some patients
viral injury to the neural innervation or ICCs of the stomach (postviral gastroparesis)

Postgastric Surgery Gastroparesis
Usually involves prior ulcer surgery

More common when vagotomy performed

Worse with history of gastric outlet obstruction

Roux-en-Y syndrome can be very severe
disordered gastric emptying
delayed small bowel transit

Newer surgeries can cause delayed gastric emptying in some patients
Nissen Fundoplication for GERD
Heart-Lung Transplantation for endstage heart/lung problems
Bariatric Surgery for Obesity
Wireless Motility Capsule Recording of Gastric Residence Time (Normal Subject)

FDA approved gastric emptying colonic transit

Breath Testing-$C^{13}$ or $C^{14}$ octanoate

$C^{13}$ - stable (non-radioactive)
Isotope

Rate-limiting step: gastric emptying
A Standardized Method for Gastric Emptying:
The EggBeaters 4 hour Scintigraphy Test

Low fat EggBeaters radiolabelled 1 mCi 99Tc
Microwaved.
Served with toast, jam, and water.
Imaging for gastric retention at 0, 1, 2, 3, 4 hr.
Abnormal Value: Retention >10% at 4 hr.

Gastric Electric Stimulation
High Frequency (Enterra) Therapy

High frequency, low energy, short pulse duration stimulation;
not gastric pacing.

Enterra is approved by the FDA as a Humanitarian Device Exemption
(HDE) for treatment of chronic, intractable (drug refractory) nausea
and vomiting secondary to diabetic or idiopathic gastroparesis.

Mechanism of action not elucidated:
Increase gastric emptying
Enhance fundic relaxation (accommodation)
Decrease gastric sensitivity
Activate afferent sensory pathways to central mechanisms for N/V
Effectiveness of Gastric Electrical Stimulation in Gastroparesis: Results from the Prospectively Collected Database of GpR

92 (14.5%) of patients had GES after GpR enrollment; 48-week data from these patients were compared to the remainder 542 (control group) who never had GES.

38% of patients with GES were diabetic and 54% idiopathic. Patients with GES had more delayed gastric emptying at 4 hrs (30.9 vs 21.8) with worse GCSI scores (3.8 vs 3.0).

After 48 weeks, GCSI scores in patients with GES improved by average of 0.9 compared with 0.3 in controls (p<0.001) with 43.6% showing improvement of at least 1 point compared with 24.7% in controls (p=0.004).

Conclusions: In this observational study in multiple practice settings, 15% of gastroparesis required GES therapy and were more likely to show clinically meaningful improvement at 48 weeks than those without GES Rx.

Abell et al. DDW 2015